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A Randomized Study of CRT-D vs. 2Ch-ICD in Ischemic Cardiomyopathy With Narrow QRS: The NARROW-CRT Study.


Background

Current recommendations require a QRS duration of ≥120 ms as a condition for prescribing cardiac resynchronization therapy (CRT). This study was designed to test the hypothesis that patients with heart failure (HF) of ischemic origin, current indications for defibrillator implantation, and QRS <120 ms may benefit from CRT in the presence of marked mechanical dyssynchrony.

Methods and Results

Patients with intraventricular dyssynchrony on echocardiography were randomly assigned to CRT or dual-chamber defibrillator implantation (CRT defibrillator and dual-chamber implantable cardioverter-defibrillator arm, respectively). The primary end point was the HF clinical composite response, which scores patients as improved, unchanged, or worsened. The secondary end point was the cumulative survival from HF hospitalization and HF death. An additional secondary end point was the composite of HF hospitalization, HF death, and spontaneous ventricular fibrillation. Twenty-three of 56 patients with CRT defibrillator showed an improvement in their clinical composite response at 1 year, compared with 9 of 55 patients with dual-chamber implantable cardioverter-defibrillator (41% versus 16%; P=0.004). After a median follow-up of 16 months, the CRT defibrillator arm showed a nonsignificant higher survival from HF hospitalization and HF death (P=0.077), and a significantly higher survival from the combined end point of HF hospitalization, HF death, and spontaneous ventricular fibrillation (P=0.028).

Conclusions

In this comparison of CRT defibrillator and dual-chamber implantable cardioverter-defibrillator, CRT improved clinical status in some patients with ischemic cardiomyopathy, mild-to-moderate symptoms, narrow QRS duration, and mechanical dyssynchrony on echocardiography.

Clinical Trial Registration: URL: http://clinicaltrials.gov. Unique identifier: NCT01577446. Keywords: CRT, dyssynchrony, heart failure, narrow QRS PMID: 23592833 // Ospedale S.Maria di Loreto Mare, Napoli, Italy.
Ilesto 7 Series Biotronik has announced the European market launch of its Ilesto 7 Series. This is the world’s first DF4 implantable cardiac defibrillator (ICD) and cardiac resynchronisation therapy (CRT) series approved for MRI. According to a company press release, the Ilesto 7 series include one of the world’s smallest ICDs and also offer the greatest longevity—up to 11.5 years for the single chamber ICD. “We see a rising need for MR scans at our clinic and nationwide, and we acknowledge the steps Biotronik has taken to develop its ProMRItm technology in order to help thousands of patients obtain the diagnostics they desperately need,” said Juan Gabriel Martinez, head of the Arrhythmia Unit of Hospital General Alicante, Spain. Martinez implanted an Ilesto 7 HF-T in a 63-year-old patient suffering from cardiomyopathy. “Before Biotronik launched its ProMRItm technology, patients with an ICD or CRT-D were prohibited from undergoing MR scans. Fortunately, with the new Ilesto system, I can offer my patients the option of an MR scan if they need one in the future. This is a very important aspect to my patients, as they have a high chance of needing an MR scan during the lifetime of their devices.” Due to its small size, the Ilesto 7 Series and the new DF4 connector system, according to a company release, simplifies and shortens the implantation procedure, is more comfortable for the patient, and also leads to better cosmetic results.

The Food and Drug Administration (FDA) has granted approval for Ilesto 7 implantable cardioverter-defibrillator/cardiac resynchronisation therapy defibrillator (ICD/CRT-D) series (Biotronik) “Biotronik lives up to its reputation for excellence in design and manufacturing with the introduction of the Ilesto family, and the new Ilesto DX device. Physicians depend on complete and timely information, and Ilesto DX with Biotronik Home Monitoring certainly delivers. With this device, physicians can receive atrial information to ensure diagnostic accuracy and identify previously undetected atrial fibrillation. They also receive peace of mind that there is less risk of complications due to the single lead,” said Paul Woodstock, executive vice president of sales and marketing at Biotronik, USA. “Ilesto’s smaller footprint will be more comfortable as well, which may present a win-win solution for patients and physicians alike.”
Biotronik’s DX platform, which combines the benefits of both single- and dual-chamber ICDs, provides atrial information to aid in diagnostic accuracy while reducing the risk of complications associated with an additional atrial lead.

“In order to meet unprecedented demand for this novel category of device, the Illesto DX version will be the first ICD we launch within this series,” said Woodstock. “In a world driven by benefits and risks, single-lead DX systems deliver on both counts. The ability to provide comprehensive atrial diagnostics while reducing potential complications associated with additional leads represents an unrivaled cutting-edge technological advancement.”

The Illesto 7 series is now approved and currently available in most international markets, including the EU and Japan. In CE markets, the Illesto 7 series is the second generation of Biotronik’s ProMRI technology, which enables patients access to potentially life-saving MR scans.

The European market release of the Illesto 7 series with ProMRI technology and the new DF4 connectors is expected in midyear 2013.

First implanters of the Illesto 7 series are:
Leonardo Calò, Polyclinic Casilino, Rome, Italy;
Pascal Defaye, Grenoble University Hospital (CHU), Grenoble, France; Paul Erne, Lucerne Cantonal Hospital (LUKS), Lucerne, Switzerland;
Juan Gabriel Martínez, General de Alicante, Alicante, Spain;
Martin Jan Schalij and Lieselot van Erven, Leiden University Medical Center (LUMC), Leiden, Netherlands;
Tamas Szili-Torok, Erasmus Medical Center, Rotterdam (EMC), The Netherlands.
Atrial Fibrillation in CRT-D: A Risk Factor for Mortality, Appropriate and Inappropriate Shocks

Nick Van Boven, Dominic Theuns, Kjell Bogaard, Jaap Ruiter, Geert Kimman, Lily Berman, Tjeerd Van Der Ploeg, Isabella Kardys, Victor Umans.

Atrial Fibrillation in Cardiac Resynchronization Therapy with a Defibrillator: A Risk Factor for Mortality, Appropriate and Inappropriate Shocks
Journal of Cardiovascular Electrophysiology 2013; DOI: 10.1111/jce.12208

Introduction

Knowledge about predictive factors for mortality and (in)appropriate shocks in cardiac resynchronization therapy with a defibrillator (CRT-D) should be available and updated to predict clinical outcome.

Methods

We retrospectively analyzed 543 consecutive patients assigned to CRT-D in 2 tertiary medical centers. The aim of this study was to assess risk factors for all-cause mortality, appropriate and inappropriate shocks.

Results

Mean follow-up was 3.2 (±1.8) years. A total of 110 (20%) patients died, 71 (13%) received ≥1 appropriate shocks, and 33 (6.1%) received ≥1 inappropriate shocks. No patients received a His bundle ablation and biventricular pacing percentage was not analyzed. Multivariable Cox regression analysis showed that a history of atrial fibrillation (AF) (HR 1.74 CI 1.06–2.86), higher creatinine (HR 1.12; CI 1.08–1.16) and a poorer left ventricular ejection fraction (LVEF) (HR 0.97; CI 0.94–1.01) independently predict all-cause mortality. In the entire cohort, history of AF and secondary prevention were independent predictors of appropriate shocks and variables associated with inappropriate shocks were history of AF and QRS ≥150ms. In primary prevention patients, history of AF also predicted appropriate shocks as did ischemic cardiomyopathy and poorer LVEF. History of AF, QRS ≥150ms and lower creatinine were associated with inappropriate shocks in this subgroup. Appropriate shocks increased mortality risk, but inappropriate shocks did not.

Conclusion

In symptomatic CHF patients treated with CRT-D, history of AF is an independent risk factor for mortality, but also for appropriate and inappropriate shocks. Further efforts in AF management may optimize the care in CRT-D patients.

No disclosures. This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jce.12208. Keywords: atrial fibrillation; heart failure; cardiac resynchronization therapy; implantable cardioverter defibrillator; mortality

Pezzali N, Curnis A, Specchia C, Carubelli V, Covolo L, Donato F, Auricchio A, Regoli F, Metra M.


AIMS:

Several factors can influence the extent of left ventricular (LV) reverse remodelling after cardiac resynchronization therapy (CRT) in patients with heart failure (HF). Polymorphism in genes involved in cardiac remodelling, namely beta-adrenergic receptors (ARs), may have a role. We studied the influence of beta-1 Arg389Gly, beta-2 Arg16Gly, and beta-2 Gln27Glu ARs gene polymorphisms on the magnitude of reverse remodelling response to CRT and its possible correlations with the incidence of appropriate implantable cardioverter-defibrillator (ICD) shocks.

METHODS AND RESULTS:

Beta-ARs were assessed in 101 patients with HF due to idiopathic (50.5%) or ischaemic (49.5%) dilated cardiomyopathy, undergoing CRT for standard indications [left ventricular ejection fraction (LVEF) 23.5 ± 7.5%, QRS ≥ 120 ms]. Left ventricular ejection fraction was measured by echocardiography at baseline, 6 months after CRT, and periodically afterwards. The LVEF change from baseline was of 3.1 ± 11 units among Gln27Gln, 8.3 ± 10.4 units among Gln27Glu, 11 ± 6.4 units among Glu27Glu carriers (P = 0.018 for Gln27Gln vs. Glu27Glu carriers), and 8.8 ± 9.8 units among Gln27Glu + Glu27Glu carriers (P = 0.006 vs. Gln27Gln). Gln27 homozygotes had a higher incidence of appropriate ICD shocks for fast ventricular tachycardia/ventricular fibrillation.

CONCLUSION:

Beta-2 Gln27Glu ARs gene polymorphism may influence LV reverse remodelling after CRT with Glu27Glu carriers showing the greatest improvement. It may also influence the incidence of malignant ventricular tachyarrhythmias.

Keywords: Beta-Adrenergic Receptors Gene Polymorphism, Cardiac Resynchronization Therapy (Crt), Icd Shocks, Left Ventricular Reverse RemodellingPMID:237294 04 / Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University and Civil Hospital of Brescia, Piazzale Spedali Civili 1, 25123 Brescia, Italy.
Points

- Note that this cohort study demonstrated a similar rate of inappropriate shocks across increasing age categories of recipients.
- Be aware that the lack of a control group limits the ability to interpret these results -- if older patients were more carefully selected than their younger counterparts their similar outcomes would not be surprising.

The decision to forgo implanting a defibrillator (ICD) in the elderly should not be based on age alone, but should include other risk factors for death, a large registry study found.

Despite the fact that the risk of death increased incrementally with age, the rates of appropriate and inappropriate shocks were similar across all age groups, according to Douglas S. Lee, MD, PhD, from the Institute for Clinical Evaluative Sciences at the University of Toronto, Ontario, and colleagues.

This held true in both primary and secondary prevention ICD patients, they reported online in *Circulation: Journal of the American Heart Association*.

The findings suggest that clinicians should "consider factors that predispose to mortality despite defibrillator implantation," they said.

Whether ICDs are beneficial for patients in their 80s or older is controversial, as there are often several competing risk factors for death. But the number of such patients eligible for ICDs is fairly sizable at an estimated 28%.

In prior studies, the mortality benefit of ICDs in the elderly has been inconsistent. In addition, most randomized trials under-represent the elderly population, researchers said.

For this study, Lee and colleagues examined 5,399 primary and secondary prevention ICD recipients from February 2003 to September 2010 taken from the Ontario ICD registry -- a "large, prospective, inclusive database designed to evaluate adjudicated clinical and device-related outcomes after ICD implantation."

The number of patients with ICDs who were 80 or older was 434 -- 275 had the devices for primary prevention and 159 for secondary prevention. Of the 1,704 patients ages 70 through 79 with ICDs, 1,242 had them for primary prevention and 462 for secondary.

In the patients with primary prevention ICDs, the rate of mortality per 100 person-years for defined age groups increased with age:

- 18 to 49 -- 2.1
- 50 to 59 -- 3
- 60 to 69 -- 5.4
- 70 to 77 -- 6.9
- 80 or greater -- 10.2

The rate of mortality for secondary prevention ICD recipients similarly increased with age:

- 18 to 49 -- 2.2
- 50 to 59 -- 3.8
- 60 to 69 -- 6.1
- 70 to 77 -- 8.7
- 80 or greater -- 15.5
But although age was an independent predictor of mortality, it was not an independent predictor of appropriate shock therapy -- in either the primary (mean 5.1 per 100 person-years) or secondary (mean 12.0 per 100 person-years) prevention recipients.

The primary prevention shock rate was similar to that reported in the literature, but the 12% rate for secondary prevention was lower, Lee and colleagues reported.

"This may be explained by a trend toward more thoughtful programming and concomitant use of antiarrhythmic medication to avert unnecessary shocks," they suggested.

After they adjusted for clinical differences and comorbidities, the appropriate shock rate for elderly patients was no different from the rest of the cohort.

This suggests that the elderly "derive benefit in reduction of arrhythmic death similar to that in younger patients."

In addition, researchers reported that appropriate shocks were highly successful, and most of the elderly patients survived more than 30 days after the shock.

The researchers pointed out that these results refute "cardiac annihilation," a term indicating the elderly are more susceptible to unsuccessful shocks or electromechanical dissociation after ICD shock.

The rate of inappropriate shocks was less than 3.5% overall; however, it was slightly higher in younger primary prevention recipients (4.1 inappropriate shocks per 100 person-years in the 18 to 49 age group versus 2.1 in the over-80 age group, for example, in the primary prevention group).

"Cardiovascular and noncardiovascular hospitalizations were elevated in the elderly, reflecting a greater impact of comorbidities," researchers wrote in conclusion.

"Consideration of prognostic factors that predict mortality in conjunction with individualized clinical judgment will help to identify older patients who are more likely to benefit from ICD implantation," they added.

The study might have limited generalizability because board-certified electrophysiologists approved all implantations on evidence-based criteria, and other centers might have more "liberal" selection policies, researchers said.

Other limitations include the lack of a control group and the use of administrative data to determine the mode or cause of death.


Funding for the study came in part from the Ontario Ministry of Health and Long-term Care and the Canadian Institutes of Health Research. Lee reported he had no conflicts of interest. Other authors reported relationships with St Jude Medical, Boston Scientific, Boehringer Ingelheim, Bayer, Bristol-Myers Squibb, Servier, Medtronic, and Biosense Webster.
Cost-Utility Analysis of the EVOLVO Study on Remote Monitoring for Heart Failure Patients With Implantable Defibrillators: Randomized Controlled Trial.


Cost-Utility Analysis of the EVOLVO Study on Remote Monitoring for Heart Failure Patients With Implantable Defibrillators: Randomized Controlled Trial.


BACKGROUND:
Heart failure patients with implantable defibrillators place a significant burden on health care systems. Remote monitoring allows assessment of device function and heart failure parameters, and may represent a safe, effective, and cost-saving method compared to conventional in-office follow-up.

OBJECTIVE:
We hypothesized that remote device monitoring represents a cost-effective approach. This paper summarizes the economic evaluation of the Evolution of Management Strategies of Heart Failure Patients With Implantable Defibrillators (EVOLVO) study, a multicenter clinical trial aimed at measuring the benefits of remote monitoring for heart failure patients with implantable defibrillators.

METHODS:
Two hundred patients implanted with a wireless transmission-enabled implantable defibrillator were randomized to receive either remote monitoring or the conventional method of in-person evaluations. Patients were followed for 16 months with a protocol of scheduled in-office and remote follow-ups. The economic evaluation of the intervention was conducted from the perspectives of the health care system and the patient. A cost-utility analysis was performed to measure whether the intervention was cost-effective in terms of cost per quality-adjusted life year (QALY) gained.

RESULTS:
Overall, remote monitoring did not show significant annual cost savings for the health care system (€1962.78 versus €2130.01; P=.80). There was a significant reduction of the annual cost for the patients in the remote arm in comparison to the standard arm (€291.36 versus €381.34; P=.01). Cost-utility analysis was performed for 180 patients for whom QALYs were available. The patients in the remote arm gained 0.065 QALYs more than those in the standard arm over 16 months, with a cost savings of €888.10 per patient. Results from the cost-utility analysis of the EVOLVO study show that remote monitoring is a cost-effective and dominant solution.

CONCLUSIONS:
Remote management of heart failure patients with implantable defibrillators appears to be cost-effective compared to the conventional method of in-person evaluations.

Trial Registration: ClinicalTrials.gov NCT00873899; http://clinicaltrials.gov/show/NCT00873899 (Archived by WebCite at http://www.webcitation.org/6H0BOA29f). Keywords: Cost-effectiveness, heart failure, implantable defibrillators, telemedicine // PMID: 23722666 // PMCID: PMC3670725 Free PMC Article // Norwegian Centre for Integrated Care and Telemedicine, University Hospital of North Norway, Tromsø, Norway. paolo.zanaboni@telemed.no.
Chronic Kidney Disease and Outcomes in Heart Failure With Preserved Versus Reduced Ejection Fraction: The Cardiovascular Research Network PRESERVE Study.

Smith DH, Thorp L, Gurwitz JH, McManus DD, Goldberg RJ, Allen LA, Hsu G, Sung SH, Magid DJ, Go AS.

Chronic Kidney Disease and Outcomes in Heart Failure With Preserved Versus Reduced Ejection Fraction: The Cardiovascular Research Network PRESERVE Study.


Background

There is scant evidence on the effect that chronic kidney disease (CKD) confers on clinically meaningful outcomes among patients with heart failure with preserved left ventricular ejection fraction (HF-PEF).

Methods and Results

We identified a community-based cohort of patients with HF. Electronic medical record data were used to divide into HF-PEF and reduced left ventricular EF on the basis of quantitative and qualitative estimates. Level of CKD was assessed by estimated glomerular filtration rate (eGFR) and by dipstick proteinuria. We followed patients for a median of 22.1 months for outcomes of death and hospitalization (HF-specific and all-cause). Multivariable Cox regression estimated the adjusted relative-risk of outcomes by level of CKD, separately for HF-PEF and HF with reduced left ventricular EF. We identified 14 579 patients with HF-PEF and 9762 with HF with reduced left ventricular EF. When compared with patients with eGFR between 60 and 89 mL/min per 1.73 m(2), lower eGFR was associated with an independent graded increased risk of death and hospitalization. For example, among patients with HF-PEF, the risk of death was nearly double for eGFR 15 to 29 mL/min per 1.73 m(2) and 7× higher for eGFR<15 mL/min per 1.73 m(2), with similar findings in those with HF with reduced left ventricular EF.

Conclusions

CKD is common and an important independent predictor of death and hospitalization in adults with HF across the spectrum of left ventricular systolic function. Our study highlights the need to develop new and effective interventions for the growing number of patients with HF complicated by CKD.

Keywords: chronic kidney disease, heart failure, hospitalization, mortality

PMID:23685625 Center for Health Research, Kaiser Permanente Northwest, Portland, OR.
Clinical Impact, Safety and Efficacy of Single versus Dual Coil ICD leads in MADIT-CRT


Journal of Cardiovascular Electrophysiology 2013; DOI: 10.1111/jce.12219

Clinical Impact, Safety and Efficacy of Single versus Dual Coil ICD leads in MADIT-CRT

Background

Current data on efficacy, safety and impact on clinical outcome of single versus dual coil implantable cardioverter-defibrillator (ICD) leads are limited and contradictory.

Methods

Defibrillation threshold (DFT) at implantation and first shock efficacy were compared in patients implanted with single versus dual coil ICD leads in MADIT-CRT. The risk for atrial tachyarrhythmias and all-cause mortality were evaluated. Short (< 30 days after the implantation) and long-term (throughout the entire study duration) complications were assessed.

Results

Patients with dual coil ICD leads had significantly lower DFT’s compared to patients with single coil ICD leads (17.6 ± 5.8 Joules versus 19.4 ± 6.1 Joules, p<0.001). First shock efficacy was similar among patients with dual and single coil ICD leads (89.6% versus 92.3%, p = 1.00). When comparing patients with dual versus single coil ICD leads, there was no difference in the risk of atrial tachyarrhythmias (HR = 1.57, 95% CI: 0.81–3.02, p = 0.18), or in the risk of all-cause mortality (HR = 1.10, 95% CI: 0.58–2.07, p = 0.77). Patients implanted with single or dual coil ICD lead had similar short and long-term complication rates (short-term HR = 0.96, 95% CI: 0.56–1.65, p = 0.88, long-term procedure-related HR = 0.99, 95% CI: 0.62–1.59, p = 1.00, long-term ICD lead related: HR = 1.2, 95% CI: 0.5–2.9, p = 0.68) during mean follow-up of 3.3 years.

