Review Article

On the Underutilization of Cardiac Resynchronization Therapy

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ABSTRACT

Cardiac resynchronization therapy (CRT) is an exciting therapy that can treat patients with systolic heart failure and left ventricular dysfunction who have a wide QRS complex. Indications for its use have been refined and expanded based on recent clinical data and guidelines, yet the rate of new CRT implants in the United States has not changed much over the past 8 years. Many patients receiving implantable cardioverter-defibrillators can benefit from, but are not receiving, appropriately-indicated CRT devices. We summarize data on CRT use, discuss reasons for probable underutilization, and provide recommendations for augmenting proper and effective use of this highly beneficial therapy. (*J Cardiac Fail 2014;20:696−705*)
Key Words: Cardiac resynchronization therapy, heart failure, implantable cardioverter defibrillator, utilization.

Cardiac resynchronization therapy (CRT) is an important adjunctive therapy developed to treat patients with systolic heart failure (HF) who have a wide (>120 ms) QRS complex and are optimally medically managed.[1−6] The therapy is commonly used, but likely not enough.

From 2002 to 2012, $>500,000$ patients received a CRT-defibrillator (CRT-D) and $>75,000$ received a CRT-pacemaker (CRT-P) in the United States (US). Randomized controlled clinical trials involving $>5,000$ patients have shown that CRT improves symptoms, exercise capacity, functional status, ventricular size and function, hospitalization rate, and mortality in selected patients with advanced HF.[1−3] This led to recommendations for CRT in patients with left ventricular ejection fraction (EF) $\leq 35\%$, wide QRS, sinus rhythm, and advanced HF symptoms despite optimal drug therapy. More recent studies in less advanced wide-QRS HF patients have demonstrated significant benefits with CRT.[4−6] These and other studies have led to revised 2012 CRT guidelines.[7] The largest, and likely most important, change was the addition of many New York Heart Association (NYHA) functional class II patients resulting in an overall broadening of the indications for CRT.

Despite strong and increasing evidence supporting CRT use in appropriate HF patients, and a rapidly growing HF population, CRT implantation rates have changed little in the US for the past 8 years. CRT is expensive, invasive, and limited to a subset of HF patients who have specific clinical criteria (low EF and wide QRS), and these factors, among others, may be limiting its use. Nevertheless, many patients who could benefit are not receiving this therapy. Here, we address trends in CRT utilization, consider potential explanations for underutilization, and discuss ways to improve appropriate use.

CRT Utilization in US and Europe

The estimated CRT-D implantation rate in the US increased steadily from $\sim 13,000$ in 2002 to $>55,000$ in 2005 (Fig. 1; data estimated as described in Appendix A). Subsequently, there has been a leveling off in the number of new CRT-D implantations, with 53,917 in 2012, despite increasing evidence of benefit and new indications for use.
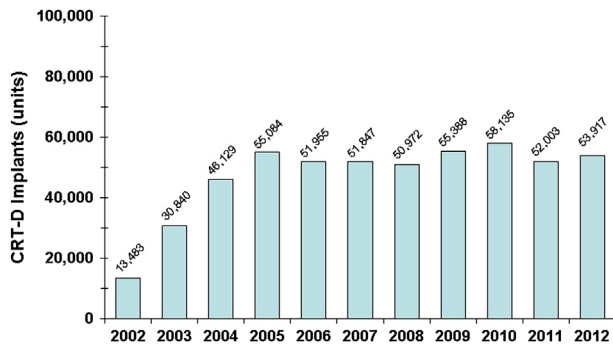
Fig. 1. Initial cardiac resynchronization therapy−defibrillator (CRT-D) implantation estimates in the United States from 2002 to 2012.

Fig. 3. Initial implantable cardioverter-defibrillator (ICD) implantation estimates in the US between 2002 and 2012. CRT, cardiac resynchronization therapy.

Figure 2 shows the estimated CRT-D implantations/million inhabitants in Europe (17 countries) since the peak US year of 2005.[8] In contrast to the flat trend in the US, CRT-D implantations (initial and replacement) have increased progressively and linearly in Europe from 2005 to 2010 (270% increase), with a continued upward trend in 2011.[8] Assuming that ∼20% of CRT-D implantations are generator change-outs,[9] the initial CRT-D implantation rate per million inhabitants in Europe in 2010 was 80 versus 188 in the US in 2010. Although the CRT-D implantation rate in Europe is lower than in the US, the gap has been closing progressively, with 2010 initial CRT-D implantation rates in several countries (Italy 136, Germany 124, Czech Republic 106, and Netherlands 103) approaching that in the US. Although it is recognized that numerous demographic, social, political, regulatory, and economic differences between the US and Europe affect the utilization of health care resources, this differential slope of the CRT-D utilization curves is striking.