Conclusions

Patients with single coil ICD leads have slightly higher DFT’s as compared to dual coil leads, but the efficacy, safety, and clinical impact on atrial tachyarrhythmias, and mortality is similar. Implantation of single coil ICD leads may be favorable in most patients.

†Both authors contributed equally to this work. The MADIT-CRT study was supported by a research grant from Boston Scientific, St. Paul, Minnesota, to the University of Rochester School of Medicine and Dentistry. This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jce.12219. Keywords: heart failure; MADIT-CRT; implantable cardioverter defibrillators; mortality; atrial arrhythmias
Coenzyme Q10 supplementation reduces HF admissions and improves survival: Q-SYMBIO

In a study bound to be scrutinized when it is finally published, the Q-SYMBIO randomized, controlled, double-blind clinical trial garnered a fair deal of attention this past week when investigators reported excellent clinical outcomes in chronic heart failure patients treated with coenzyme Q10 (CoQ10).

**Metabolic modulation and energetic manipulation in the failing heart is the next frontier of heart-failure management. I want this stuff to work.**

Presenting the study at Heart Failure Congress 2013 of the European Society of Cardiology Heart Failure Association, lead investigator Dr Svend Aage Mortensen (Copenhagen University Hospital, Denmark) reported that, at two years, major adverse cardiovascular events (MACE), a composite of unplanned hospitalization due to worsening heart failure, cardiovascular death, and the need for urgent cardiac transplantation and mechanical support, occurred in 14% of patients treated with CoQ10 compared with 25% of patients who received a placebo, a statistically significant difference (p=0.003). All-cause mortality was also significantly lower in the CoQ10-treated patients, with 9% dying compared with 17% in the placebo arm (p=0.01).

In addition to these outcomes, the Q-SYMBIO investigators reported that cardiovascular mortality and admissions for heart failure were significantly lower in those who received CoQ10. In their conclusions, the researchers stated that "CoQ10 should be considered as a part of the maintenance therapy of patients with chronic heart failure."

**Yellow light: Go slow, caution urged**

Some, however, considered the recommendations to alter clinical practice on the basis of this 420-patient clinical trial premature. Dr Sanjay Kaul (Cedars-Sinai Medical Center, Los Angeles), for example, said he wants to reserve judgment on the data until they have stood up against the scrutiny of the peer-review process. He noted that the mortality data were first presented at the meeting of the International Coenzyme Q10 Association last November, but these are yet to be published.

"Clinicians should view implausibly large treatment effects observed in small underpowered trials with skepticism, as they are seldom replicated in subsequently conducted large controlled trials," Kaul told the press. "The examples of vesnarinone in heart failure, [glucose-insulin-potassium] GIK post-STEMI, and perioperative beta-blockers in high-risk vascular surgery quickly come to mind. None of the impressive preliminary results could be replicated. If a finding appears to be 'too good to be true,' it usually is."

One curiosity that also needs to be addressed, added Kaul, is why the Q-SYMBIO trial took more than 10 years to complete. The trial design was first published in 2003. It was asked
Mortensen to comment on the study and the results, but he declined, saying he wants to wait until after the study is published to discuss the findings.

**What other treatments were they taking?**

CoQ10 is an antioxidant involved in cellular-energy production. It is postulated that heart-failure patients, who have a measurable deficiency in CoQ10, would benefit from receiving the supplement.

The Q-SYMBO study included 202 patients randomized to CoQ10 and 218 patients randomized to placebo. All patients included in the study had moderate to severe heart failure (NYHA class 3 or 4) and were receiving "current" pharmacologic therapy. Patients had an average ejection fraction of 31%, and the average age was 62 years. Within three months of treatment, investigators observed a trend toward lower levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP). The clinical improvements in MACE were observed after two years of receiving 100 mg of CoQ10 three times daily compared with those who received the placebo. In addition, 44% of those who received CoQ10 had an improvement in NYHA class compared with 45% of those who received placebo (p=0.047).

To us, Dr David Kao (University of Denver, Aurora, CO) also said there are some questions that need to be answered before any heart-failure patient should start taking CoQ10 supplements. Specifically, it is not known exactly what "current pharmacologic therapy" entailed for the treated patients. Like Kaul, he would like to see the paper published in order to determine the background regimens, but if it turns out that they were receiving ACE inhibitors/angiotensin-receptor blockers and beta-blockers and CoQ10 still reduced HF admissions and mortality, "that would certainly be a big deal."

Still, even with all the relevant information, Kao said the trial needs to be replicated in a larger cohort. To substantiate any claims of mortality reduction, the next trial, if Q-SYMBO stands up once published, would need to include several thousand patients at least.

"I think this is a fascinating area," Kao told the press. "Metabolic modulation and energetic manipulation in the failing heart is the next frontier of heart-failure management. I want this stuff to work. The CoQ10 story has been murky, and there just isn't quite enough information available on this trial yet to know how to interpret it."

The study was funded by the International Coenzyme Q10 Association, as well as Kaneka and Pharma Nord, maker of products that contain CoQ10. Kaul and Kao report no conflicts of interest related to the study.
CRT in pacemaker-dependent patients with LV dysfunction

John Gierula, RM Cubbon, HA Jamil, R Byrom, PD Baxter, S Pavitt, MS Gilthorpe, J Hewison, MT Kearney, Klaus K.A. Witte.

Cardiac resynchronization therapy in pacemaker-dependent patients with left ventricular dysfunction

Aims

Heart failure and left ventricular (LV) systolic dysfunction (LVSD) are common in patients with permanent pacemakers. The aim was to determine if cardiac resynchronization therapy (CRT) at the time of pulse generator replacement (PGR) is of benefit in patients with unavoidable RV pacing and LVSD.

Methods and results

Fifty patients with unavoidable RV pacing, LVSD, and mild or no symptoms of heart failure, listed for PGR were randomized 1 : 1 to either standard RV-PGR (comparator) or CRT. The primary endpoint was the difference in change in LV ejection fraction (LVEF) between RV-PGR and CRT groups from baseline to 6 months. Secondary endpoints included peak oxygen consumption, quality of life, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels. At 6 months there was a difference in change in median (interquartile range) LVEF [9 (6–12) vs. −1.5 (−4.5 to −0.8)%; P < 0.0001] between the CRT and RV-PGR arms. There were also improvements in exercise capacity (P = 0.007), quality of life (P = 0.03), and NT-proBNP (P = 0.007) in those randomized to CRT. After 809 (729–880) days, 17 patients had died or been hospitalized (6 in CRT group and 11 in the comparator RV-PGR group) and two patients in the RV-PGR arm had required CRT for deteriorating heart failure. Patients with standard RV-PGR had more days in hospital during follow-up than those in the CRT group [4 (2–7) vs. 11 (6–16) days; P = 0.047].

Conclusion

Performing CRT in pacemaker patients with unavoidable RV pacing and LVSD but without severe symptoms of heart failure, at the time of PGR, improves cardiac function, exercise capacity, quality of life, and NT-pro-BNP levels.

Key words Left ventricular dysfunction Pacemaker Heart failure

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Cardiovascular Implantable Electronic Device Implantation with Uninterrupted Dabigatran: Comparison to Uninterrupted Warfarin


Background

While continuation of oral anticoagulation (OAC) with warfarin may be preferable to interruption and bridging with heparin for patients undergoing cardiovascular implantable electronic device (CIED) implantation, it is uncertain whether the same strategy can be safely used with dabigatran.

Objective and Methods

To determine the risk of bleeding and thromboembolic complications associated with uninterrupted OAC during CIED implantation, replacement, or revision the outcomes of patients receiving uninterrupted dabigatran (D) were compared to those receiving warfarin (W).

Results

D was administered the day of CIED implant in 48 patients (age 66 ± 12.4 yrs, 13F and 35M, 21 ICDs and 27 PMs), including new implant in 25 patients, replacement in 14 patients, and replacement plus lead revision in 9 patients. D was held the morning of the procedure in 14 patients (age 70 ± 11 yrs, 4F and 10M, 5 ICDs and 9 PMs). W was continued in 195 patients (age 60 ± 14.4 yrs, 54F and 141M), including new implant in 122 patients, replacement in 33 patients, and replacement plus lead revision or upgrade in 40 patients. Bleeding complications occurred in 1 of 48 patients (2.1%) with uninterrupted dabigatran (a late pericardial effusion), 0 of 14 with interrupted D, and 9 of 195 patients (4.6%) on W (9 pocket hematomas), p = 0.69. Fifty percent of bleeding complications were associated with concomitant antiplatelet medications.

Conclusions

The incidence of bleeding complications is similar during CIED implantation with uninterrupted D or W. The risks are higher when OAC is combined with antiplatelet drugs.

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Comparison of Rate Versus Rhythm Control in Patients With Atrial Fibrillation and a Pacemaker.


The effect of rate versus rhythm control in patients with atrial fibrillation who have undergone previous pacemaker (PM) implantation is unknown. We evaluated the mortality in patients with atrial fibrillation and a PM randomized to rate or rhythm control treatment strategies. The Atrial Fibrillation Follow-up Investigation of Rhythm Management data set was stratified by the presence (n = 250) or absence (n = 3,810) of a PM at randomization into the rate or rhythm control arm. Kaplan-Meier curves were used for univariate analysis, and proportional hazards were used for multivariate analysis. The subjects with a PM (n = 250) were older (73 vs 69 years, p <0.01) and had a greater prevalence of coronary artery disease (53% vs 37%, p <0.01) and congestive heart failure (33% vs 23%, p <0.01). All-cause mortality was significantly greater in the PM patients who were randomized to the rhythm control arm (n = 128) than in the patients enrolled in the rate control arm with or without a PM (n = 2,027, p <0.01) and those in the rhythm control arm without a PM (n = 1,905, p <0.01). Multivariate analysis revealed that predictors of all-cause mortality included PM patients randomized to the rhythm control arm (hazard ratio 2.59, 95% confidence interval 1.46 to 4.58, p <0.01) and the presence of congestive heart failure (hazard ratio 2.42, 95% confidence interval 1.40 to 4.16, p <0.01). In conclusion, all-cause mortality was greater among patients with atrial fibrillation with a PM, who were randomized to the rhythm control arm of the Atrial Fibrillation Follow-up Investigation of Rhythm Management study compared with all other patients enrolled in the Atrial Fibrillation Follow-up Investigation of Rhythm Management study. The rhythm control strategy in patients with a PM was an independent predictor of mortality.

PMID: 23540545 Division of Cardiology, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida.
Comparison of Bacterial Adherence to Titanium Versus Polyurethane for Cardiac Implantable Electronic Devices.


Implantation of cardiac implantable electronic devices (CIED) has dramatically increased over the past several years. Although several preventive measures have been implemented, there has been a disproportional increase in the number of CIED-related infections. To evaluate the adherence of bacteria to polyurethane and titanium, the 2 surfaces that coat the CIED, we proceeded with an in vitro study using the most common microorganisms responsible for CIED-related infections. Original, unused 1 × 1 centimeter titanium and polyurethane flat plates were incubated with coagulase-negative staphylococci, methicillin-resistant Staphylococcus aureus, and Pseudomonas aeruginosa. Each experiment was repeated 5 times. After incubating the titanium and polyurethane plates for 3, 6, 12, or 24 hours, all 3 organisms displayed a higher grade of bacterial adherence to the polyurethane versus titanium surfaces (p = 0.01).

In conclusion,

to decrease the rate of bacterial adherence, especially during the immediate postimplantation period when the CIED is at high risk for bacterial adherence, colonization, and infection, it may be prudent to consider constructing CIED surfaces with a higher proportion of titanium over polyurethane. Animal studies are warranted to explore the relevance of these laboratory findings.

Division of Medicine, Department of Infectious Diseases, the University of Texas MD Anderson Cancer Center, Houston, Texas; Baylor College of Medicine, Houston, Texas. Electronic address: GMViola@mdanderson.org PMID: 23523061
Cancer patients with cardiac pacemakers needing radiation treatment: A systematic review.

Munshi A, Agarwal JP, Pandey KC.


With improving average life expectancy of individuals in most countries, there has been increase in the incidence of cardiovascular diseases and cancers. Radiation oncologists therefore are likely to encounter an increasing number of cancer patients with in situ cardiac pacemaker devices needing radiation treatments. Pacemaker technology has advanced rapidly in recent years. As a result, the potential interactions of these devices with radiation therapy have changed since American Association of Physicists in Medicine (AAPM) issued guidelines in 1994. Current approaches to treatment in patients who have these devices vary among radiation oncology centers. Furthermore, the recommendations given by the devices' manufacturers differ considerably. Common knowledge about pacemaker in radiation oncology community is vital as radiation management needs to be tailored to individual patients in accordance to the information of available for the device. Some general practical guidelines can be gleaned from the literature. It is felt that more robust information is required using web based database sharing to develop total safe practice guidelines in such patients. This article reviews the information available to help create such guidelines and presents recommendations for treatment in this increasingly common clinical situation.

PMID: 23771357 // Department of Radiation Oncology, Fortis Memorial Research Institute, Gurgaon, Haryana, India.
Delayed intrinsicoid deflection onset in surface ECG lateral leads predicts left ventricular reverse remodeling after cardiac resynchronization therapy.

Del-Carpio Munoz F, Powell BD, Cha YM, Wiste HJ, Redfield MM, Friedman PA, Asirvatham SJ.

BACKGROUND:

Up to one-third of the patients who undergo cardiac resynchronization therapy (CRT) are not responders.

OBJECTIVE:

To demonstrate that delayed lateral left ventricular activation time determined through time to intrinsicoid deflection onset (ID) predicts response after CRT.

METHODS:

The ID in leads I, aVL, V1 and V2, and V5 and V6 were measured in 135 patients who underwent CRT. A CRT response was defined as a decrease in left ventricular end-systolic volume (LVESV) exceeding 15% at 6 months.

RESULTS:

In patients with left bundle branch block or nonspecific intraventricular conduction delay, response was predicted by longer ID in lead I (odds ratio [OR] 3.23; 95% confidence interval (CI) 1.4-7.4; per 20-ms increase), in lead aVL (OR 3.0; 95% CI 1.2-7.3; per 20-ms increase), and in lead I minus lead V1 (OR 2.4; 95% CI 1.2-4.7) adjusting for baseline QRS duration and LVESV. Results were similar after adjusting for postimplant or change in QRS duration. The ID parameters were better predictors of response than QRS duration parameters. ID in lead I/QRS duration ratio (OR 3.1; 95% CI 1.6-5.9) also increased the odds of response after adjusting for baseline LVESV. Cutoff values for ID in leads-I, 110 ms; aVL, 130 ms; I minus V1, 90 ms-and ID in lead I/QRS duration ratio of 0.69 yielded a sensitivity and a specificity as high as 83% and 81%.

CONCLUSIONS:

Measurement of ID on surface electrocardiography permits a preimplant, noninvasive means of determining left ventricle activation delay; is a good predictor of CRT response; and represents a promising alternative to QRS duration parameters.

PMID: 23542361 // Division of Cardiovascular Diseases.
Depression, psychological distress, and quality of life in patients with ICD with or without CRT.


Congestive heart failure is frequent and leads to reduced exercise capacity, reduced quality of life (QoL), and depression in many patients. Cardiac resynchronization therapy (CRT) and implantable cardioverter defibrillators (ICD) offer therapeutic options and may have an impact on QoL and depression. This study was performed to evaluate physical and mental health in patients undergoing ICD or combined CRT/ICD-implantation (CRT-D). Echocardiography, spiroergometry, and psychometric questionnaires [Beck Depression Inventory, General World Health Organization Five Well-being Index (WHO-5), Brief Symptom Inventory and 36-Item Short Form (SF-36)] were obtained in 39 patients (ICD: 17, CRT-D: 22) at baseline and 6-month follow-up (FU) after device implantation. CRT-D patients had a higher NYHA class and broader left bundle branch block than ICD patients at baseline. At FU, ejection fraction (EF), peak oxygen uptake, and NYHA class improved significantly in CRT-D patients but remained unchanged in ICD patients. Patients with CRT-D implantation showed higher levels of depressive symptoms, psychological distress, and impairment in QoL at baseline and FU compared to ICD patients. These impairments remained mostly unchanged in all patients after 6 months.

Overall,

these findings imply that there is a need for careful assessment and treatment of psychological distress and depression in ICD and CRT-D patients in the course of device implantation as psychological burden seems to persist irrespective of physical improvement.

PMID: 23732755 / Department of Cardiology, Maastricht University Medical Centre, PO Box 5800, 6202 AZ, Maastricht, The Netherlands, c.knackstedt@mumc.nl.
Evaluation of Acute Cardiac and Chest Wall Damage after Shocks with a Subcutaneous ICD in Swine.

Killingsworth CR, Melnick SB, Litovsky SH, Ideker RE, Walcott GP.
Evaluation of Acute Cardiac and Chest Wall Damage after Shocks with a Subcutaneous Implantable Cardioverter Defibrillator in Swine.

BACKGROUND:

A subcutaneous implantable cardioverter defibrillator (S-ICD) could ease placement and reduce complications of transvenous ICDs, but requires more energy than transvenous ICDs. Therefore we assessed cardiac and chest wall damage caused by the maximum energy shocks delivered by both types of clinical devices.

METHODS:

During sinus rhythm, anesthetized pigs (38 ± 6 kg) received an S-ICD (n = 4) and five 80-Joule (J) shocks, or a transvenous ICD (control, n = 4) and five 35-J shocks. An inactive S-ICD electrode was implanted into the same control pigs to study implant trauma. All animals survived 24 hours. Troponin I and creatine kinase muscle isoenzyme (CK-MM) were measured as indicators of myocardial and skeletal muscle injury. Histopathological injury of heart, lungs, and chest wall was assessed using semiquantitative scoring.

RESULTS:

Troponin I was significantly elevated at 4 hours and 24 hours (22.6 ± 16.3 ng/mL and 3.1 ± 1.3 ng/mL; baseline 0.07 ± 0.09 ng/mL) in control pigs but not in S-ICD pigs (0.12 ± 0.11 ng/mL and 0.13 ± 0.13 ng/mL; baseline 0.06 ± 0.03 ng/mL). CK-MM was significantly elevated in S-ICD pigs after shocks (6,544 ± 1,496 U/L and 9,705 ± 6,240 U/L; baseline 704 ± 398 U/L) but not in controls. Electrocardiogram changes occurred postshock in controls but not in S-ICD pigs. The myocardium and lungs were histologically normal in both groups. Subcutaneous injury was greater in S-ICD compared to controls.

CONCLUSION:

Although CK-MM suggested more skeletal muscle injury in S-ICD pigs, significant cardiac, lung, and chest wall histopathological changes were not detected in either group. Troponin I data indicate significantly less cardiac injury from 80-J S-ICD shocks than 35-J transvenous shocks.

PMID: 23713608 // Cardiac Rhythm Management Laboratory, Division of Cardiovascular Diseases, Department of Medicine.
ECG Quantification of Myocardial Scar and Risk Stratification in MADIT-II


ECG Quantification of Myocardial Scar and Risk Stratification in MADIT-II
Annals of Noninvasive Electrocardiology 2013 ; Article first published online: 9 JUN 2013
DOI: 10.1111/anec.12065

Background

Low left ventricular ejection fraction (LVEF) increases risk for both sudden cardiac death (SCD) and for heart failure (HF) death; however, implantable cardioverter-defibrillators (ICDs) reduce the incidence of SCD, not HF death. Distinguishing individuals at risk for HF death (non-SCD) versus SCD could improve ICD patient selection.

Objective

This study evaluated whether electrocardiogram (ECG) quantification of myocardial infarction (MI) could discriminate risk for SCD versus non-SCD.

Methods

Selvester QRS scoring was performed on 995 MADIT-II trial subjects' ECGs to quantify MI size. MIs were categorized as small (0–3 QRS points), medium (4–7) or large (≥8). Mortality, SCD and non-SCD rates in the conventional medical therapy (CMT) arm and mortality and ventricular tachycardia/fibrillation (VT/VF) rates in the ICD arm were analyzed by QRS score group. Both arms were analyzed to determine ICD efficacy by QRS score group.

Results

In the CMT arm, mortality, SCD and non-SCD rates were similar across QRS score groups (P = 0.73, P = 0.92, and P = 0.77). The ICD arm showed similar rates of mortality (P = 0.17) and VT/VF (P = 0.24) across QRS score groups. ICD arm mortality was lower than CMT arm mortality across QRS score groups with greatest benefit in the large scar group.

Conclusion

Recently, QRS score was shown to be predictive of VT/VF in the SCD-HeFT population consisting of both ischemic and nonischemic HF and having a maximum LVEF of 35% versus 30% for MADIT-II. Our study found that QRS score did not add prognostic value in the MADIT-II population exhibiting relatively more severe cardiac dysfunction.

Keywords: sudden death; heart failure; implantable cardioverter-defibrillator; electrocardiography; electrophysiology; tachyarrhythmias
Efficacy of ICD in young patients with catecholaminergic polymorphic ventricular tachycardia: success depends on substrate.


Background

The effectiveness of implantable cardioverter-defibrillator (ICD) therapy for the management of catecholaminergic polymorphic ventricular tachycardia (VT) in young patients is not known. ICD discharges are not always effective and inappropriate discharges are common, both resulting in morbidity and mortality.

Methods and Results

This is a multicenter, retrospective review of young patients with catecholaminergic polymorphic VT and ICDs from 5 centers. ICD discharges were evaluated to determine arrhythmia mechanism, appropriateness, efficacy of therapy, and complications. A total of 24 patients were included. Median (interquartile range) ages at onset of catecholaminergic polymorphic VT symptoms and ICD implant were 10.6 (5.0-13.8) years and 13.7 (10.7-16.3) years, respectively. Fourteen patients received 140 shocks. Ten patients (42%) experienced 75 appropriate shocks and 11 patients (46%) received 65 inappropriate shocks. On actuarial analysis, freedom from appropriate shock at 1 year after ICD implant was 75%. Of appropriate shocks, only 43 (57%) demonstrated successful primary termination. All successful appropriate ICD discharges were for ventricular fibrillation. No episodes of polymorphic VT or bidirectional VT demonstrated successful primary termination. The adjusted mean (95% confidence interval) cycle length of successful discharges was significantly shorter than unsuccessful discharges (168 [152-184] ms versus 245 [229-262] ms; adjusted P=0.002). Electrical storm occurred in 29% (4/14) and induction of more malignant ventricular arrhythmias in 36% (5/14). There were no deaths.

Conclusions

ICD efficacy in catecholaminergic polymorphic VT depends on arrhythmia mechanism. Episodes of ventricular fibrillation were uniformly successfully treated, whereas polymorphic and bidirectional VT did not demonstrate successful primary termination. Inappropriate shocks, electrical storm, and ICD complications were common.

Keywords: arrhythmia, catecholaminergic polymorphic ventricular tachycardia, electrical storm, implanted cardioverter defibrillator, pediatric, ventricular tachycardia PMID: 23667268 // Department of Pediatrics, Lucile Packard Children's Hospital, Stanford University, Palo Alto, CA.
A 55-year-old male patient presented after a single shock caused by oversensing of isolated nonphysiologic signals on both the distal HV and pace-sense channels. No other abnormalities were found. He subsequently returned complaining of device “vibration” and his St. Jude implantable defibrillator (ICD; St. Jude Medical, St. Paul, MN, USA) was found to be in VVI backup mode and could not be interrogated. Direct testing in the electrophysiology lab showed normal lead impedances and thresholds with an inability to reproduce the abnormal signals. Detailed cine fluoroscopy of the leads found no abnormalities. A new ICD was connected and successfully delivered a 20-joule shock but failed to deliver a maximum output (39-joule) shock. The new ICD was again found to be in backup mode. A new Endotak Reliance G lead (Boston Scientific, Natick, MA, USA) was implanted and a maximum-output shock was successful using a new Fortify DR ICD. This case likely represents a Durata lead insulation defect in the form of an inside-out abrasion under the distal HV coil. Increased awareness of this defect is warranted, particularly since routine interrogation and submaximum-output shocks may fail to detect the problem.
Effectiveness of remote monitoring of CIEDs in detection and treatment of clinical and device-related cardiovascular events in daily practice: the HomeGuide Registry


Effectiveness of remote monitoring of CIEDs in detection and treatment of clinical and device-related cardiovascular events in daily practice: the HomeGuide Registry

Aims

The HomeGuide Registry was a prospective study (NCT01459874), implementing a model for remote monitoring of cardiac implantable electronic devices (CIEDs) in daily clinical practice, to estimate effectiveness in major cardiovascular event detection and management.

Methods and results

The workflow for remote monitoring [Biotronik Home Monitoring (HM)] was based on primary nursing: each patient was assigned to an expert nurse for management and to a responsible physician for medical decisions. In-person visits were scheduled once a year. Seventy-five Italian sites enrolled 1650 patients [27% pacemakers, 27% single-chamber implantable cardioverter defibrillators (ICDs), 22% dual-chamber ICDs, 24% ICDs with cardiac resynchronization therapy]. Population resembled the expected characteristics of CIED patients. During a 20+13 month follow-up, 2471 independently adjudicated events were collected in 838 patients (51%): 2033 (82%) were detected during HM sessions; 438 (18%) during in-person visits. Sixty were classified as false-positive, with generalized estimating equation-adjusted sensitivity and positive predictive value of 84.3% [confidence interval (CI), 82.5–86.0%] and 97.4% (CI, 96.5–98.2%), respectively. Overall, 95% of asymptomatic and 73% of actionable events were detected during HM sessions. Median reaction time was 3 days [interquartile range (IQR), 1–14 days]. Generalized estimating equation-adjusted incremental utility, calculated according to four properties of major clinical interest, was in favour of the HM sessions: +0.56 (CI, 0.53–0.58%), \( P < 0.0001 \). Resource consumption: 3364 HM sessions performed (76% by nurses), median committed monthly manpower of 55.5 (IQR, 22.0–107.0) min x health personnel/100 patients.

Conclusion

Home Monitoring was highly effective in detecting and managing clinical events in CIED patients in daily practice with remarkably low manpower and resource consumption.

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Electric Jolt May Ease Sleep Apnea

Upper airway stimulation with an implanted neurostimulator was a safe and effective treatment for moderate-to-severe obstructive sleep apnea, researchers reported here.

After 12 months with the implanted device, patients saw significant reductions in apnea hypopnea index ($P<0.0001$) and oxygen desaturation index ($P<0.0001$) from baseline, according to Patrick Strollo, Jr., MD, of the University of Pittsburgh Medical Center, and colleagues.

Patients who had the device installed also saw significant improvements in scores for sleepiness ($P<0.0001$) and quality of life ($P<0.0001$) from baseline after 12 months, Strollo said during an oral presentation at the SLEEP meeting.

Although obstructive sleep apnea is often effectively treated with continuous positive airway pressure (CPAP), efficacy can be hindered by lack of adherence, and some patients are intolerant to the treatment route.

The researchers studied the efficacy and safety of electrical stimulation of the hypoglossal nerve in treated obstructive sleep apnea in a population of 124 CPAP-intolerant or -naive patients enrolled in the STAR trial who had moderate-to-severe obstructive sleep apnea.

The primary outcome measures were changes in apnea hypopnea index and oxygen desaturation index, while secondary endpoints were Epworth Sleepiness Scale ratings and Functional Outcomes of Sleep Questionnaire score.

Participants were enrolled in a prospective, multicenter trial with a randomized therapy withdrawal arm and received a screen polysomnographic study, surgical consultation, and drug-induced sleep endoscopy. Patients were followed 12 months after implantation of the neurostimulator before being randomized to the on treatment or off treatment withdrawal arm.

Inclusion criteria included apnea hypopnea index of 20 to 50, failed or not tolerated CPAP, central and mixed sleep apnea that accounted for less than 25% of all apnea hypopnea index events, and absence of significant apnea when sleeping in a nonsupine position, Strollo said during his presentation.

Participants were a mean 54.5 years old, mostly male (83%), mostly white (97%), had a mean body mass index of 28.4 kg/m$^2$, had a mean neck circumference of 41.2 cm, a mean systolic blood pressure of 128.7 mm/Hg, and a mean diastolic blood pressure of 81.5 mm/Hg.

Thirty eight percent also had hypertension, 9% had diabetes, 5% asthma, 2% congestive heart failure, and 18% had received a prior uvulopalatopharyngoplasty.

At 12 months following device implantation, mean scores for apnea hypopnea index, oxygen desaturation index, sleepiness scale, and quality of life all significantly improved ($P<0.0001$).

Among patients who were randomized to stop treatment after 12 months on, apnea hypopnea index scores grew significantly worse than those who were randomized to continue treatment ($P<0.0001$).
Adverse events included one serious device revision, procedure-related pain in 25% of participants, tongue discomfort in 33% of participants, and mild-to-moderate infection in 1%. There was also one death that was unrelated to the trial.

Tongue discomfort was related to tongue positioning during neurostimulation.

Strollo concluded that upper airway stimulation "can play a significant role in the management of at-risk patients who do not accept or adhere to CPAP therapy," based on significant improvements in all measurements in the study and based on their ability to tolerate treatment.


The study was supported by Inspire Medical Systems. Authors received support from the NIH, Philips-Respironics, ResMed, Inspire Medical Systems, the National Football League, the Will Rogers Foundation, the ResMed Foundation, and ApniCure.
Percutaneous biventricular cardiac assist device in cardiogenic shock

Patrick Hunziker, Lukas Hunziker

Percutaneous biventricular cardiac assist device in cardiogenic shock


Patients with cardiogenic shock who require mechanical circulation support may profit from more effective, less invasive devices. Panel A shows the first-in-man use of biventricular percutaneous support with impeller devices (Abiomed Impella, Danvers, MA, USA). The 54-year-old patient presented with acute myocardial infarction and shock due to biventricular pump failure. When angioplasty of the RCA, intravascular volume optimization, and high-dose inotropes failed to stabilize the patient, a percutaneous left ventricular-assist device was implanted. Pulmonary oedema resolved, but severe right heart failure with multi-organ failure (liver, kidney) persisted despite nitric oxide therapy. Additional percutaneous device implantation in the right heart led to circulatory stabilization and progressive organ function recovery, with successful device weaning on Day 8. Echocardiography on Day 44 showed a normal right ventricular function. Panel B shows the pump head and Panel C the topology of the devices.

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Impact of Carvedilol and Metoprolol on Inappropriate ICD Therapy in the MADIT-CRT Trial.


OBJECTIVES:
This study sought to evaluate the effects of carvedilol and metoprolol on the end point of inappropriate ICD therapy in the MADIT-CRT study.

BACKGROUND:
The impact of carvedilol and metoprolol on inappropriate therapy in heart failure patients with devices has not yet been investigated.

METHODS:
All patients in the MADIT-CRT study who received a device (N=1790) were identified. Using time-dependent Cox regression analysis we compared patients treated with different types of beta-blockers or no beta-blockers on the primary end point of inappropriate therapy yielded as anti-tachycardia pacing (ATP) or shocks. Secondary end points were inappropriate therapy due to atrial fibrillation and atrial tachyarrhythmias also evaluated as ATP or shock.

RESULTS:
Inappropriate therapy occurred in 253 of 1790 patients (14%) during a mean follow-up period of 3.4 years (SD ±1.1) Treatment with carvedilol was associated with a significantly decreased risk of inappropriate therapy when compared to metoprolol (HR 0.64, [CI: 0.48-0.85], p=0.002). The reduction in risk was consistent for inappropriate ATP (HR 0.66 [CI: 0.48-0.90], p=0.009) and inappropriate shocks (HR 0.54 [CI: 0.36-0.80], p=0.002). The risk of inappropriate therapy caused by atrial fibrillation was also reduced in patients on carvedilol compared to metoprolol (HR 0.50, [CI: 0.32-0.81], p=0.004). General use of beta-blocker (93%) and adherence in this study was high.

CONCLUSIONS:
In heart failure patients with either a CRT-D or ICD device, carvedilol was associated with a 36% reduction of inappropriate ATP and shock therapy compared to metoprolol. Inappropriate therapy due to atrial fibrillation was reduced by 50% in patients on carvedilol compared to metoprolol.

PMID:23770172 // Heart Research Follow-up Program, Cardiology Division, University of Rochester Medical Center, Rochester, New York, USA; Department of Cardiology, Gentofte Hospital, Hellerup, Denmark. Electronic address: mruwald@hotmail.com.
Fear of ICD Shock Impairs Sexual Function

Points

Note that this cohort study of patients with and without ICD's for congenital heart disease demonstrated that shock-anxiety negatively impacted sexual function.

Be aware that of those with ICD's, 30% had received at least one shock with the device.

Fear of receiving an ill-timed shock from an implantable-cardioverter defibrillator (ICD) during sex is adversely affecting the bedroom performance of people with congenital heart disease, new research confirmed.

In the multicenter study, 70 patients with ICDs (mean age 32) reported a high level of anxiety as measured by the validated Florida Shock Anxiety Scale (score 16, interquartile range 12-23.5), which was slightly higher than the median score for the general population of ICD recipients (15.4, \( P=0.057 \)), wrote Stephen Cook, MD, of the Children's Hospital of Pittsburgh, and colleagues in the June issue of *HeartRhythm*.

In addition, a higher level of shock-related anxiety was associated with poorer sexual function scores in men as measured by the Sexual Health Inventory for Men (SHIM) questionnaire (\( P<0.001 \)), while in women, higher ICD-related anxiety also correlated with lower sexual function as measured by the Female Sexual Function Index (\( P<0.01 \)).

The study is the first to link shock-related anxiety to sexual dysfunction in young ICD recipients, the authors stated. This study updates data reported by Cook at the 2011 American Heart Association meeting.

As many as 1.3 million people in the U.S. have congenital heart disease (CHD), and an increasing number are being treated with ICDs to prevent sudden cardiac death, the researchers reported.

"Despite the overall success of the ICD in preventing premature mortality in at-risk patients, the psychological cost of living with an ICD can be considerable," Cook's group wrote, adding that as many as one in three patients with ICDs display symptoms of anxiety and depression.

This prospective, multicenter, cross-sectional study was conducted on adult CHD patients with and without an ICD. Forty-four percent of the participants were women. The complexity of CHD was classified as mild in 18% of the patients, moderate in 52%, and severe in 30%.

Among ICD recipients, devices were implanted a median of 5.5 years prior to study enrollment and 30% sof patients had received an inappropriate shock from their device.

The authors found that higher total anxiety scores were associated with poorer sexual function (Spearman's rank correlation= -0.480, \( P<0.001 \)).
Having an ICD was not associated with erectile dysfunction (relative risk 0.94, 95% CI 0.4-2.2, \( P \) not significant), but higher total anxiety scores related to ICD shock were inversely correlated to erectile function as measured by SHIM (Spearman's rank correlation= -0.432, \( P < 0.003 \)).

Having an ICD was also associated with self-reported depressive symptoms (Spearman rank correlation=0.536, \( P < 0.001 \)).

The study had some limitations. Subgroup analyses were limited by the number of enrolled adults with CHD and the study did rely on patient self-report. Also, the issue of sexual inactivity (lack of interest; lack of partner) was not addressed in this research.

Nonetheless, "ICDs are increasingly being implanted in this young and vulnerable patient population, yet the psychosocial issues are often overlooked," Cook said in a statement. "Our study is an example of dynamic research intended to help us better understand this growing population."

They suggested wider use of anxiety questionnaires like the Florida Shock Anxiety Scale to assess patient fears about inappropriate shock and identify those who are especially vulnerable.

"It remains to be demonstrated whether systematic screening assessments combined with directed interventions may prove beneficial in ICD recipients with congenital heart disease," the authors wrote. "In the interim, it appears essential for healthcare providers to address these issues in order to optimize the health, sexual function, and psychological well-being of their patients."

reference:

The study was funded by the Alliance for Adult Research in Congenital Cardiology. No information on conflict of interest was reported by the authors.

**Shock-related anxiety from heart devices is associated with sexual dysfunction in young adults**

A new study shows young adults with congenital heart disease also living with an implantable cardioverter- defibrillator (ICD) experience a high level of shock-related anxiety. The multicentre study, published in the June edition of Heart Rhythm, is the first to discover that shock-related anxiety is associated with sexual dysfunction in young adults and calls on healthcare providers to address these issues to improve the quality of life for patients.

Patients in this study, lead by Stephen Cook, Adult Congenital Heart Disease Center, Heart Institute, Children's Hospital of Pittsburgh of University of Pittsburgh Medical Center, USA, were prospectively enrolled from four adult congenital heart disease outpatient clinics within the Alliance for Adult Research in Congenital Cardiology. The Florida Shock Anxiety Scale (FSAS), a 10-item tool designed to provide a quantitative measure about the ability to cope with the impact of a shock, was administered to patients with an ICD. Men completed the Sexual Health Inventory for Men (SHIM), a questionnaire for screening and diagnosing erectile dysfunction and its severity. Additionally, women completed the Female Sexual Function Index (FSFI), a self-report questionnaire that assesses sexual function in women in a variety of dimensions.
A total of 180 patients (70 patients with an ICD, 110 patients without an ICD) and an average age of 32 years old were enrolled in the study. In ICD recipients, a high level of shock-related anxiety was identified, which was slightly higher than the median score for ICD recipients in the general population revealing a high level of device specific fears and anxiety. A higher level of shock-related anxiety was associated with poorer sexual function score in both men and women.

“ICDs are increasingly being implanted in this young and vulnerable patient population, yet the psychosocial issues are often overlooked. Our study is an example of dynamic research intended to help us better understand this growing population,” said Cook. “Improving outcomes and the quality of life in these young adults is critical and our results clearly show the importance of addressing their psychological well-being.”

Early identification of shock-related anxiety may pave the way for targeted interventions such as educational initiatives, treatment planning and psychological referral. Despite the overall access of ICDs in preventing premature mortality in at-risk patients, the psychological cost of living with an ICD can be significant. Proposed strategies to improve psychological well-being should include an effective communication strategy between patients and health-care professionals in regarding education and sexual concerns.
Fragmented QRS Complex Predicts The Arrhythmic Events in Patients with Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia


Journal of Cardiovascular Electrophysiology 2013. DOI: 10.1111/jce.12202

Background

Fragmented QRS (frQRS) complex, with various morphology, has been recently described as a diagnostic criterion of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D). However, there is little data regarding the prognostic role of frQRS in these patients. Therefore, we aimed to investigate the association of frQRS with arrhythmic events in patients with ARVC/D.

Methods

Seventy-eight patients (51 men, 65.4%; mean age: 31.25 ± 11.5 years) with the diagnosis of ARVC/D according to 2010 modified Task Force Criteria were analyzed retrospectively. Baseline ECG evaluation revealed frQRS complex in 46 patients (59%). Eleven patients with complete/incomplete right bundle branch block were excluded from the study. The phenomenon of frQRS was defined as deflections at the beginning of the QRS complex, on top of the R-wave, or in the nadir of the S-wave similar to the definition in CAD in either one right precordial lead or in more than one lead including all standard ECG leads.

Results

During 38 ± 14 months follow-up period, 3 patients (3.8%) died suddenly, 36 patients (46.1%) experienced arrhythmic events (32 VTs and 4 VF, 30 in the ICD group). frQRS was significantly associated with arrhythmic events (P < 0.001). Also, the number of ECG leads with frQRS complex was higher in patients with arrhythmic events (5.08 ± 2.5 vs 1.14 ± 1.7, P < 0.001, respectively).

Conclusion

frQRS complex on standard 12-lead ECG predicts fatal and non-fatal arrhythmic events in patients with ARVC/D. Therefore, large scale and prospective studies are needed to confirm those findings.