One potential explanation is that US physicians were initially more aggressive about implanting CRT-D devices and that the Europeans are simply "catching up." A 2nd explanation is that HF device safety recalls beginning in 2005 caused this flat trend in the US. Supporting this argument is the fact that initial implantable cardioverter-
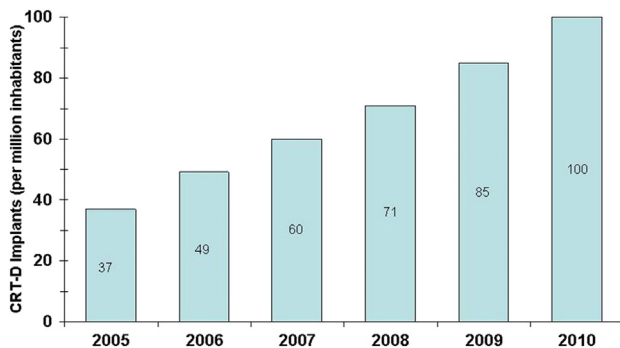
defibrillator (ICD) implantation has progressively decreased from a peak of 99,867 in 2006 (Fig. 3). Although this may be an important factor in declining CRT-D utilization, it does not explain the observation entirely, because safety recalls were well known to physicians in Europe, yet implantation of CRT-D devices increased. In addition, ICD implantation increased in Europe at the same time but at a slower increase of 176% from 2005 to 2010.[10]

A 3rd explanation is that US physicians shifted toward a greater percentage of CRT-P versus CRT-D implantations. However, this was not the case, with the percentage of CRT-P devices implanted remaining stable at ∼16% in the US.[11]

A 4th explanation is that there is now a better understanding of those who benefit from CRT, such as those with left bundle branch block (LBBB) and/or those with very wide (>150 ms) QRS complexes, and those who may not benefit at all. It is rather clear that non-LBBB patients do not derive the same benefit from a CRT device. Similarly, not all atrial fibrillation patients benefit. Additionally, some are simply too sick with NYHA functional class IV HF, have uncorrectable HF at the end of life, or are on their death bed because of another cause. Furthermore, the lack of response in ∼1/3 patients considered to be candidates may have affected recent CRT implantation enthusiasm. Undisclosed or undefined changes in health care may also play a role. We discuss these issues further below.

Is CRT Underutilized?

The IMPROVE HF study, was a prospective real-world study involving ∼35,000 HF patients.[11,12] Approximately 38% of eligible patients without documented contraindications received a CRT device (with or without an ICD) and 49% received an ICD (with or without CRT).[12] With the use of these and other data, Fonarow et al estimated that the number of HF patients in the US eligible for CRT was 326,151, or 5.6% of the 5.8 million patients with HF.[13] In light of new guideline changes,[7] we generated aggressive

Fig. 2. Total cardiac resynchronization therapy−defibrillator (CRT-D) implantation estimates for Europe (17 countries) per 1,000,000 population from 2005 to 2010.
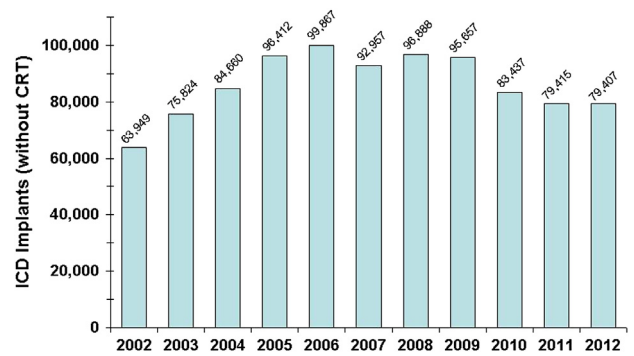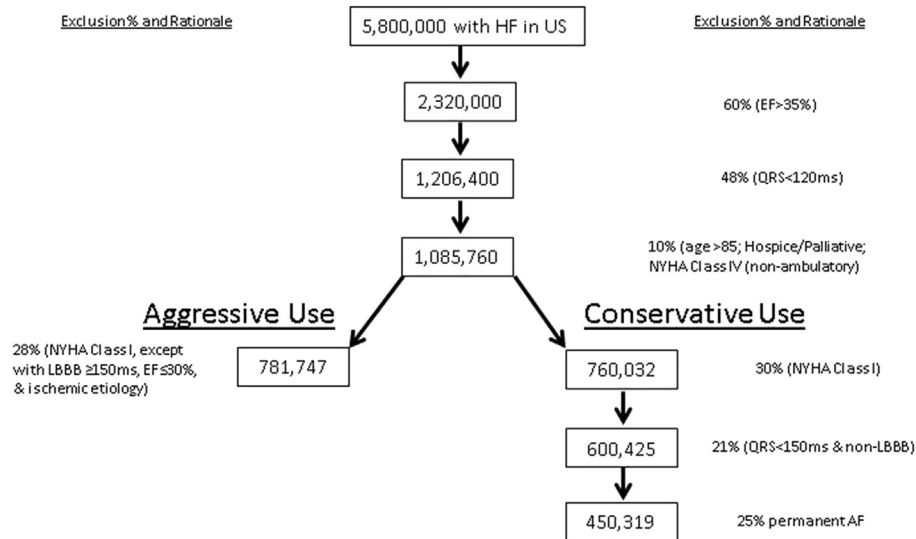
Fig. 4. Aggressive and conservative estimates of heart failure (HF) patients eligible for cardiac resynchronization therapy under current guidelines. AF, atrial fibrillation; EF, ejection fraction; LBBB, left bundle branch block; NYHA, New York Heart Association.