No disclosures. This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jce.12202. Keywords: arrhythmogenic right ventricular cardiomyopathy; QRS fragmentation; ventricular arrhythmia; implantable cardioverter defibrillator; sudden cardiac death.
Improved Survival in Patients with Continuous-Flow Ventricular Assist Device for Bridge to Heart Transplantation

Improved Survival in Patients with Continuous-Flow Ventricular Assist Device for Bridge to Heart Transplantation
Transplantation Proceedings 2013 ; 45 / 5 : 2017-2018 (June 2013)

Background

Contemporary continuous-flow ventricular assist devices (CFVADs) have greatly improved patient survival for indications of bridge to transplantation (BTT) and destination therapy. In Japan, CFVAD is limited for BTT use. The waiting period for heart transplantation (HT) is long owing to donor shortage. We examined the results of CFVAD for BTT indication.

Methods

Eighty-nine VAD treatments were performed among subjects whose preimplantation condition was profile 1 (n = 49) or profile 2 or 3 (n = 40). The device was the paracorporeal pulsatile Nipro VAD (n = 67) or CFVAD (n = 22). All CFVAD patients were profile 2 or 3.

Results

The median assist period was 529 days (Nipro VAD, 530; CFVAD, 528). Twenty-six patients were on the device for >2 years. Actuarial survival was 81.6%, 69.5%, and 61.1% at 1, 3, and 5 years. Survival in profile 1 was significantly worse than in profile 2 or 3. Survival of CFVAD patients was superior to that of paracorporeal VAD. Six-month mortality rate of 20% in cases before 2009 (n = 60) was dramatically improved to 3% among those after 2010 (n = 29). All patients with CFVAD were alive and discharged home. 26 patients were transplanted, 7 had been weaned from VAD and 27 were on a device. The rate of events requiring hospital admission was 0.98 per patient-year in CFVAD patients.

Conclusions

Contemporary CFVADs have enabled advanced heart failure patients to await HT safely with an improved quality of life. The advent of CFVAD has also shifted their preimplantation condition to a less sick status. CFVADs were the safest, most reliable circulatory support devices for long-term waiting periods for the BTT indications.
ICD Not to Blame for Higher CV Mortality After Shock

**Points**

- It may be the underlying arrhythmia that is more detrimental to patient health than the shock from an implantable cardioverter defibrillator, a study has found.
- Note that the first inappropriate shock for nonventricular arrhythmia (atrial fibrillation or flutter) was associated with an increased relative risk of death compared with ICD recipients without known shock.
- Certain inappropriate shocks from an implantable cardioverter defibrillator (ICD) are associated with an increased mortality risk, but it may be the underlying arrhythmia that is more detrimental to patient health, the observational ALTITUDE study found.

The first inappropriate shock for a nonventricular arrhythmia (atrial fibrillation or flutter) was associated with a 61% increased relative risk of death compared with ICD recipients who did not experience a known shock (HR 1.61), according to Brian D. Powell, MD, of the Sanger Heart & Vascular Institute in Charlotte, N.C., and colleagues.

In contrast, mortality risk did not increase in patients whose first shock was associated with "benign" arrhythmias such as sinus tachycardia, supraventricular tachycardia, or lead noise or oversensing (HR 0.97), researchers wrote in the study published in the *Journal of the American College of Cardiology*.

The increased risk of death associated with atrial fibrillation or atrial flutter is "secondary to the underlying substrate and comorbidities associated with atrial fibrillation," Powell and colleagues suggested.

In addition, they wrote, a shock due to rapid ventricular rates in the setting of atrial fibrillation or atrial flutter may be a marker of inadequate doses of beta-blockers or worsening heart failure.

The researchers concluded that a poor prognosis after a first shock may be more related to the underlying arrhythmia than to any adverse effect from the shock itself.

"If shocks were bad for you, there should be an increased mortality regardless of the nature of the inappropriate shock," Vivek Reddy, MD, director of arrhythmia services at the Mount Sinai Medical Center in New York City, told MedPage Today.

"We know that defibrillators are good for you overall," said Reddy, who was not part of the study. "But we also know that once the first appropriate or inappropriate shock is delivered, the risk of mortality is greater."

The current study, he said, was large enough to tease out the nature of the inappropriate shocks -- mainly that inappropriate shocks for atrial fibrillation or atrial flutter led to increased mortality, while inappropriate shocks for sinus tachycardia and other benign arrhythmias did not increase mortality.

These data also suggest that ventricular arrhythmias may "represent a final common pathway in otherwise terminal conditions such as end-stage heart failure or multi-organ failure," wrote Eric S. Williams, MD, and Jeanne E. Poole, MD, of the University of Washington Medical Center in Seattle, in an accompanying editorial.

If that is the case, "the debate as to whether an ICD shock carries an additional risk to the patient from shock-induced myocardial damage becomes a futile exercise, since the patient would have died either without or in spite of the shock," the editorialists added.
Preclinical and small studies have shown an increase in troponin levels following ICD shock; however, randomized trials such as MADIT II and SCD-HeFT have shown a long-term mortality benefit for ICD recipients.

"Now, in light of the ALTITUDE study results, the alternative explanation is more reasonable: the occurrence of morbid arrhythmias, specifically ventricular arrhythmias and atrial fibrillation, identifies a high-risk patient population," Williams and Poole wrote.

The current study drew its data from the ALTITUDE project, which comprises remotely acquired prospective data from patients with ICDs and cardiac resynchronization therapy plus defibrillator (CRT-D) devices.

The database, at the time of the study, comprised 127,134 patients from 1,550 U.S. centers. The average follow-up was 3 years from implant and 2 years from first shock.

The overall mean age was 64, with ICD recipients being nonsignificantly younger than CRT-D patients (62 versus 70). Most patients were male.

Of the 3,809 matched patients in the study group, the type of device broke down as follows:

- 25% with single-chamber ICD
- 35% dual-chamber ICD
- 40% CRT-D

In contrast to the inappropriate first shocks of benign arrhythmias, all first appropriate shocks were associated with an increased risk of subsequent mortality.

The investigators noted that the MADIT-RIT trial found that those randomized to conventional ICD programming incurred more shocks and increased mortality, compared with those who had either delayed or high-rate therapy -- which actually produced a better-than-50% mortality benefit.

Do the MADIT-RIT results contradict these observational findings? No, said Powell and colleagues.

They suggested, not unlike the MADIT-RIT investigators, that the mortality benefit was driven mostly by the decreased rate of anti-tachycardia therapy (ATP).

When episodes of ATP were taken into consideration, the first-shock episodes were not significantly different between the groups in MADIT-RIT, Powell and colleagues said.

The study is limited by its observational nature, limited clinical data that does not allow for further analysis, no data on medications, and the use of a single manufacturer's devices.


On 11 June, the US Food and Drug Administration (FDA) approved St Jude Medical’s next-generation Ellipse and SJM Assura portfolio of implantable cardioverter defibrillators (ICDs) and cardiac resynchronisation therapy defibrillators (CRT-Ds). The new devices are designed to lower the risk of lead abrasion and to ensure high-voltage therapy delivery.

According to a company release, the Ellipse and SJM Assura family of devices feature the DynamicTx Over-Current Detection Algorithm, which automatically adjusts shocking configurations to ensure the delivery of high-voltage therapy even if an electrical short in one portion of the system were to occur. In addition, the next-generation Ellipse and SJM Assura portfolio of implantable defibrillators have a low-friction coating on the device can, which has been demonstrated in testing to significantly reduce the friction between the device and leads.

As such, the low-friction coating provides an extra layer of insulation and is designed to reduce the risk for lead-to-can abrasion, the most common type of lead insulation failure in the industry.

“The new safety features in these devices are an excellent example of innovation that improves patient safety,” said Anne Curtis, chairman of the Department of Medicine with the University at Buffalo, USA. “The DynamicTx feature in the new Ellipse and SJM Assura devices provides an additional safeguard to ensure the patient receives life-saving therapy delivery even if an electrical short were to occur. In addition, St Jude Medical is the first company to help address the problem of lead-to-can abrasion by providing increased insulation on the ICD device itself, rather than the lead.”

These advanced technologies provide preventative and adaptive capabilities to address potential failures that can result in the inability to deliver high-voltage therapy when needed, especially in systems using silicone-only insulated defibrillation leads, which are known to be at higher risk of abrasion. It is estimated that over 400,000 silicone-only insulated defibrillation leads from all manufacturers remain active worldwide.

“St Jude Medical strives to deliver the highest levels of patient safety. The new Ellipse ICD and SJM Assura family of devices support those efforts by providing added features that ensure effective therapy delivery,” said Eric S Fain, president of the St Jude Medical Implantable Electronic Systems Division. “We are pleased that the FDA approved these devices, allowing us to bring important safety and system reliability enhancements to patients.”
Fewer comorbidities key to ICD effectiveness in elderly: Registry analysis

Elderly and younger patients received appropriate and inappropriate therapy from their implantable cardioverter defibrillators (ICDs) at about the same rates, whether they had primary- or secondary-prevention devices, in a prospective population-based registry study [Source Yung D, et al.]

It’s known and the current study confirms that the elderly have greater mortality after ICD implantation compared with younger patients. And that, according to senior author Dr Douglas S Lee (University of Toronto, ON), might lead one to believe, incorrectly, that ICDs are less effective in the elderly. "Our study is showing the other side of the equation, now that we have information about treatments delivered by the devices for life-threatening rhythms. It shows that although elderly patients are at higher risk for dying, they also have similar rates of appropriate therapies that potentially saved their lives."

The findings underscore the importance of selecting patients for ICDs who are most likely to benefit, and "those are patients with fewer life-limiting cardiac and noncardiac comorbidities," Lee told the press.

Indeed, "Our study suggests that ICD implantation in the elderly requires individualized consideration," state Lee and his colleagues in their report published in the June 18, 2013 issue of Circulation, with lead author Dr Derek Yung (University of Ottawa, ON).

Their analysis points to NYHA functional class, peripheral vascular disease, and use of loop diuretics as multivariable predictors of mortality in both primary- and secondary-prevention patients and to syncope, reduced glomerular filtration rate, and left atrial size as predictors solely in the primary-prevention group.

The group looked at 5399 patients receiving ICDs from 2007 to 2010 in the prospective Ontario ICD Database. Mortality increased significantly with age group by decade among the 3939 and 1460 patients with primary- and secondary-prevention devices, respectively. There were no significant increases in risk of appropriate shocks by age.

Covariate-adjusted competing risk analysis demonstrated higher risk of death but no significant decline in appropriate shocks with older age in either ICD-indication group.

<table>
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<th>Age cohorts, range in years</th>
<th>Death (p for trend)</th>
<th>Appropriate shock</th>
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<td>Primary-prevention</td>
<td>&lt;0.001</td>
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Covariate adjusted hazard ratio* (95% CI) for death and appropriate shock by age cohort and ICD indication in the Ontario ICD Database
"The findings shouldn't be interpreted as showing that all elderly patients who meet the minimum requirements for an ICD should actually be ICD candidates," Lee cautions. Rather, the message was that ICD-therapy rates in a well-selected elderly population were similar to those in younger patients. And "there were fairly low rates of certain comorbidities that would indicate, overall, that these were fairly well-selected patients, even at the population level."


The study was supported by a grant from the Canadian Institutes of Health Research and the Ontario Ministry of Health and Long-term Care. Lee is a clinician scientist of the Canadian Institutes of Health Research; he had no other disclosures. Disclosures for the coauthors are listed in the paper
Impact of extending device longevity on the long-term costs of ICD therapy: a modelling study with a 15-year time horizon.

Boriani G, Braunschweig F, Deharo JC, Leyva F, Lubinski A, Lazzaro C.

Impact of extending device longevity on the long-term costs of implantable cardioverter-defibrillator therapy: a modelling study with a 15-year time horizon.

Europace 2013 May 21. [Epub ahead of print]

AIMS:

To determine the long-term costs of extending device longevity in four patient populations requiring a single-chamber implantable cardioverter-defibrillator (ICD) or requiring cardiac resynchronization therapy with defibrillation (CRT-D) device over a 15-year time window.

METHODS AND RESULTS:

We considered patient populations with an accepted indication for a single-chamber ICD for prevention of sudden cardiac death in the context of preserved (Population A) or impaired (Population B) left ventricular function; or with indication for a CRT-D device in the context of heart failure in New York Heart Association class II (Population C) or III (Population D). Expected patient survival and a cost analysis, including the cost of complications, was undertaken from a hospital perspective. Extended device longevity of 5 vs. 9 years for ICDs (Populations A and B); 4 vs. 7 years for CRT-Ds (Populations C and D) were considered. Over a 15-year time horizon, total, yearly, and per diem savings, per patient, from extending ICD longevity to 9 years were €10 926.91, €728.46, and €1.99 for Population A, and €7661.32, €510.75, and €1.40 for Population B. Total, yearly, and per diem savings from extending CRT-D longevity to 7 years were €13 630.38, €908.69, and €2.49 for Population C, and €10 968.29, €731.22, and €2.00 for Population D. Avoidance of a generator replacement amounted up to 46.6-62.5% of the saving.

CONCLUSION:

Extending device longevity has an important effect on the long-term cost of device therapy, both for ICD and CRT-D. This has important implications for device choice.

Keywords: Budget, Cardiac resynchronization therapy, Cost, Cost analysis, Device longevity, Economics, Implantable cardioverter-defibrillator, Primary prevention, Sudden death PMID: 23696624 // Istituto di Cardiologia, Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES), Università di Bologna, Azienda Ospedaliera S. Orsola-Malpighi, Via Massarenti 9, 40138 Bologna, Italy.
Gender-specific differences in clinical outcome of primary prevention implantable cardioverter defibrillator recipients.

Gender-specific differences in clinical outcome of primary prevention implantable cardioverter defibrillator recipients.
Heart. 2013 May 30. [Epub ahead of print]

OBJECTIVE:
To assess differences in clinical outcome of implantable cardioverter-defibrillator (ICD) treatment in men and women.

DESIGN:
Prospective cohort study.

SETTING:
University Medical Center.

PATIENTS:
1946 primary prevention ICD recipients (1528 (79%) men and 418 (21%) women). Patients with congenital heart disease were excluded for this analysis.

MAIN OUTCOME MEASURES:
All-cause mortality, ICD therapy (antitachycardia pacing and shock) and ICD shock.

RESULTS:
During a median follow-up of 3.3 years (25th-75th percentile 1.4-5.4), 387 (25%) men and 76 (18%) women died. The estimated 5-year cumulative incidence for all-cause mortality was 20% (95% CI 18% to 23%) for men and 14% (95% CI 9% to 19%) for women (log rank p<0.01). After adjustment for potential confounding covariates all-cause mortality was lower in women (HR 0.65; 95% CI 0.49 to 0.84; p<0.01). The 5-year cumulative incidence for appropriate therapy in men was 24% (95% CI 21% to 28%) as compared with 20% (95% CI 14% to 26%) in women (log rank p=0.07). After adjustment, a non-significant trend remained (HR 0.82; 95% CI 0.64 to 1.06; p=0.13).

CONCLUSIONS:
In clinical practice, 21% of primary prevention ICD recipients are women. Women have lower mortality and tend to experience less appropriate ICD therapy as compared with their male peers.

PMID: 23723448 Leiden University Medical Center, , Leiden, The Netherlands.
ICDs in ARVD-C: patient outcomes, incidence of appropriate and inappropriate interventions, and complications.

Schinkel AF.

Background- Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a cardiomyopathy characterized by ventricular arrhythmias and an abnormal right ventricle. Implantable cardioverter defibrillator (ICD) therapy may prevent sudden cardiac death in patients with ARVD/C. Currently, an overview of outcomes, appropriate and inappropriate interventions, and complications of ICD therapy in ARVD/C is lacking. Methods and Results- A literature search was performed to identify studies reporting outcome and complications in patients with ARVD/C who underwent ICD implantation. Of 641 articles screened, 24 studies on 18 cohorts were eligible for inclusion. In case of multiple publications on a cohort, the most recent publication was included in the meta-analysis. There were 610 patients (mean age, 40.4 years; 42% women), who had an ICD for primary or secondary prevention of sudden cardiac death. Risk factors for sudden cardiac death were presyncope (61%), syncope (31%), previous cardiac arrest (14%), ventricular tachycardia (58%), and ventricular fibrillation (6%). Antiarrhythmic medication consisted mostly of β-blockers (38%), amiodarone (14%), or sotalol (30%). During the 3.8-year follow-up, annualized cardiac mortality rate was 0.9%, annualized noncardiac mortality rate was 0.8%, and annualized heart transplant rate was 0.9%. The annualized appropriate and inappropriate ICD intervention rates were 9.5% and 3.7%, respectively. ICD-related complications consisted of difficult lead placement (18.4%), lead malfunction (9.8%), infection (1.4%), lead displacement (3.3%), and any complication (20.3%). Conclusions- Cardiac and noncardiac mortality rates after ICD implantation in patients with ARVD/C are low. Appropriate ICD interventions occur at a rate of 9.5%/y. Inappropriate ICD interventions and complications lead to considerable ICD-related morbidity.

Keywords: arrhythmogenic right ventricular dysplasia/cardiomyopathy, complication, implantable cardioverter defibrillator, prognosis, sudden cardiac death // PMID: 23673907 // Department of Cardiology, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands.
Permanent cardiac pacing in children: choosing the optimal pacing site: a multicenter study.


BACKGROUND:

We evaluated the effects of the site of ventricular pacing on left ventricular (LV) synchrony and function in children requiring permanent pacing.

METHODS AND RESULTS:

One hundred seventy-eight children (aged <18 years) from 21 centers with atrioventricular block and a structurally normal heart undergoing permanent pacing were studied cross-sectionally. Median age at evaluation was 11.2 (interquartile range, 6.3-15.0) years. Median pacing duration was 5.4 (interquartile range, 3.1-8.8) years. Pacing sites were the free wall of the right ventricular (RV) outflow tract (n=8), lateral RV (n=44), RV apex (n=61), RV septum (n=29), LV apex (n=12), LV midlateral wall (n=17), and LV base (n=7). LV synchrony, pump function, and contraction efficiency were significantly affected by pacing site and were superior in children paced at the LV apex/LV midlateral wall. LV dyssynchrony correlated inversely with LV ejection fraction (R=0.80, P=0.031). Pacing from the RV outflow tract/lateral RV predicted significantly decreased LV function (LV ejection fraction <45%; odds ratio, 10.72; confidence interval, 2.07-55.60; P=0.005), whereas LV apex/LV midlateral wall pacing was associated with preserved LV function (LV ejection fraction ≥55%; odds ratio, 8.26; confidence interval, 1.46-47.62; P=0.018). Presence of maternal autoantibodies, gender, age at implantation, duration of pacing, DDD mode, and QRS duration had no significant impact on LV ejection fraction.

CONCLUSIONS:

The site of ventricular pacing has a major impact on LV mechanical synchrony, efficiency, and pump function in children who require lifelong pacing. Of the sites studied, LV apex/LV midlateral wall pacing has the greatest potential to prevent pacing-induced reduction of cardiac pump function.

PMID: 23275383 // Children’s Heart Center, University Hospital Motol, V Úvalu 84, 150 06 Prague 5, Czech Republic. jan.janousek@lfmotol.cuni.cz
LV mechanical dyssynchrony by cardiac MRI is greater in pts with strict vs nonstrict ECG criteria for LBBB.


BACKGROUND:

Left bundle-branch block (LBBB) is a marker of increased delay between septal and left ventricular (LV) lateral wall electrical activation and is a predictor of which patients will benefit from cardiac resynchronization therapy. Recent analysis has suggested that one-third of patients meeting the conventional electrocardiogram criteria for LBBB are misdiagnosed, and new strict LBBB criteria have been proposed. We tested the hypothesis that patients with strict LBBB have greater LV mechanical dyssynchrony than do patients meeting the nonstrict LBBB criteria, whereas there is no difference between patients with nonstrict LBBB and LV conduction delay with a QRS duration of 110 to 119 ms.

METHODS:

Sixty-four patients referred for primary prevention implantable cardioverter-defibrillators underwent 12-lead electrocardiogram and cardiac magnetic resonance myocardial tagging. The patients were classified as strict LBBB, nonstrict LBBB, or non-LBBB (nonspecific LV conduction delay with a QRS duration of 110-119 ms). The time delay between septal and lateral LV wall peak circumferential strain (septal-to-lateral wall delay) was measured by cardiac magnetic resonance.

RESULTS:

Patients with strict LBBB (n = 31) had a greater septal-to-lateral wall delay compared with patients with nonstrict LBBB (n = 19) (210 ± 137 ms vs 122 ± 102 ms, P = .045). There was no significant difference between nonstrict LBBB and non-LBBB (n = 14) septal-to-lateral wall delay (122 ± 102 ms vs 100 ± 86 ms, P = .51).

CONCLUSIONS:

Strict LBBB criteria identify patients with greater mechanical dyssynchrony compared with patients only meeting the nonstrict LBBB criteria, whereas there was no significant difference between patients with nonstrict LBBB and non-LBBB. The greater observed LV dyssynchrony may explain why patients with strict LBBB have a better response to cardiac resynchronization therapy.

PMID: 23708167 // Department of Clinical Physiology, Cardiac MR Group, Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden; Duke Clinical Research Institute, Durham, MD.
BACKGROUND:

Contemporary implantable cardiac defibrillators (ICD) enable storage of multiple, preepisode R-R recordings in patients who suffered from ventricular tachyarrhythmia (VTA). Timely prediction of VTA, using heart rate variability (HRV) analysis techniques, may facilitate the implementation of preventive and therapeutic strategies.

AIM:

To evaluate the novel multipole method of the HRV analysis in prediction of imminent VTAs in ICD patients.

METHODS:

We screened patients from the Biotronik HAWAI Registry (Heart Rate Analysis with Automated ICDs). A total of 28 patients from the HAWAI registries (phase I and II), having medical records, who had experienced documented, verified VTA during the 2-year follow-up, were included in our analysis. HRV during preepisode recordings of 4,500 R-R intervals were analyzed using the Dyx parameter and compared to HRV of similar length recordings from the same patients that were not followed by arrhythmia.

RESULTS:

Our study population consisted mainly of men 25 of 28 (89%), average age of 64.8 ± 9.4 years, 92% with coronary artery disease. HRV during 64 preevent recordings (2.3 events per patient on average) was analyzed and compared with 60 control recordings. The multipole method of HRV analysis showed 50% sensitivity and 91.6% specificity for prediction of ventricular tachycardia/ventricular fibrillation in the study population, with 84.5% positive predictive value. No statistically significant correlation was found between various clinical parameters and the sensitivity of imminent VTA predetection in our patients.

CONCLUSION:

The multipole method of HRV analysis emerges as a highly specific, possible predictor of imminent VTA, providing an early warning allowing to prepare for an arrhythmic episode.

PMID: 23713754 // Davidai Arrhythmia Center, Leviev Heart Center, Sheba Medical Center, Ramat Gan, Israel; Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.
Left bundle-branch block: The relationship between electrocardiogram electrical activation and echocardiography mechanical contraction


Background
The relationship between myocardial electrical activation by electrocardiogram (ECG) and mechanical contraction by echocardiography in left bundle-branch block (LBBB) has never been clearly demonstrated. New strict criteria for LBBB based on a fundamental understanding of physiology have recently been independently published for both ECG and echocardiography. The relationship between the 2 modalities and the relation to cardiac resynchronization therapy (CRT) response was investigated.

Methods
Sixty-six patients with LBBB by conventional criteria had a standard 12-lead ECG and 2-dimensional strain echocardiography performed before CRT implantation. Criteria for LBBB by echocardiography included early termination of contraction in one wall and prestretch and late contraction in opposing wall(s). New strict criteria by ECG included QRS duration ≥ 140 ms (men) or 130 ms (women), QS or rS in leads V1 and V2, and mid-QRS notching or slurring in ≥ 2 of leads V1, V2, V5, V6, I, and aVL. Response was defined as > 15% decrease in left ventricular end-systolic volume after 6 months.

Results
In 64 of 66 patients, ECG analysis was possible. Echo and ECG readings for LBBB presence were concordant in 54 (84%) of 64. Thirty-seven (82%) of 45 patients with LBBB by strict ECG criteria responded to CRT, whereas only 4 (21%) of the 19 patients without LBBB responded (sensitivity 90% and specificity 65%). Thirty-six (95%) of 38 patients with concordance for the presence of LBBB responded to CRT. In patients with concordance for the absence of LBBB, 15 (94%) of 16 did not respond.

Conclusion
For the first time, a close relation has been demonstrated between electrical activation by ECG and mechanical contraction by echocardiography. These findings may help identify CRT candidates.
Multicenter Experience with Transvenous Lead Extraction in ARVC.


BACKGROUND:

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is becoming a more commonly diagnosed entity with frequent need for coincident implantable cardioverter defibrillator (ICD) therapy. Given predominant right ventricular disease with thinning of the wall, there is concern regarding the safety of transvenous lead extraction (TLE) in ARVC.

METHODS:

We performed a retrospective study of consecutive patients with ARVC undergoing TLE of ICD leads at three high-volume centers. Patient and lead characteristics, indications, outcomes, and extraction sheath (ES) use were analyzed.

RESULTS:

Between 1999 and 2012, more than 2,000 lead extractions were performed at the three centers. Of these, 11 patients underwent 14 extractions meeting inclusion criteria. Mean implant duration was 74.5 months (range 6-140). In 11 patients, a total of 22 leads (16 high-voltage and six pace-sense leads) were extracted in 14 procedures. The cohort was 50% male with a mean age of 45 years (range, 25-56) and mean ejection fraction 55 ± 13%. The majority (64%) of leads were extracted due to lead malfunction, three patients had an ICD lead removed for exit block, and three patients underwent TLE for infectious complications (two local, one systemic). ES assistance with laser or mechanical cutting sheaths was employed in the vast majority of cases (85.7%). All leads were removed completely. There were no major procedural complications. In five cases, lead reimplantation encountered low-amplitude R waves requiring multiple attempted lead positions before final successful implant.

CONCLUSIONS:

This is the first reported series of TLE in ARVC patients. TLE can be performed safely and effectively in patients with ARVC by experienced operators at high-volume centers with a low complication rate.

PMID: 23786517 // Brigham and Women's Hospital, Boston, Massachusetts.
Mutation Positive ARVD-C: The Triangle of Dysplasia Displaced


Mutation Positive Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy: The Triangle of Dysplasia Displaced
Journal of Cardiovascular Electrophysiology 2013 ; DOI: 10.1111/jce.12222

Introduction

The traditional description of the Triangle of Dysplasia in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C) predates genetic testing and excludes biventricular phenotypes.

Methods and Results

We analyzed Cardiac Magnetic Resonance (CMR) studies of 74 mutation-positive ARVD/C patients for regional abnormalities on a 5-segment RV and 17-segment LV model. The location of electroanatomic endo- and epicardial scar and site of successful VT ablation was recorded in 11 ARVD/C subjects. Among 54/74 (73%) subjects with abnormal CMR, the RV was abnormal in almost all (96%), and 52% had biventricular involvement. Isolated LV abnormalities were uncommon (4%). Dyskinetic basal inferior wall (94%) was the most prevalent RV abnormality, followed by basal anterior wall (87%) dyskinesis. Subepicardial fat infiltration in the posterolateral LV (80%) was the most frequent LV abnormality. Similar to CMR data, voltage maps revealed scar (<0.5 mV) in the RV basal inferior wall (100%), followed by the RV basal anterior wall (64%) and LV posterolateral wall (45%). All 16 RV VTs originated from the basal inferior wall (50%) or basal anterior wall (50%). Of 3 LV VTs, 2 localized to the posterolateral wall. In both modalities, RV apical involvement never occurred in isolation.

Conclusion

Mutation-positive ARVD/C exhibits a previously unrecognized characteristic pattern of disease involving the basal inferior and anterior RV, and the posterolateral LV. The RV apex is only involved in advanced ARVD/C, typically as a part of global RV involvement. These results displace the RV apex from the Triangle of Dysplasia, and provide insights into the pathophysiology of ARVD/C.

The authors wish to acknowledge funding from the Dutch Heart Foundation (to ASJMtR), the Alexandre Suerman Stipend (to ASJMtR), the Interuniversity Cardiology Institute of the Netherlands (to JAG), the National Heart, Lung, and Blood Institute (K23HL093350 to HT), the St. Jude Medical Foundation, and Medtronic Inc. The Johns Hopkins ARVD/C Program (ARVD.com) is supported by the Bogle Foundation, the Healing Hearts Foundation, the Campanella family, and Wilmerding Endowments, and the Dr. Francis P. Chiaramonte Private Foundation. Dr. Calkins received research support from Medtronic and St. Jude Medical. Other authors: No disclosures. This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jce.12222 Keywords: arrhythmogenic right ventricular dysplasia/cardiomypathy; magnetic resonance imaging; electroanatomic mapping; ventricular tachcardia; phenotype; genetics;implantable cardioverter defibrillator
New mineralocorticoid-receptor antagonist passes in phase 2 study.

A next-generation mineralocorticoid-receptor antagonist (MRA) cleared one hurdle this past week when investigators reported data showing that the drug decreased levels of B-type natriuretic peptide (BNP) as much as spironolactone in patients with chronic heart failure and kidney disease and did so without increasing serum potassium concentrations [source: Pitt B, et al.].

Patients treated with the drug, known only as BAY94-8862 (Bayer) at the moment, had a significantly lower incidence of hyperkalemia than patients treated with spironolactone, as well as a lower incidence of worsening renal failure. Presenting the results of the study at Heart Failure Congress 2013 of the European Society of Cardiology Heart Failure Association, Dr Faiez Zannad (Université de Lorraine, Nancy, France) said the safety and efficacy profile of the drug suggests "it has the potential to overcome the limitations of available first- and second-generation steroidal MRAs."

Dr Andrew Stewart Coates (Monash University, Melbourne, Australia) said the study is welcomed among heart-failure physicians for many reasons. An additional agent, on top of the two that are already available, would provide physicians with flexibility, especially since there are growing numbers of patients with heart failure and impaired renal function, patients who are typically excluded from clinical trials. However, he cautioned that the study was not a double-blind randomized trial.

"A negative feature that we have to recognize is having an open-label comparator," said Coates, the discussant during the late-breaking clinical-trials session. "We don't know whether physician or patient behavior, such as advice or diet, might be different among the patients known to be taking spironolactone."

Early results are positive

The phase 2 study consisted of two parts: Part A was a safety and tolerability study of BAY94-8862 (2.5, 5, or 10 mg once daily) in 65 heart-failure patients with reduced left ventricular ejection fractions (HF-REF) and mild chronic kidney disease (CKD). In part B, investigators compared BAY94-8862 (2.5, 5, or 10 mg once daily or 5 mg twice daily) and open-label spironolactone in 392 HF-REF patients with moderate CKD.

In the larger study, which was initiated after they received the go-ahead from an independent data safety and monitoring committee that analyzed part A, the MRA-treated patients had significantly lower rates of renal failure, renal impairment, and hyperkalemia.

Regarding the primary end point in part B, which was the change in serum potassium levels up to one month, patients treated with BAY94-8862 at all doses had significantly smaller increases compared with spironolactone (average dose 36.9 mg/day). The once-daily 2.5-mg and 5-mg doses of BAY94-8862 had no significant change in serum potassium levels compared with placebo, while there were increases in potassium concentrations with the 10-mg once-daily and 5-mg twice-daily doses (compared with placebo).

Changes in serum potassium up to day 7
<table>
<thead>
<tr>
<th>End point</th>
<th>Placebo (%)</th>
<th>BAY94-8862 2.5 mg once daily (%)</th>
<th>BAY94-8862 5 mg once daily (%)</th>
<th>BAY94-8862 10 mg once daily (%)</th>
<th>BAY94-8862 5 mg twice daily (%)</th>
<th>Spironolactone (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in serum potassium</td>
<td>0.08</td>
<td>0.04</td>
<td>0.16</td>
<td>0.21</td>
<td>0.3</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Treatment-emergent adverse events (pooled data from part B of all BAY94-8862-treated patients)

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>BAY94-8862 (%)</th>
<th>Spironolactone (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal failure</td>
<td>1.5</td>
<td>7.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>3.8</td>
<td>28.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>5.3</td>
<td>12.7</td>
<td>0.05</td>
</tr>
</tbody>
</table>

BNP and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) decreases in part B in patients receiving the BAY94-8862 were comparable to those observed in the spironolactone-treated patients, and there was a trend toward larger reductions in those who received higher doses of the MRA. At day 15, the median concentrations of BNP and NT-proBNP decreased from baseline in all patients who received the new MRA. At one month, the median BNP and NT-proBNP decreased from baseline in patients receiving the higher doses of BAY94-8862, but BNP increased slightly among those receiving the 2.5-mg and 5-mg once-daily doses, and NT-proBNP increased slightly with the 2.5-mg dose.

In the present study, as noted by Zannad during the session, Coates said the doses tested were not as effective at blocking aldosterone as spironolactone.

"If we believe that BNP and N-terminal proBNP changes are telling us what the beneficial effects of the MRA are, this is a major advance because we can separate the side-effect profile from the beneficial-effect profile," said Coates. "If, however, we're not certain that a hemodynamic biomarker, BNP and N-terminal proBNP, over a short period are telling us of a beneficial effect, and rather we believe that it's blocking the effect of aldosterone, then the extent of the mineralocorticoid-receptor antagonism is important."


Zannad reports consulting for Bayer, Biotronik, Boston Scientific, Gambro, Janssen, Novartis, Pfizer, Resmed, Servier, and Takeda, receiving payment for lectures from Pfizer and AstraZeneca, and travel support from Bayer. Coates has no conflicts of interest.
Novel HF Drug Works with Normal EF, Too

**Points**

- Note that these studies were published as abstracts and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.
- Serelaxin works as well in patients with heart failure and preserved ejection fraction (EF) as it does in those with impaired EF.
- Point out that in another study of patients with acute heart failure, serelaxin was associated with a decrease in the pulmonary capillary wedge pressure, a lower pulmonary arterial pressure, and improved systemic and pulmonary vascular resistance.

Serelaxin works as well in patients with heart failure and preserved ejection fraction (EF) as it does in those with impaired EF, a subanalysis of the RELAX-AHF trial showed.

On the co-primary endpoint of dyspnea relief through day 5 -- which was significantly improved with serelaxin in the entire trial population -- there was no difference in the effect between those with an EF of 50% or higher and those with an EF below 50% ($P=0.88$), according to Gerasimos Filippatos, MD, of the University of Athens in Greece.

However, on the other coprimary endpoint of the percentage of patients reporting moderately or markedly improved dyspnea through 24 hours -- which was not affected by serelaxin in the overall patient population -- there was a significant interaction ($P=0.03$) in which patients with preserved EF derived a benefit from the treatment and those with impaired EF did not, Filippatos reported at the Heart Failure Congress here.

Serelaxin did not reduce rehospitalizations, but did reduce cardiovascular and all-cause mortality -- similar to the overall trial -- without significant differences in the effects between the groups defined by EF.

In a commentary delivered after Filippatos' presentation, Mihai Gheorghiade, MD, of Northwestern University Feinberg School of Medicine in Chicago, underscored the importance of trying to find therapies that work for patients with heart failure with preserved EF, who make up about 50% of all heart failure patients (a number that is growing) and who have no proven treatments.

The subanalysis had some limitations, he said, including the relatively low number of patients with preserved EF (26% of the patients), the lack of EF measurements in the hospital, the lack of an effect on rehospitalizations, and the relatively low mortality compared with other trials.

But it also had its strengths, including the early enrollment of patients in the trial, the older age of those with preserved EF (mean age 75), the high percentage of women, and the relatively high average EF in the preserved group (average of about 60%).

Gheorghiade said the importance of the substudy was that it proved the hypothesis that "short-time intervention in patients admitted with heart failure can affect post-discharge event rates in a population that represents 50% of all admissions and for which there are no available therapies -- evidence-based therapies -- to treat this condition."

The findings need to be validated further, he said, in another large randomized trial in which ejection fraction is measured in the hospital, patients are randomized early after admission,
and researchers evaluate early signs and symptoms, myocardial injury, effects on blood pressure, and the effects on rehospitalizations.

RELAX-AHF randomized 1,161 patients hospitalized with acute heart failure with normal-to-high systolic blood pressure and mild-to-moderate renal impairment to receive either serelaxin -- a recombinant form of human relaxin-2 -- or placebo on top of standard therapies.

Filippatos and his colleagues decided to look specifically at effects in the subset of patients with preserved EF because of the lack of evidence-based therapies in that group.

Compared with the patients with impaired EF, the patients with preserved ejection fraction had similar clinical signs of congestion, but -- on average -- they were older, had a higher percentage of females, had higher systolic and lower diastolic blood pressure, took longer to be randomized after presentation, and had fewer hospitalizations in the previous year.

Also, they were less likely to be taking a beta-blocker or aldosterone antagonist at baseline, and were more likely to have hypertension and atrial fibrillation. Despite those differences, the effects of serelaxin were largely similar in the two ejection fraction groups, not only on the clinical endpoints but also on levels of various biomarkers.

The results of a second randomized trial reported by Piotr Ponikowski, MD, PhD, of the Medical University and Clinical Military Hospital in Wroclaw, Poland, showed changes in various hemodynamic variables that might help explain some of the findings in RELAX-AHF.

The trial included 71 patients with acute heart failure who received serelaxin at the same dose as in RELAX-AHF or placebo. This trial also had co-primary endpoints -- peak change from baseline in pulmonary capillary wedge pressure and change in cardiac index during the first 8 hours of the infusion.

The peak change in the pulmonary capillary wedge pressure during the first 8 hours of the infusion was greater in the serelaxin group (6.69 versus 4.25 mm Hg; difference 2.44 mm Hg, 95% CI 0.78-4.10), but cardiac index increased slightly with no difference between the groups. Serelaxin treatment had other benefits, however, including a lower pulmonary arterial pressure and improved systemic and pulmonary vascular resistance and brachial systolic and diastolic pressure.

In addition, serelaxin increased creatinine clearance and reduced N-terminal pro-brain natriuretic peptide levels.

Rates of serious adverse events during the study were 8.8% in the serelaxin group and 21.6% in the placebo group. There were two deaths in each group.

"We believe that the hemodynamic effects are consistent with the changes in signs and symptoms of congestion observed with serelaxin in previous clinical studies and perhaps may explain the beneficial effects we have been observing in the [RELAX-AHF] trial," Ponikowski said.

reference:

RELAX-AHF was funded by Corthera Inc., an affiliate of Novartis. Filippatos has received fees from Vifor Pharma in connection to the FAIR-HF trial. Ponikowski has received honoraria related to activities as chairman of the current trial, which was sponsored by Novartis. He has received speaker’s fees from and has served as a consultant to the company.
Noninvasive Assessment of LV Contraction Patterns Using CMR to Identify Responders to CRT.

Noninvasive Assessment of LV Contraction Patterns Using CMR to Identify Responders to CRT.

OBJECTIVES:
Type II activation describes the U-shaped electrical activation of the left ventricle (LV) with a line of block in patients with left bundle branch block (LBBB). We sought to determine if a corresponding pattern of contraction could be identified using cardiac magnetic resonance (CMR) cine imaging and whether this predicted response to cardiac resynchronization therapy (CRT).

BACKGROUND:
U-shaped LV electrical activation in LBBB has been shown to predict favorable response to CRT. It is not known if the degree of electromechanical coupling is such that the same is true for LV contraction patterns.

METHODS:
A total of 52 patients (48% ischemic) scheduled for CRT implantation prospectively underwent pre-implantation CMR cine analysis using endocardial contour tracking software to generate time-volume curves and contraction propagation maps. These were analyzed to assess the contraction sequence of the LV. The effect of contraction pattern on CRT response in terms of reverse remodeling (RR) and clinical parameters (New York Heart Association functional class, 6-min walk distance and Heart Failure Questionnaire score) was assessed at 6 months.