and conservative estimates of patients in the US currently eligible for CRT (Fig. 4).

Estimates of the percentage of patients in each category are based on data from several sources and detailed in Appendix B. In both conservative and aggressive analyses we excluded all HF patients with EF $>$35% or QRS $<$ 120 ms. We also excluded an estimated 10% of wide-QRS systolic-dysfunction HF patients for whom a CRT may be inappropriate (age $>$85 years, hospice or palliative care, or no-ambulatory NYHA functional class IV HF symptoms). We did not include HF patients with high-grade atrioventricular (AV) block (and left ventricular ejection fraction [LVEF] $>$ 35%) though a recent multicenter randomized trial showed benefit.[14]

In the aggressive estimate, we also excluded most NYHA functional class I patients, leaving ~780,000 HF patients (~13.5%) eligible for CRT. In the conservative estimate patients with either NYHA functional class I HF, QRS $<$ 150 ms with non-LBBB or permanent atrial fibrillation were additionally excluded, leaving ~450,000 (~7.8%) CRT-eligible HF patients. With the use of implantation data from Fig. 1 and an assumption of 8%, 9%, and 10% annual mortality (Appendix C), the number of CRT-D patients implanted from 2002 to 2012 and alive in the US in 2013 should be ~315,000−348,000, leaving a gap of ~100,000−430,000 patients potentially eligible for CRT.

Underutilization of CRT in Patients Receiving an ICD

Most patients who are eligible for CRT also meet American College of Cardiology/American Heart Association guideline criteria for an ICD because many of the criteria, such as EF $\leq$35%, overlap. In the US, the majority (~84%) of CRT recipients are treated with a concomitant ICD.[11] In those patients who receive CRT-P rather than CRT-D, typical reasons are advanced age, a contraindication for ICD (eg, psychiatric issues), or a patient/physician choice not to implant an ICD. Therefore, the remainder of this paper will focus on CRT-D with the understanding that some of the issues mentioned also apply to CRT-P. Review of the relative benefits and risks of CRT-P versus CRT-D is outside the scope of this paper and will not be discussed.

Based on data from Figs. 1 and 3, the percentage of US ICD patients who received concomitant CRT was 36% −41% from 2005 to 2012 with an upward trend in the last few years (Fig. 5). National ICD Registry data from 2006−2007 showed that 32.2% of patients receiving an ICD met criteria for CRT.[15] Of those eligible patients, 80.7% received a CRT-D and 19.3% an ICD only. The IMPROVE HF registry demonstrated a larger percentage of patients who received an ICD alone despite meeting standard indications for CRT,[11] with only a little more than one-half of the CRT-indicated patients who received an ICD being implanted with the correct device (CRT-D). The percentage of patients receiving an indicated ICD
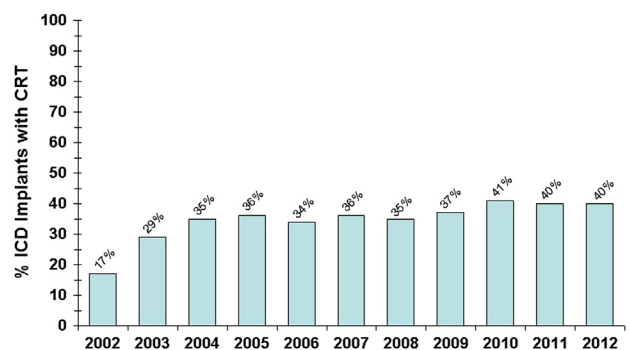

Fig. 5. Proportion of ICD implants that were CRT-D in the US between 2002 and 2012. Abbreviations as in Fig. 3.

Table 1. Response Rate to Question, "In Your Opinion What Are the Top 2 Reasons Why Some CRT Indicated Patients Get an ICD Device Rather Than a CRT Device?"