RESULTS:
Two types of contraction pattern were identified; homogenous spread from septum to lateral wall (type I, n = 27) and presence of block with a subsequent U-shaped contraction pattern (type II, n = 25). Rates of RR in those with a type 2 pattern were significantly greater at 6 months (80% vs. 26%, p < 0.001) as was mean increase in 6-min walk distance (126 ± 106 m vs. 55 ± 60 m; p = 0.004).

CONCLUSIONS:
Cine CMR can identify a U-shaped pattern of contraction which predicts increased echocardiographic and clinical response rates to CRT in patients with LBBB.

PMID: 23735442 Division of Imaging Sciences and Biomedical Engineering, King's College, London, United Kingdom; Cardiovascular Directorate, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom.
Minder röntgenstraling

De hoeveelheid röntgenstraling tijdens live beeldgeleide hartinterventies kan met de helft worden verminderd. Dat blijkt uit onderzoek dat is gepresenteerd tijdens het jaarcongres van de European Association for Percutaneous Cardiovascular Interventions in Parijs. De studie is opgezet door een Duits hartcentrum en eind 2012 uitgevoerd door UMC St Radboud in Nijmegen. In deze studie werden twee reeksen röntgenopnames (angiogrammen) bij dezelfde patiënt vergeleken. Het ging om een populatie van 39 patiënten. De eerste reeks beelden werd gemaakt met de conventionele röntgentechnologie en de tweede reeks werd gemaakt met de Philips Allura Clarity IQ nieuwe scanner. Zes onafhankelijke interventiecardiologen uit vijf Europese landen beoordeelden de beelden. Uit de resultaten bleek dat de beeldkwaliteit met de nieuwe scanner even goed is, met de helft minder straling. De cardiologen kunnen inmiddels de meeste vormen van angiografische diagnostiek uitvoeren met een stralingsniveau van 1 microsievert. Eerder bleek ook al dat de inzet van de technologie zorgt voor minder straling bij vaatprocedures. Daarnaast wordt gekeken naar mogelijkheden op het gebied van neuroradiologie en electrofysiologie. De resultaten van deze studies worden later dit jaar verwacht.
Revised ACC/AHA HF guidelines address aldosterone, device use, quality of life

The just-released 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for heart failure present a strong evidence-based approach that covers the spectrum from screening for the disease, through treatments, to discussing end-of-life care [source Circulation].

This is the third full rewrite of the previous guidelines that were issued in 2000, and it reflects the advance in medicine and the growing body of evidence that has become available to guide treatment decisions. The guidelines will be published in the August 27, 2013 issue of the Journal of the American College of Cardiology.

Speaking to the press, writing committee cochair Dr Clyde Yancy (Northwestern University, Chicago, IL) highlighted three important changes.

First, the guidelines present a better characterization and understanding of the disease and its natural history. At one end of the care spectrum, the guidelines address screening family members and doing genetic testing in patients with idiopathic cardiomyopathy. At the other end, the guidelines prompt conversations about palliative care.

"It really is important to have this bookend approach to HF, where we think carefully about who gets this disease and why. . . . For those with the disease, [it is important] to have discussions about quality of life, about outcomes, and being courageous enough to have the conversation about palliative care and hospice." The guidelines provide direction for this broad patient management.

Second, the guidelines provide updated treatment strategies. What's new is the earlier use of certain medical therapies such as aldosterone antagonists and the earlier, more precise use of device therapy in heart failure. "We have data now that help us better orchestrate how patients are treated," Yancy said.

The writing committee uses the term "guideline-directed medical therapy" to represent optimal medical therapy (primarily class I). After sifting through more than 900 papers and armed with this strong evidence, the task force was "bold enough to say, here is a one-page algorithm with guideline-recommended [treatment]," such that the practitioner can match the patient's characteristics and come up with a personalized treatment plan that allows the patient to have the best outcome.

Third, "we developed steps that are evidence-based to reduce readmission, to improve the transition of care . . . and we repositioned the performance measures," he said.

Some specific new features are:

- Earlier use of aldosterone antagonists.
- Extending cardiac resynchronization therapy (CRT) device use to patients with mild to moderate heart failure.
- More emphasis on quality of care and adherence to performance measures for heart failure.
- Updated strategies to prevent heart failure.
- Updated guidelines for genetic testing.
A greater focus on quality of life, patient-centric outcomes, and a shared decision-making strategy in heart failure.

"Our big picture approach was to make it clear that heart failure, classically regarded as a futile disease, now carries a more hopeful outlook. Patients can and should do better with this disease than before, and the exhaustive burden of this disease can be lessened. Patients deserve a chance at best medical therapy for all diseases but especially for heart failure. This guideline statement is a big effort to help make that happen," Yancy and writing committee cochair Dr Mariell Jessup (University of Pennsylvania, Philadelphia) said in a statement.

Source: Yancy CW, Jessup M, Bozkurt B. 2013 ACCF/AHA guideline for the management of heart failure. JACC 2013; DOI: 10.1016/j.jacc.2013.05.019. or Circulation 2013; DOI:10.1161/CIR.0b013e31829e8776.
Remote monitoring and worldwide adoption: Is it already changing clinical practice

Thomas Vogtmann reviews expert consensus and guidelines on the adoption of remote monitoring, and discusses how clinical practice might change for the better as a result of its increased usage. He gave this talk at the XV International Symposium on Progress in Clinical Pacing in Rome, Italy.

As the number of patients with cardiovascular implantable electronic devices increases rapidly, a clear need has arisen for new technologies that ease patient management and reduce workload and costs. Remote monitoring provides a worthwhile solution to these issues, and the medical technology community has taken note, with four different remote monitoring systems now on the market. Today, they are available in all developed countries on all five continents with rapidly increasing usage.

Indeed, there has been a worldwide proliferation of remote monitoring in a relatively short period of time. A 2010 survey by the European Heart Rhythm Association (EHRA) indicates that by 2015, 57% of centres plan to use remote monitoring in most or all pacemaker patients and 86% of centres plan to use it in most or all ICD patients (Halimi for EHRA, Europace 2010; 12: 1778-80).

Everyone can agree on one thing: remote monitoring is an important and safe tool in reducing in-office follow-ups. The TRUST trial (Varma et al, Circulation 2010, 122, 325–332 and Varma et al, Circ Arrhythm Electrophysiol 2010, 3:428–436) has also proven this for ICDs, and COMPAS (Mabo P et al, Eur Heart J 2012, 33 (9): 1105-1111) for pacemakers. By 2008, the Heart Rhythm Society (HRS) and EHRA had already acknowledged that remote monitoring has the potential to provide timelier information on cardiovascular implantable electronic devices and early detection of relevant technical and clinical events, as studies have clearly demonstrated.

Several new studies added evidence to the time efficiency of Home Monitoring. The MonIC (Model project monitor center) study was recently published on EP Europace (Vogtmann T et al, EP Europace 2012, 15: 219-226). MonIC evaluated the efficiency gains in clinics using Biotronik Home Monitoring and showed that this system is reliable, beneficial and efficient.

Basic screening and communication of relevant arrhythmic and technical events required a total of 1.1 minutes of a physician’s time and 30 minutes of a trained nurse’s time each day per 100 patients monitored by the centre. A study by Ricci et al (Europace 2008; 10: 164-170) also backs-up these findings. Showing that screening and evaluation of Home Monitoring data required 12 minutes of a trained nurse’s time each day per 100 patients and two minutes of a physician’s time.
In spite of the proven clinical benefits of remote monitoring, however, as well as its reduction of costs, many countries have not yet solved the problem of reimbursement, even though remote monitoring has already been acknowledged in their guidelines—the most important step for the further adoption of the technology. In 2012 the Netherlands Society of Cardiology made a significant step by releasing its own specific set of guidelines for remote monitoring. These guidelines include issues of programming and address the open questions regarding reimbursement, demanding cost-effectiveness studies (de Cock for Netherlands Society of Cardiology, *Neth Heart J* 2012; 20: 53-65).

In this new era of cardiovascular implantable electronic devices patient management, the course is set to provide patients with highly reliable and convenient follow-up options while reducing clinical workload and costs to service providers. Next, a strengthened set of clinical guidelines and wider recognition by the local reimbursement systems are needed, bringing the benefits of remote monitoring to a growing number of patients.

*Thomas Vogtmann is a cardiologist and electrophysiologist at the Kardiologische Gemeinschaftspraxis Potsdam, Germany, and is a principal investigator of the MoniC study*
OBJECTIVES:

The aim of this study was to examine rapid-rate nonsustained ventricular tachycardia (RR-NSVT) during routine implantable cardioverter-defibrillator (ICD) evaluation in patients with heart failure and its relationship to outcomes.

BACKGROUND:

The clinical implications of RR-NSVT identified during routine ICD interrogation are unclear. In this study, the occurrence of RR-NSVT and its association with ICD shocks and mortality in SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) were examined.

METHODS:

The 811 patients who received ICDs in SCD-HeFT constituted the study population. The occurrence of RR-NSVT and its association with ICD shocks and mortality in SCD-HeFT were examined.

RESULTS:

RR-NSVT was documented on ICD interrogation in 186 of 811 patients (22.9%). The mean duration of RR-NSVT was 26.4 ± 9.1 beats (7.5 ± 2.6 s), with a mean cycle length of 259 ± 32 ms. Polymorphic RR-NSVT accounted for 56% of episodes. Compared with patients without RR-NSVT, those with RR-NSVT were less likely to be taking beta-blockers, statins, or aspirin at enrollment. After adjusting for other known predictors of mortality in SCD-HeFT, RR-NSVT was independently associated with appropriate ICD shocks (hazard ratio: 4.25; 95% confidence interval: 2.94 to 6.14; p < 0.0001), with all-cause mortality (hazard ratio: 2.40; 95% confidence interval: 1.62 to 3.54; p < 0.0001), and with a composite of all-cause mortality and appropriate ICD shocks (hazard ratio: 3.03; 95% confidence interval: 2.21 to 4.15; p < 0.0001).

CONCLUSIONS:

RR-NSVT identified on routine ICD interrogation should be considered an important clinical event. RR-NSVT during ICD interrogation is associated with appropriate ICD shocks and all-cause mortality. The clinical evaluation of patients with RR-NSVT should include
intensification of medical therapy, particularly beta-blockers, or other appropriate clinical interventions. (Sudden Cardiac Death in Heart Failure Trial [SCD-HeFT]; NCT00000609).


**Predictors and Risk of Pacemaker Implantation After the Cox-Maze IV Procedure.**

Robertson JO, Cuculich PS, Saint LL, Schuessler RB, Moon MR, Lawton J, Damiano RJ, Maniar HS.
Predictors and Risk of Pacemaker Implantation After the Cox-Maze IV Procedure.

**BACKGROUND:**

The incidence of and causes for permanent pacemaker implantation (PPM) after surgical arrhythmia procedures remain poorly understood because of the varied lesion patterns and energy sources reported in small series. This study characterized the incidence, indications, and risk factors for PPM after the Cox-maze IV (CMIV) procedure when performed as either a lone or a concomitant procedure.

**METHODS:**

A retrospective analysis of 340 patients undergoing a CMIV as either a lone (n = 112) or a concomitant (n = 228) procedure was conducted. The incidence, indication, and variables associated with PPM implantation within 1 year of the operation were assessed. Follow-up was conducted at 30 days and 1 year and was 90% complete.

**RESULTS:**

The incidence of PPM after a lone CMIV procedure was 5%. Patients with concomitant cardiac operations had a nonsignificant increase in PPM insertion at 30 days (11% vs 5%, p = 0.14) and 1 year (15% vs 6%, p = 0.06) when compared with lone CMIV patients. Of patients who required pacemakers, sinus node dysfunction was present in 79% (35/44) of patients in the entire series and in 88% (8/9) after lone CMIV. After PPM, 84% (37/44) of patients remained paced at last follow-up. Multivariate analysis identified age (odds ratio = 1.10 [1.06-1.14], p < 0.001) as the only variable associated with higher risk of a PPM after any CMIV procedure.

**CONCLUSIONS:**

The risk of PPM implantation after a lone CMIV is 5% and increases with age. The need for a PPM after a CMIV is largely due to SA node dysfunction, which appears unlikely to recover. These data should help physicians counsel patients regarding the perioperative risks associated with the CMIV.

PMID:23642681 // Division of Cardiothoracic Surgery, Barnes-Jewish Hospital/Washington University, St. Louis, Missouri.
Percutaneous LA Appendage Closure with the Amplatzer Cardiac Plug Device in Patients with Non-Valvular Atrial Fibrillation and Contraindications for Anticoagulation Therapy.


Percutaneous Left Atrial Appendage Closure with the Amplatzer Cardiac Plug Device in Patients with Non-Valvular Atrial Fibrillation and Contraindications for Anticoagulation Therapy.


OBJECTIVES:

To evaluate the results associated with left atrial appendage closure (LAAC) with the Amplatzer Cardiac Plug (ACP) in patients with non-valvular atrial fibrillation (NVAF) and absolute contraindication for anticoagulation therapy.

BACKGROUND:

Little data exist on the late outcomes following LAAC in patients with absolute contraindication for warfarin.

METHODS:

A total of 52 patients underwent LAAC using the ACP device in 7 Canadian centers. Most patients received short-term (1-3 months) dual antiplatelet therapy following the procedure and single antiplatelet therapy thereafter. A transesophageal echocardiography (TEE) was performed in 74% of patients at 6-month follow-up. No patient was lost to follow-up (≥12 months in all patients).

RESULTS:

Mean age and median CHADS2 score were 74± 8 years and 3 [2-4], respectively. The procedure was successful in 98.1% of the patients and the main complications were device embolization (1.9%) and pericardial effusion (1.9%), with no cases of periprocedural stroke. At a mean follow-up of 20 ± 5 months, the rates of death, stroke, systemic embolism, pericardial effusion, and major bleeding were 5.8%, 1.9%, 0%, 1.9%, and 1.9%, respectively.

The presence of mild peridevice leak was observed in 16.2% of patients at 6-month follow-up as evaluated by TEE. There were no cases of device thrombosis.

CONCLUSION:

In patients with NVAF at high risk for cardioembolic events and absolute contraindication for anticoagulation, LAAC using the ACP device followed by dual/single antiplatelet therapy was associated with a low rate of embolic and bleeding events after a mean follow-up of 20 months. No cases of severe residual leak or device thrombosis were observed at 6-month follow-up.

PMID:23665098 // Quebec Heart & Lung Institute, Quebec City, Quebec, Canada.
Pacemaker or Defibrillator Surgery without Interruption of Anticoagulation

David H. Birnie, J S Healey, GA Wells, A Verma, AS Tang, AD Krahn, CS Simpson, F Ayala-Paredes, B Coutu, TLL Leiria, V Essebag, for the BRUISE CONTROL Investigators


BACKGROUND

Many patients requiring pacemaker or implantable cardioverter–defibrillator (ICD) surgery are taking warfarin. For patients at high risk for thromboembolic events, guidelines recommend bridging therapy with heparin; however, case series suggest that it may be safe to perform surgery without interrupting warfarin treatment. There have been few results from clinical trials to support the safety and efficacy of this approach.

METHODS

We randomly assigned patients with an annual risk of thromboembolic events of 5% or more to continued warfarin treatment or to bridging therapy with heparin. The primary outcome was clinically significant device-pocket hematoma, which was defined as device-pocket hematoma that necessitated prolonged hospitalization, interruption of anticoagulation therapy, or further surgery (e.g., hematoma evacuation).

RESULTS

The data and safety monitoring board recommended termination of the trial after the second prespecified interim analysis. Clinically significant device-pocket hematoma occurred in 12 of 343 patients (3.5%) in the continued-warfarin group, as compared with 54 of 338 (16.0%) in the heparin-bridging group (relative risk, 0.19; 95% confidence interval, 0.10 to 0.36; P<0.001). Major surgical and thromboembolic complications were rare and did not differ significantly between the study groups. They included one episode of cardiac tamponade and one myocardial infarction in the heparin-bridging group and one stroke and one transient ischemic attack in the continued-warfarin group.

CONCLUSIONS

As compared with bridging therapy with heparin, a strategy of continued warfarin treatment at the time of pacemaker or ICD surgery markedly reduced the incidence of clinically significant device-pocket hematoma.

Source Information

From the University of Ottawa Heart Institute, Ottawa (D.H.B., G.A.W., A.S.T.); Population Health Research Institute, Hamilton, ON (J.S.H.); Southlake Regional Health Centre, Newmarket, ON (A.V.); Island Medical Program, University of British Columbia, Vancouver (A.S.T.); University of British Columbia, Vancouver (A.D.K.); Queen's University and Kingston General Hospital, Kingston, ON (C.S.S.); Université de Sherbrooke, Sherbrooke, QC (F.A.-P.); Hôpital Hotel-Dieu Centre Hospitalier de l'Université de Montréal, Montreal (B.C.); and McGill University Health Centre and Hôpital du Sacré-Coeur de Montréal, Montreal (V.E.) — all in Canada; and Instituto de Cardiologia Fundação Universitaria Cardiologia, Porto Alegre, Brazil (T.L.L.L.). Address reprint requests to Dr. Birnie at the University of Ottawa Heart Institute, 40 Ruskin St., Ottawa, ON K1Y 4W7, Canada, or at dbirnie@ottawaheart.ca. Investigators in the Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial (BRUISE CONTROL) are listed in the Supplementary Appendix, available at NEJM.org.

Management of Antithrombotic Therapy in Patients Undergoing Invasive Procedures

Todd H. Baron, M.D., Patrick S. Kamath, M.D., and Robert D. McBane, M.D.


When patients receiving anticoagulation therapy undergo invasive procedures, management requires an individualized assessment of the risk of bleeding versus the risk of thrombosis. This review explains management, including bridging anticoagulation for patients receiving warfarin.
Source Information
From the Divisions of Gastroenterology and Hepatology (T.H.B., P.S.K.), Cardiovascular Diseases (R.D.M.), and Hematology (R.D.M.), Mayo Clinic, Rochester, MN.
Disclosure forms provided by the authors are available with the full text of this article at NEJM.org. No potential conflict of interest relevant to this article was reported. Address reprint requests to Dr. Baron at the Division of Gastroenterology and Hepatology, Mayo Clinic, 200 First St. SW, Rochester, MN 55905, or at baron.todd@mayo.edu
Multi-Institutional Study of Implantable Defibrillator Lead Performance in Children and Young Adults
Results of the Pediatric Lead Extractability and Survival Evaluation (PLEASE) Study

Multi-Institutional Study of Implantable Defibrillator Lead Performance in Children and Young Adults - Results of the Pediatric Lead Extractability and Survival Evaluation (PLEASE) Study Circulation. 2013; 127: 2393-2402 Published online before print May 21, 2013 doi: 10.1161/CIRCULATIONAHA.112.001120

Background

Implantable cardioverter-defibrillator (ICD) therapy in children and congenital heart disease patients is hampered by poor long-term lead survival. Lead extraction is technically difficult and carries substantial morbidity. We sought to determine the outcomes of ICD leads in pediatric and congenital heart disease patients.

Methods and Results

The Pediatric Lead Extractability and Survival Evaluation (PLEASE) is a 24-center international registry. Pediatric and congenital heart disease patients with ICD lead implantations from 2005 to 2010 were eligible. Study subjects comprised 878 ICD patients (44% congenital heart disease). Mean±SD age at implantation was 18.6±9.8 years. Of the 965 total leads, 54% were thin (≤7F), of which 57% were Fidelis, and 23% were coated with expanded polytetrafluoroethylene. There were 139 ICD lead failures (14%) in 132 patients (15%) at a mean lead age of 2.0±1.4 years, causing shocks in 53 patients (40%). Independent predictors of lead failure included younger implantation age and Fidelis leads. Actuarial analysis showed an incremental risk of lead failure with younger age at implantation: <8 years compared with >18 years ($P=0.015$). The actuarial yearly failure rate was 2.3% for non-Fidelis and 9.1% for Fidelis leads. Extraction was performed on 143 leads (80% thin, 7% expanded polytetrafluoroethylene coated), with lead age as the only independent predictor for advanced extraction techniques. There were 6 major extraction complications (4%) but no procedural mortality.

Conclusions

This study demonstrates that ICD leads in children and congenital heart disease patients have an age-related suboptimal performance, further compounded by a high failure rate of Fidelis leads. Advanced extraction techniques were common and correlated with older lead age.

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Remote monitoring after recent hospital discharge in patients with heart failure: a systematic review and network meta-analysis.


Remote monitoring after recent hospital discharge in patients with heart failure: a systematic review and network meta-analysis.
Heart 2013 May 16. [Epub ahead of print]

CONTEXT:

Readmission to hospital for heart failure is common after recent discharge. Remote monitoring (RM) strategies have the potential to deliver specialised care and management and may be one way to meet the growing needs of the heart failure population.

OBJECTIVE:

To determine whether RM strategies improve outcomes for adults who have been recently discharged (<28 days) following an unplanned admission due to heart failure.

STUDY DESIGN:

Systematic review and network meta-analysis.

DATA SOURCES:

Fourteen electronic databases (including MEDLINE, EMBASE and PsycINFO) were searched to January 2012, and supplemented by hand-searching relevant articles.

STUDY SELECTION:

All randomised-controlled trials (RCTs) or observational cohort studies with a contemporaneous control group were included. RM interventions included home telemonitoring (TM) (including implanted monitoring devices) with medical support provided during office hours or 24/7 and structured telephone support (STS) programmes delivered via human-to-human contact (HH) or human-to-machine interface (HM).

DATA EXTRACTION:

Data were extracted and validity was assessed independently by two reviewers.

RESULTS:

Twenty-one RCTs that enrolled 6317 patients were identified (11 studies evaluated STS (10 of which were HH, while 1 was HM), 9 studies assessed TM, and 1 study assessed both STS and TM). No trial of implanted monitoring devices met the inclusion criteria. Compared with usual care, although not reaching statistical significance, RM trended to reduce all-cause mortality for STS HH (HR: 0.77, 95% credible interval (Crl): 0.55, 1.08), TM during office hours (HR: 0.76, 95% Crl: 0.49, 1.18) and TM24/7 (HR: 0.49, 95% Crl: 0.20, 1.18). Exclusion
of one trial that provided better-than-usual support to the control group rendered each of the above comparisons statistically significant. No beneficial effect on mortality was observed with STS HM. Reductions were also observed in all-cause hospitalisations for TM interventions but not for STS interventions. Care packages generally improved health-related quality-of-life and were acceptable to patients.

CONCLUSIONS:

STS HH and TM with medical support provided during office hours showed beneficial trends, particularly in reducing all-cause mortality for recently discharged patients with heart failure. Where 'usual' care is less good, the impact of RM is likely to be greater.

KEYWORDS: EBM, HEART FAILURE PMID:23680885 // ScHARR, University of Sheffield, , Sheffield, UK.
Plasma adiponectin in heart failure with and without cachexia: Catabolic signal linking catabolism, symptomatic status,


Plasma adiponectin in heart failure with and without cachexia: Catabolic signal linking catabolism, symptomatic status,
Metabolism & Cardiovascular Diseases 2013 ; Article in Press

Background and aims

Adiponectin (ADPN) as an adipose tissue hormone contributes to regulation of energy metabolism and body composition and is associated with cardiovascular risk profile parameters. Cardiac cachexia may develop as a result of severe catabolic derangement in chronic heart failure (CHF). We aimed to determine an abnormal ADPN regulation as a link between catabolic signalling, symptomatic deterioration and poor prognosis.

Methods and results

We measured plasma ADPN in 111 CHF patients (age 65 ± 11, 90% male, left ventricular ejection fraction (LVEF) 36 ± 11%, peak oxygen consumption (peakVO₂) 18.1 ± 5.7 l/kg*min, body mass index (BMI) 27 ± 4 kg/m², all mean ± standard deviation) and 36 healthy controls of similar age and BMI. Body composition was assessed by dual energy X-ray absorptiometry, insulin sensitivity was evaluated by homoeostasis model assessment, exercise capacity by spiroergometry. Plasma ADPN did not differ between CHF vs. controls (13.5 ± 11.0 vs. 10.5 ± 5.3 mg/l, p > 0.4), but increased stepwise with NYHA functional class (I/II/III: 5.7 ± 1.4/10.7 ± 8.3/19.2 ± 14.0 mg/l, ANOVA p < 0.01). Furthermore, ADPN correlated with VO₂ at anaerobic threshold (r = −0.34, p < 0.05). ADPN was highest in cachectic patients (cCHF, 16%) vs. non-cachectic (ncCHF) (18.7 ± 15.0 vs. 12.5 ± 9.9 mg/l; p < 0.05). ADPN indicated mortality risk independently of established prognosticators (HR: 1.04 95% CI: 1.02–1.07; p < 0.0001). ADPN above the mean (13.5 mg/l) was associated with a 3.4 times higher mortality risk in CHF vs. patients with ADPN levels below the mean.

Conclusion

Circulating ADPN is abnormally regulated in CHF. ADPN may be involved in impaired metabolic signalling linking disease progression, tissue wasting, and poor outcome in CHF.

Keywords: Chronic heart failure, Cachexia, Metabolism, Adiponectin // Abbreviations: ADPN, adiponectin, AT, anaerobic threshold, BMI, body mass index, cCHF, cachectic chronic heart failure, CHF, chronic heart failure, DEXA, dual energy X-ray absorptiometry, HOMA, homoeostasis model assessment, LVEF, left ventricular ejection fraction, ncCHF, non-cachectic chronic heart failure, NYHA, New York Heart Association, proANP, pro-atrial natriuretic peptide, peakVO₂, peak oxygen uptake, RER, respiratory exchange ratio, VE, ventilation volume per minute, VCO₂, exhaled carbon dioxide, VO₂, oxygen intake, VO₂ at AT, oxygen intake at anaerobic threshold // Received 21 December 2012; received in revised form 5 March 2013; accepted 17 April 2013. published online 19 June 2013.
Risk stratification for ICD therapy: the role of the wearable cardioverter-defibrillator.


The benefit of implantable cardioverter-defibrillator (ICD) therapy depends upon appropriate evaluation of a persisting risk of sudden death and estimation of the patient's overall survival. Assessment of a stable and unchangeable arrhythmogenic substrate is often difficult. Structural abnormality and ventricular dysfunction, the two major risk parameters, may recover, and heart failure symptoms can improve so that ICD therapy may not be indicated. Risk stratification can take time while the patient continues to be at high risk of arrhythmic death, and patients may need temporary bridging by a defibrillator in cases of interrupted ICD therapy. The wearable cardioverter-defibrillator (WCD) combines a long-term electrocardiogram (ECG)-monitoring system with an external automatic defibrillator. The LifeVest® (ZOLL, Pittsburgh, PA, USA) is composed of a garment, containing two defibrillation patch electrodes on the back, and an elastic belt with a front-defibrillation patch electrode and four non-adhesive ECG electrodes, connected to a monitoring and defibrillation unit. The WCD is a safe and effective tool to terminate ventricular tachycardia/ventricular fibrillation events, unless a conscious patient withholds shock delivery. It may be used in patients in the early phase after acute myocardial infarction with poor left ventricular function, after acute coronary revascularization procedures (percutaneous coronary intervention or coronary artery bypass grafting) and reduced left ventricular ejection fraction (≤35%), in patients with acute heart failure in non-ischaemic cardiomyopathy of uncertain aetiology and prognosis. The WCD may be helpful in subjects with syncope of assumed tachyarrhythmia origin or in patients with inherited arrhythmia syndromes. The WCD may replace ICD implantation in patients waiting for heart transplantation or who need a ventricular-assist device.

This review describes the technical details and characteristics of the WCD, discusses its various potential applications, and reports the currently available experience with the wearable defibrillator.

Keywords: ICD therapy, Risk stratification, Sudden cardiac death, Wearable cardioverter-defibrillator PMID: 23729691
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Usefulness of Step Counts to Predict Mortality in Japanese Patients With Heart Failure.


Usefulness of Step Counts to Predict Mortality in Japanese Patients With Heart Failure.


The purpose of this study was to determine both an association between mortality and physical activity (PA) objectively measured by accelerometer and cutoff values for PA in Japanese outpatients with heart failure (HF). This prospective observational study comprised 170 HF outpatients (mean age, 65.2 years; 77% men). Peak oxygen uptake (VO$_2$) and the relation between ventilation and carbon dioxide production (VE/VCO$_2$ slope) as indices of exercise capacity were measured during cardiopulmonary exercise testing with a cycle ergometer. PA was assessed by accelerometer-measured average step count (steps) per day for 1 week. Study endpoint was cardiovascular-related death. Over an average follow-up of 1,377.1 (median, 1,335) days, 31 cardiovascular-related deaths occurred. Patients were then divided into survivor (n = 139) and nonsurvivor (n = 31) groups. Brain natriuretic peptide level was significantly different between groups. Peak VO$_2$ and steps were also significantly lower and VE/VCO$_2$ slope higher in the nonsurvivors versus survivors. Univariate Cox proportional hazards analysis showed brain natriuretic peptide, peak VO$_2$, VE/VCO$_2$ slope, and steps to be significant prognostic indicators of survival. Multivariate analysis showed PA of ≤4,889.4 steps/day to be a strong and independent predictor of prognosis (hazard ratio: 2.28, 95% confidence interval: 1.31-6.30; p = 0.008). Kaplan-Meier curves after log-rank test showed significant prognostic difference between PA of ≤4,889.4 and >4,889.4 steps/day in the 2 groups (log-rank: 12.19; p = 0.0005).

In conclusion,

step count as objectively measured by accelerometer may be a prognostic indicator of mortality in Japanese outpatients with HF.

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Variation among hospitals in selection of higher-cost, "higher-tech," ICDs: NCDR ICD Registry.


BACKGROUND:

New implantable cardioverter/defibrillator (ICD) models are regularly introduced, incorporating technological advantages. The purpose of this study was to determine factors associated with use of a newer, higher-tech/higher-cost device, as opposed to a previously released device, among patients undergoing ICD implantation.

METHODS:

We analyzed the 78,494 cases receiving new ICD implants submitted by 978 hospitals to the NCDR ICD Registry between January 2005 and June 2007. Devices were categorized as "previously released" 3 months after a new model from the same manufacturer was released. A nonparsimonious model including all demographic, clinical, provider, and hospital characteristics was created using logistic regression to predict use of a previously released device.

RESULTS:

Overall, 36% of implants involved previously released devices. However, no demographic (race, gender, payor status), clinical, or provider characteristics had a meaningful impact on use of previously released devices. The model C-statistic was 0.602, suggesting that measured characteristics had a limited ability to differentiate those receiving a previously released device. However, individual hospitals varied greatly in use of "previously released" devices, from 3% in the lowest decile to 91% in the top decile. Among physicians implanting at >1 hospital, there was minimal correlation between use of previously released devices between hospitals, suggesting hospital policies or culture, rather than physician preference, drives the large interhospital variation seen.

CONCLUSIONS:

The use of "previously released" devices is influenced minimally by measured patient or provider characteristics. Rather, the main determinant of whether patients receive the newest, versus a previously released device, appears to be practice patterns at individual hospitals.

PMID: 23708175 //
The Impact of Drug Discontinuation in Patients Treated with Temporary Pacemaker due to Atrioventricular Block

Maria Bisgaard Knudsen, Anna Margrethe Thøgersen, Søren Pihlkjær Hjortshøj, Sam Riahi.

Introduction

Patients treated with a temporary pacemaker (TPM) due to atrioventricular (AV) block are often monitored after discontinuation of AV node blocking drugs to evaluate the indication for permanent pacing. However, the impact of drug discontinuation is sparsely documented. We investigated to what extent drug discontinuation abolished the need for permanent pacemaker (PPM) implantation.

Methods and results

All hospital records of patients who received a TPM at Aalborg Hospital, Denmark, between January 2000 and March 2011 (n = 575) were retrospectively reviewed. Patients with AV block who were treated with a TPM and concomitant cessation of drug therapy were included if there was no other underlying mechanism causing the AV block. AV blocking drugs included antiarrhythmic agents class II, III, and IV and digoxin. Fifty-five patients fulfilled our inclusion criteria.

Forty-seven patients had an indication for a PPM at the initial hospital admission, despite drug discontinuation. Of the remaining 8 patients who were discharged without a PPM, 3 subsequently experienced events: 2 had recurrence of AV block requiring a PPM, and 1 experienced syncope. Thus, in total, 49 (89%) patients had a final indication for a permanent pacemaker (PPM).

Of patients receiving beta-blocker monotherapy, 26 (96%) had an indication for a PPM. TPM implantation was complicated by infection or displacement in 11% of cases.

Conclusions

The vast majority of patients treated with a TPM due to AV block and who receive beta-blockers alone or in combination with digoxin have a final indication for a PPM despite cessation of drug treatment. TPM are frequently associated with complications.


BACKGROUND:
Implantable Cardioverter Defibrillators (ICDs) have been demonstrated to reduce mortality in survivors of life-threatening arrhythmias (secondary prevention) and in patients at increased risk of sudden cardiac death (primary prevention). Other nations have reported significant increases in ICD use in recent years. We examined Australian nationwide trends of ICD procedures over a 10-year period (2000-2009).

METHODS:
A retrospective analysis of the Australian Institute of Health and Welfare’s National Hospital Morbidity Database was performed to determine the annual number of ICD implantation and replacement procedures between 2000-2009. Rates were calculated using Australian Bureau of Statistics data on the annual estimated population. Time trends in the yearly procedure number and rate were analysed using negative binomial regression models with comparisons made by age and sex.

RESULTS:
The number of new ICD implantations increased from 708 to 3198 procedures between 2000-2009. Replacement procedures increased from 290 to 1378. The implantation rate (per million) increased from 37.0 to 145.6 and the replacement rate from 15.1 to 62.7. When rates were adjusted for age and sex, the implantation rate increased annually by 15.8% and the replacement rate by 16.6% (p<0.0001). Procedures occurred most commonly in men (implantations: 80.1%; replacements: 78.0%) between ages 70-79.

CONCLUSIONS:
ICD procedures increased significantly in Australia between 2000-2009. Despite these increases, other studies have suggested ICD devices are currently under-utilised. During the study period, males accounted for the majority of ICD procedures. While there are numerous reasons for this, it is not known if device under-use is more common in females.

PMID:23734916 // Centre for Heart Rhythm Disorders (CHRD), University of Adelaide and the Royal Adelaide Hospital, Adelaide, Australia
The Prognostic Significance of Narrow Fragmented QRS on Admission Electrocardiogram in Patients Hospitalized for Decompensated Systolic Heart Failure

Sevgi Ozcan, Huseyin Altug Cakmak, Baris Ikitimur, Ece Yurtseven, Berna Stavileci, Ebru Yucel Tufekcioglu, Rasim Enar.

The Prognostic Significance of Narrow Fragmented QRS on Admission Electrocardiogram in Patients Hospitalized for Decompensated Systolic Heart Failure
Clinical Cardiology 2013 : Article first published online: 10 JUN 2013 //
DOI: 10.1002/clc.22158

Background
Narrow fragmented QRS (fQRS) has recently been recognized as a significant predictor of prognosis in various cardiovascular diseases.

Hypothesis
We hypothesized that the presence of narrow fQRS on admission electrocardiogram (ECG) in patients with decompensated systolic heart failure (HF) of any cause would be associated with long-term prognosis.

Methods
Patients hospitalized for decompensated HF due to ischemic or nonischemic dilated cardiomyopathy (left ventricular ejection fraction <35%) were retrospectively analyzed. The primary clinical end points were cardiovascular mortality, sudden cardiac death, and rehospitalization for HF.

Results
The mean duration of follow-up was 3.73 ± 1.41 years. Patients were classified as fQRS(+) group (n = 114; mean age, 63.49 ± 12.04 years) and fQRS(−) group (n = 113 patients; mean age, 65.04 ± 11.95 years). fQRS on ECG was significantly correlated with New York Heart Association (NYHA) functional class (P = 0.001). In multivariate Cox proportional hazard analysis, narrow fQRS (odds ratio [OR]: 3.130, 95% confidence interval [CI]: 1.560-2.848, P = 0.001), chronic renal failure (OR: 2.455, 95% CI: 1.120-5.381, P = 0.025), NYHA class (OR: 8.305, 95% CI: 2.568-26.855, P < 0.0001), and hypoalbuminemia (OR: 2.099, 95% CI: 1.122-3.926, P = 0.020) were independent predictors of cardiovascular mortality. In Kaplan-Meier survival analysis, narrow fQRS on admission ECG predicted worse survival rate at 84 months; survival probability significantly decreased in the fQRS(+) group compared with fQRS(−) group (P < 0.0001).

Conclusions
Presence of narrow fQRS is associated with worse NYHA functional class in patients hospitalized for decompensated HF. Narrow fQRS predicts cardiovascular mortality in a specific subgroup of systolic HF patients, namely those hospitalized for decompensated HF of both ischemic and nonischemic causes.
Time-dependent effect of CRT on ventricular repolarization and ventricular arrhythmias.

Time-dependent effect of cardiac resynchronization therapy on ventricular repolarization and ventricular arrhythmias. Europace 2013 Jun 4. [Epub ahead of print]

AIMS:
Cardiac resynchronization therapy (CRT) improves the clinical status of patients with congestive heart failure, although left ventricular epicardial pacing may increase transmural dispersion of repolarization (TDR). The aim of this study was to investigate the time-dependent effect of CRT on ventricular repolarization and ventricular arrhythmia at mid-term follow-up.

METHODS AND RESULTS:
The study group consisted of 84 patients treated with CRT. Twelve-lead electrocardiogram was digitally recorded and Tpeak-to-Tend interval (Tp-e) was measured at baseline, 1 week, 1 month, and 3, 6, and 12 months after device implantation. We determined the time-dependent changes in Tp-e, ventricular tachycardia and ventricular fibrillation (VT/VF) during 12 months of follow-up, in both CRT responders and non-responders. Seventeen of 84 patients (20%) had VT/VF during first year. Six of those 17 patients (35%) experienced VT/VF within 1 month of implantation and diminished over time. Tp-e decreased significantly at 6 and 12 months after implantation compared with 1 week [108 ± 14 ms at 1 week vs. 97 ± 21 ms at 6 months (P = 0.03) and 95 ± 19 ms at 12 months (P = 0.01)]. Responders demonstrated a greater time-dependent reduction of Tp-e at 6 and 12 months of CRT and had a lower rate of VT/VF compared with non-responders (log-rank test, P = 0.004).

CONCLUSION:
Transmural dispersion of repolarization and the number of patients with VT/VF decreased over time after CRT. Patients with reverse remodelling demonstrated a lower rate of VT/VF and a greater time-dependent reduction of TDR.

Keywords: Cardiac resynchronization therapy, Responder, Tp–e interval, Transmural dispersion of repolarization, Ventricular arrhythmia / PMID: 23736809 // Section of Arrhythmia, Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, 7-5-2, Kusunoki-Cho, Chuo-Ku, Kobe, Hyogo 650-0017, Japan.
The mode of death in ICD and CRT-D pts: results from routine clinical practice.

The mode of death in implantable cardioverter-defibrillator and cardiac resynchronization therapy with defibrillator patients: results from routine clinical practice.

BACKGROUND:

Although data on the mode of death of implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy with defibrillator (CRT-D) patients have been examined in randomized clinical trials, in routine clinical practice data are scarce. To provide reasonable expectations and prognosis for patients and physicians, this study assessed the mode of death in routine clinical practice.

OBJECTIVE:

To assess the mode of death in ICD/CRT-D recipients in routine clinical practice.

METHODS:

All patients who underwent an ICD or CRT-D implantation at the Leiden University Medical Center, the Netherlands, between 1996 and 2010 were included. Patients were divided into primary prevention ICD, secondary prevention ICD, and CRT-D patients. For patients who died during follow-up, the mode of death was retrieved from hospital and general practitioner records and categorized according to a predetermined classification: heart failure death, other cardiac death, sudden death, noncardiac death, and unknown death.

RESULTS:

A total of 2859 patients were included in the analysis. During a median follow-up of 3.4 years (interquartile range 1.7-5.7 years), 107 (14%) primary prevention ICD, 253 (28%) secondary prevention ICD, and 302 (25%) CRT-D recipients died. The 8-year cumulative incidence of all-cause mortality was 39.9% (95% confidence interval 37.0%-42.9%). Heart failure death and noncardiac death were the most common modes of death for all groups. Sudden death accounted for approximately 7%-8% of all deaths.

CONCLUSION:

For all patients, heart failure and noncardiac death are the most common modes of death. The proportion of patients who died suddenly was low and comparable for primary and secondary ICD and CRT-D patients.

PMID: 22522066 // Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands.
Modes of death in defibrillator patients: learning from clinical experience.
The effect of dual-chamber CLS on syncope recurrence in healthy patients with tilt-induced vasovagal cardioinhibitory syncope: a prospective, randomised, single-blind, crossover study.


BACKGROUND:

The closed-loop stimulation (CLS) pacemaker algorithm is a system that permanently monitors the contractile state of the myocardium and converts the intrinsic information into rate regulation. The role that the CLS algorithm plays in the prevention of syncope recurrences still remains unclear. The aim of our prospective, randomised, single-blind, crossover study was to evaluate the effect of dual-chamber CLS in the prevention of syncope recurrence in patients with refractory vasovagal syncope (VVS) and a cardioinhibitory response to head-up tilt test (HUT) during a 36 months follow-up.

METHODS AND RESULTS:

We studied 50 patients (mean age 53±5.1; 33 male) with the indication for permanent dual-chamber cardiac pacing for HUT-induced vasovagal cardioinhibitory syncope. They were randomised after 1 month of stabilisation period to CLS algorithm features programmed OFF or ON for 18 months each, using a crossover design. The number of syncopal and presyncopal episodes during active treatment was lower than those registered during no treatment (n syncopal episodes: 2 vs 15; p=0.007; n presyncopal episodes: 5 vs 30; p = 0.004). Lead parameters remained stable over time, and there were no lead-related complications.

CONCLUSIONS:

Based on these 36 months follow-up data, it is concluded that dual-chamber CLS is an effective algorithm for preventing syncope recurrences in healthy patients with tilt-induced vasovagal cardioinhibitory syncope.

Keywords: Autonomic Nervous System PMID:23723446 Syncope Unit, Second University of Naples, Italy.
**Toddler: TV Snacks Up Risk for Heart Disease**

**Points**
- Certain eating behaviors in small children, including eating in front of the TV, were significantly associated with a surrogate marker for heart disease later in life.
- Note that although the cross-sectional study could not show causality, the results raise the possibility that eating behaviors are more closely related to health outcomes than dietary intake.

Certain eating behaviors in small children, including chowing down in front of the TV, were significantly associated with a surrogate marker for heart disease later in life, researchers found.

In a cross-sectional study of kids, ages 3 to 5, each unit increase in an eating behavior score suggested greater nutritional risk indicated by an increase of 0.02 mmol/L (95% CI, 0.002 to 0.05, \(P=0.03\)) in serum non-high density lipoprotein (non-HDL) cholesterol, according to Navindra Persaud, MD, of St. Michael's Hospital and the University of Toronto, and colleagues reported in *CMAJ*.

The authors pointed out that serum concentration of non-HDL cholesterol, which includes LDL cholesterol, is an "emerging surrogate marker for cardiovascular risk ... the American Academy of Pediatrics recommends non-HDL cholesterol concentration as the key measure for screening for cardiovascular risk in children."

They added that an earlier study that included a subgroup of children, ages 2 to 15, "found an association between LDL cholesterol concentration (which is highly correlated with non-HDL cholesterol) and asymptomatic atherosclerosis at autopsy" (*N Engl J Med* 1998; 338: 1650-1656).

While the authors cautioned that their cross-sectional study could not show causality, "these results raise the possibility that eating behaviors are more closely related to health outcomes than dietary intake. The relations between eating behaviors and LDL cholesterol and apolipoprotein B are not surprising given the correlation of these indices with serum non-HDL cholesterol concentration. In addition, apolipoprotein B is known to be correlated with cardiometabolic risk factors in adolescents."

They assessed 1,076 children from seven primary care practices in Toronto between 2008 and 2011. They administered the NutriSTEP (Nutritional Screening Tool for Every Preschooler) questionnaire, which asked about eating behaviors, dietary intake, parental concerns about food and activity, eating habits while engaged in screen time, and supplement use.

They used nonfasting blood samples from the children to assess lipid profile, insulin level, blood glucose level, and apolipoprotein A1 and B levels.

Finally, the authors collected body mass index (BMI) data from the children and the parents. They had parental BMI from 17.2% of the fathers and 75% of the mothers.

Based on a regression model, the authors found an association between serum non-HDL cholesterol level and NutriSTEP subscores for eating behaviors (0.02) and screen time (0.09).
The eating behaviors subscore was significantly associated with LDL cholesterol and apolipoprotein B concentration, both of which are correlated with serum non-HDL cholesterol (correlation coefficients of 0.90 and 0.89, respectively, \( P<0.001 \)).

Male sex and parental BMI were significantly related to serum non-HDL cholesterol levels.

However, the dietary intake subscore was not associated with non-HDL cholesterol and neither was parental concern or supplement use.

"I think this is an important study because it brings to fore something that we already know, which is children's behavior learned early in life can translate into results that affect all of their future health," Rae-Ellen Kavey, MD, MPH, of the University of Rochester Medical Center in New York, told Medpage Today.

"One of the most important things they brought up is ... watching television while eating. That's a behavior that's very common now, and it's a very difficult one to break," Kavey said. "If you grew up with the habit of eating in front of the television -- and that's strongly associated with the development of obesity -- that's a behavior that parents can eliminate."

The authors acknowledged some study limitations: The Toronto cohort may not represent children in other settings, and the participants' mothers had high levels of education. Also, food records might have been a better measurement of food intake than recall.

Kavey added that Canadian children are more active and have lower obesity rates than children in the U.S.

"Our results support previous arguments for interventions aimed at improving the eating behaviors of preschool-aged children," the authors concluded. "To do so, evidence suggests promoting responsive feeding, where adults provide appropriate access to healthy foods and children use internal cues -- not parent-directed cues or cues from the television -- to determine the timing, pace, and amount they consume."


Persaud is an associate Editor for CMAJ. One co-author received grant funding from the Canadian Institutes of Health Research (CIHR), is a board member for the Danone Institute of Canada, consultant for Dietitians of Canada, receives royalties for NutriSTEP licenses, and has been reimbursed for travel expenses by the CIHR. Another co-author is a board member for Medpace, consultant for Eli Lilly, Merck, and Bristol-Myers-Squibb, and has received grant funding from AstraZeneca. Other co-authors work for institutions that have received grants from the CIHR. No other competing interests were declared.
The effect of left ventricular electrical delay on AV optimization for cardiac resynchronization therapy.


The effect of left ventricular electrical delay on AV optimization for cardiac resynchronization therapy.

BACKGROUND:

The role of atrioventricular optimization (AVO) for cardiac resynchronization therapy (CRT) is controversial. Identifying subgroups that benefit from optimization is important to improve CRT outcomes. Pacing at sites of late electrical activation, as assessed by the QLV interval, improves remodeling with CRT.

OBJECTIVE:

To evaluate whether pacing at sites of long left ventricular (LV) electrical delay increases the effectiveness of AVO.

METHODS:

This substudy of the SMART-AV trial included 280 subjects who were randomized to either an electrogram-based AVO (SmartDelay) or nominal atrioventricular delay (120 ms). The QLV interval was defined as the time from the onset of QRS to the LV electrogram peak. CRT response was defined prospectively as a >15% reduction in left ventricular end systolic volume from implant to 6 months.

RESULTS:

The cohort was 68% men, with a mean age of 66 ± 11 years and LV ejection fraction of 28% ± 8%. Longer QLV durations were significantly associated with CRT response (P < .01) for the entire cohort. Moreover, the benefit of AVO increased as QLV prolonged. At the longest QLV quartile, there was more than a 6-fold increase in the likelihood of a remodeling response compared with nominal atrioventricular delays.

CONCLUSIONS:

Baseline electrical dyssynchrony, as measured by the QLV interval, predicted CRT response. At long QLV intervals, AVO can increase the likelihood of structural response to CRT. AVO and QLV optimized that LV lead location may work synergistically to maximize CRT response.

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Safety and tolerability of the novel non-steroidal mineralocorticoid receptor antagonist BAY 94-8862 in patients with chronic heart failure and mild or moderate chronic kidney disease: a randomized, double-blind trial.


Safety and tolerability of the novel non-steroidal mineralocorticoid receptor antagonist BAY 94-8862 in patients with chronic heart failure and mild or moderate chronic kidney disease: a randomized, double-blind trial. Eur Heart J. 2013 May 27. [Epub ahead of print]

AIMS:

Mineralocorticoid receptor antagonists (MRAs) improve outcomes in patients with heart failure and reduced left ventricular ejection fraction (HFrEF), but their use is limited by hyperkalaemia and/or worsening renal function (WRF). BAY 94-8862 is a highly selective and strongly potent non-steroidal MRA. We investigated its safety and tolerability in patients with HFrEF associated with mild or moderate chronic kidney disease (CKD).

METHODS AND RESULTS:

This randomized, controlled, phase II trial consisted of two parts. In part A, the safety and tolerability of oral BAY 94-8862 [2.5, 5, or 10 mg once daily (q.d.)] was assessed in 65 patients with HFrEF and mild CKD. In part B, BAY 94-8862 (2.5, 5, or 10 mg q.d., or 5 mg twice daily) was compared with placebo and open-label spironolactone (25 or 50 mg/day) in 392 patients with HFrEF and moderate CKD. BAY 94-8862 was associated with significantly smaller mean increases in serum potassium concentration than spironolactone (0.04-0.30 and 0.45 mmol/L, respectively, P < 0.0001-0.0107) and lower incidences of hyperkalaemia (5.3 and 12.7%, respectively, P = 0.048) and WRF. BAY 94-8862 decreased the levels of B-type natriuretic peptide (BNP), amino-terminal proBNP, and albuminuria at least as much as spironolactone. Adverse events related to BAY 94-8862 were infrequent and mostly mild.

CONCLUSION:

In patients with HFrEF and moderate CKD, BAY 94-8862 5-10 mg/day was at least as effective as spironolactone 25 or 50 mg/day in decreasing biomarkers of haemodynamic stress, but it was associated with lower incidences of hyperkalaemia and WRF.

KEYWORDS: Aldosterone, Antagonist, Chronic kidney disease, Heart failure, Mineralocorticoid receptor PMID:23713082
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Serelaxin reduces dyspnea in HF-PEF patients in first 24 hours: RELAX-AHF analysis

new analysis of the Relaxin for the Treatment of Acute Heart Failure (RELAX-AHF) trial, which stratified patients based on ejection-fraction status, suggests that serelaxin (Novartis Pharmaceuticals) may be more effective in reducing shortness of breath during the first 24 hours in heart-failure patients with preserved ejection fractions (HF-PEF) than in those with reduced ejection fractions (HF-REF).

In contrast, treatment with serelaxin, a novel recombinant form of human relaxin 2, resulted in similar improvements in area-under-the-curve (AUC) from baseline to day 5 on a dyspnea visual analog scale (VAS) in patients with HF-PEF and HF-REF. "There was no interaction between the two groups," lead investigator Dr Gerasimos Filippatos (Athens University Hospital Attikon, Greece) said regarding dyspnea on day five. "The results were similar for those with preserved ejection fraction and those with reduced ejection fraction."

In contrast, while there was only a numerical decrease in dyspnea measured at 24 hours using the Likert scale in the overall trial, Filippatos noted, "there was a better effect in those with left ventricular ejection fractions greater than 50%.

The results of the RELAX-AHF analysis were presented during a late-breaking clinical-trials session here today at the Heart Failure Congress 2013 of the European Society of Cardiology Heart Failure Association.

Limited treatment options for HF-PEF

In RELAX-AHF, 26% of the study cohort had preserved ejection fractions, defined as >50%. In terms of patient characteristics, those with preserved and reduced ejection fractions did differ in some ways. For example, those with HF-PEF were older, had slightly higher systolic blood pressure, were more likely to be female, arrived a little later at hospital, were more likely to have hypertension, and were more likely to be treated with an aldosterone antagonist.

As in the overall study population, which showed no improvement in cardiovascular death or hospitalization for heart or renal failure through day 60, there was no improvement in clinical outcomes in patients with HF-PEF or HF-REF. Cardiovascular death and all-cause mortality at day 180 were both significantly reduced by 37% overall, but investigators did not observe a significant interaction based on ejection-fraction status. In addition, there was no significant interaction with regard to changes in biomarkers, such as cardiac cystatin C or N-terminal prohormone of brain natriuretic peptide (NT-proBNP).

On the whole, Filippatos said that the data confirm that the drug is equally effective for the reduction of dyspnea through day 5 in both types of heart-failure patients and is "also equally effective at improving short- and long-term outcomes, including survival, irrespective of the ejection fraction."
Commenting on the study results, Dr Mihai Gheorghiade (Northwestern University Feinberg School of Medicine, Chicago, IL) said that while progress has been made in the treatment of outpatients living with heart failure, the same progress has not been observed among patients hospitalized with heart failure. This is evident by the unacceptably high rates of postdischarge mortality and readmission—rates that haven't changed in the past 10 years. Regarding patients with heart failure, he noted that regardless of their ejection-fraction status, hospitalizations for heart failure affect patients equally, even though the number of patients with HF-PEF is growing.

"What's interesting is that once you admit the patient for heart failure, the ejection fraction is no longer a major prognostic indicator," said Gheorghiade. "The readmission and mortality [rates] are almost equal in patients with preserved and reduced ejection fractions."

**RELAX-AHF, in a nutshell**

The RELAX-AHF study included 1160 patients with acute heart failure and systolic blood pressure >125 mm Hg randomized to serelaxin (via a 48-hour intravenous infusion within 16 hours of presentation) or placebo. As reported by heartwire, serelaxin resulted in a 19% improvement in AUC from baseline to day 5 on a dyspnea VAS, as well as a moderate—but not statistically significant—improvement in dyspnea at 24 hours measured using a Likert scale.

Days alive out of the hospital at day 60 and cardiovascular death or heart-failure/renal-failure hospitalizations up to day 60—the secondary end points—were not significantly improved with serelaxin. Overall, there was a significant 37% reduction in both risk of all-cause and cardiovascular mortality at six months with serelaxin.
Subclinical Hypothyroidism and Survival: The Effects of Heart Failure and Race.

Rhee CM, Curhan GC, Alexander EK, Bhan I, Brunelli SM.
Subclinical Hypothyroidism and Survival: The Effects of Heart Failure and Race.
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Context: Studies examining the association between subclinical hypothyroidism and mortality have yielded conflicting results. Emerging data suggest these associations may depend upon underlying congestive heart failure (CHF) and/or race, but this has not been empirically determined. Objective: Our objective was to examine the association between subclinical hypothyroidism and hypothyroidism overall with mortality according to pre-existing CHF and race. Design and Participants: We examined the associations of subclinical hypothyroidism (TSH higher than assay upper limit of normal; total T4 within reference) and hypothyroidism overall (TSH higher than assay upper limit of normal; total T4 below lower limit of normal or within reference) with all-cause mortality among Third National Health and Nutrition Examination Survey participants stratified by CHF and race using multivariable Cox models. To confirm whether differences between strata were statistically significant, we tested for interaction on the basis of CHF (separately) and race by likelihood ratio testing. Results: There were 14,130 (95.0%) euthyroid controls and 749 (5.0%) participants with hypothyroidism, 691 (4.6%) of whom had subclinical disease. Subclinical hypothyroidism vs euthyroidism was associated with greater mortality in those with CHF but not in those without: adjusted hazard ratios (HRs) (95% confidence intervals [CIs]) = 1.44 (1.01-2.06) and 0.97 (0.85-1.11), respectively (P interaction = .03). Similar findings were observed for hypothyroidism overall. Hypothyroidism overall vs euthyroidism was associated with greater mortality in Black participants (HR = 1.44 [95% CI = 1.03-2.03]) but not in non-Blacks (HR = 0.95 [95% CI = 0.83-1.08]) (P interaction = .03). Conclusion: Among participants with CHF, subclinical hypothyroidism and hypothyroidism overall are associated with greater death risk. Additional studies are needed to confirm findings and explore possible mechanisms for the differential hypothyroidism-mortality association across race.

PMID: 23720788 // Renal Division (C.M.R., G.C.C., S.M.B.), Department of Medicine; Channing Division of Network Medicine (G.C.C.), Department of Medicine; Division of Endocrinology, Diabetes, and Hypertension (E.K.A.), Department of Medicine; and Division of Pharmacoepidemiology and Pharmacoeconomics (S.M.B.), Department of Medicine, Brigham and Women's Hospital; Harvard Medical School (C.M.R., G.C.C., E.K.A., I.B., S.M.B.); Department of Epidemiology (G.C.C.), Harvard School of Public Health, Boston, Massachusetts 02115; Renal Division (I.B.), Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts 02114; and DaVita Clinical Research (S.M.B.), Minneapolis, Minnesota 55404.
Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry.

Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry.

BACKGROUND:

The risks of sports participation for implantable cardioverter-defibrillator (ICD) patients are unknown.

METHODS AND RESULTS:

Athletes with ICDs (age, 10-60 years) participating in organized (n=328) or high-risk (n=44) sports were recruited. Sports-related and clinical data were obtained by phone interview and medical records. Follow-up occurred every 6 months. ICD shock data and clinical outcomes were adjudicated by 2 electrophysiologists. Median age was 33 years (89 subjects <20 years of age); 33% were female. Sixty were competitive athletes (varsity/junior varsity/traveling team). A pre-ICD history of ventricular arrhythmia was present in 42%. Running, basketball, and soccer were the most common sports. Over a median 31-month (interquartile range, 21-46 months) follow-up, there were no occurrences of either primary end point-death or resuscitated arrest or arrhythmia-related injury during sports. There were 49 shocks in 37 participants (10% of study population) during competition/practice, 39 shocks in 29 participants (8%) during other physical activity, and 33 shocks in 24 participants (6%) at rest. In 8 ventricular arrhythmia episodes (device defined), multiple shocks were received: 1 at rest, 4 during competition/practice, and 3 during other physical activity. Ultimately, the ICD terminated all episodes. Freedom from lead malfunction was 97% at 5 years (from implantation) and 90% at 10 years.

CONCLUSIONS:

Many athletes with ICDs can engage in vigorous and competitive sports without physical injury or failure to terminate the arrhythmia despite the occurrence of both inappropriate and appropriate shocks. These data provide a basis for more informed physician and patient decision making in terms of sports participation for athletes with ICDs.

Keywords: defibrillators, implantable, sports PMID: 23690453 // Yale University School of Medicine, 789 Howard Ave, Dana 319, New Haven, CT 06511. rachel.lampert@yale.edu.
OBJECTIVE:

To assess the proportion of current implantable cardioverter defibrillator (ICD) recipients who would be suitable for a subcutaneous lead ICD (S-ICD).

DESIGN:

A retrospective cohort study.

SETTING:

Tertiary care facility in the Netherlands.

PATIENTS:

All patients who received a single- or dual-chamber ICD in the Leiden University Medical Center between 2002 and 2011. Patients with a pre-existent indication for cardiac pacing were excluded.

MAIN OUTCOME MEASURE:

Suitability for an S-ICD defined as not reaching one of the following endpoints during follow-up: (1) an atrial and/or right ventricular pacing indication, (2) successful antitachycardia pacing without a subsequent shock or (3) an upgrade to a CRT-D device.

RESULTS:

During a median follow-up of 3.4 years (IQR 1.7-5.7 years), 463 patients (34% of the total population of 1345 patients) reached an endpoint. The cumulative incidence of ICD recipients suitable for an initial S-ICD implantation was 55.5% (95% CI 52.0% to 59.0%) after 5 years. Significant predictors for the unsuitability of an S-ICD were: secondary prevention, severe heart failure and prolonged QRS duration.

CONCLUSIONS:

After 5 years of follow-up, approximately 55% of the patients would have been suitable for an S-ICD implantation. Several baseline clinical characteristics were demonstrated to be useful in the selection of patients suitable for an S-ICD implantation.