Reason	Implanter (n = 50)	Cardiologist (n = 50)	Device Nurse (n = 50)
Lack of documented QRS	46%	64%	30%
Patient's anatomy sometimes dictates	34%	34%	28%
Indicated patients too ill for lengthy CRT procedure	28%	12%	18%
Lack of documented NYHA Class	22%	18%	32%
Some implanters do not want to implant CRT	14%	22%	10%
CRT procedure too complicated and lengthy	14%	16%	8%
Patient insurance issues	6%	8%	22%
ICD implant more time- and cost-efficient than CRT	8%	6%	14%
Patient refuses CRT but not ICD	8%	0	0
There are other medical alternatives	6%	0	8%
Published responder rates to CRT	6%	4%	2%

without appropriate CRT is likely higher now that many NYHA functional class II HF patients are eligible under revised guidelines.[7]

Initial ICD patients are not the only group frequently receiving the wrong device. Patients requiring generator change often are not appropriately upgraded to CRT-D. The ALTITUDE study group analyzed ICD replacement data from 19,591 patients followed via remote monitoring.[16] Approximately 25% had ≥40% right ventricular pacing and therefore were at significant risk of progressively worsening left ventricular function and clinical deterioration.[17] Yet only 38.1 % of ∼5,000 eligible patients were upgraded to a CRT-D. Whether any of these patients could be reprogrammed to minimize ventricular pacing without need for upgrade to CRT is unknown.

An online survey tried to determine why an ICD alone was implanted when criteria for a CRT device was met (Medtronic, personal communication). The survey questioned 50 ICD implanters, 50 referring cardiologists, and 50 device nurses. The following was asked: "ICD Registry data indicate that ∼25% of patients implanted with an ICD meet indications for a CRT. In your opinion, what are the top 2 reasons why some CRT indicated patients get an ICD device rather than a CRT device?" Table 1 presents the survey results. The following paragraphs discuss the response and some additional reasons.

Benefit is Underappreciated

Perhaps, therapy benefit is underappreciated because the terminology of nonresponse is applied to CRT but not to HF drug therapy. CRT is a potent therapy with changes in left ventricular function and structure as good as, or better than, many established drug therapies; yet, by echocardiographic remodeling criteria 30%−45% of CRT patients are called nonresponders.[19] In addition, the definition of CRT response is variable, with 17 unique criteria used to define CRT response in different studies.[18] Because HF is a progressive condition, the lack of HF progression after CRT could indicate benefit. In fact, CRT may benefit even those who deteriorate. In 88% of 40 consecutive CRT patients admitted for hemodynamic derangements, the QRS widened and mechanical dyssynchrony increased with

CRT programmed off, suggesting important hemodynamic benefit of CRT even in those who appeared to deteriorate.[19]

Physicians may assume that the results from large randomized clinical trials do not apply to clinical practice. Trials performed at specialized centers often exclude the elderly, noncompliant patients, and those with multiple comorbidities. This may result in greater benefits and lower risks than occur in real-world clinical practice. For example, spironolactone use after publication of the RALES trial resulted in significant increases in hyperkalemia-related hospitalizations and deaths among older HF patients.[20] Data from that experience and others have led to the belief that "they [pivotal trials] are likely to yield a higher estimate of benefit and a lower estimate of harm than will be seen after penetrance into practice."[21]

Survival after ICD implantation is similar between patients enrolled in clinical trials and comparable patients treated in clinical practice.[22] What about CRT? There is increasing evidence that CRT in the real world provides benefit similar to, or better than, that in clinical trials. We analyzed data from 429 consecutive patients receiving CRT-D for standard indications in our clinic.[23] Survival was similar to the CRT-D arm of COMPANION, and survival free of cardiovascular hospitalization exceeded that of COMPANION without as well as with propensity matching. The Medicare Implantable Cardioverter-Defibrillator Registry data (∼15,000 patients) demonstrated 1- and 3-year survivals of 88% and 68%, respectively.[24] The ALTITUDE Survival Study (∼78,000 patients) showed 1- and 3-year survivals of 88% and 71%, respectively.[25] These survival rates are similar to those in the CRT-D arm of the COMPANION Study (∼88% and ∼65% at 1 and 3 years, respectively).[1] These data, however, must be considered cautiously in light of potential unmeasured treatment selection bias and differences in patient populations.

CRT is very different from drug therapy for HF. This may lead to clinical effectiveness in the real-world that exceeds clinical efficacy shown in research trials. Compliance with prescribed drug therapy is <80% in the HF population.[26] With CRT, the patient receives therapy regardless of compliance and follow-up noncompliance usually does not affect delivery of CRT (although compliance with follow-up could result in more optimal programming).[27]

Physicians may become more experienced with selecting patients for drug therapy and dosing drugs, yet drug therapy usually does not change much over time. With CRT, the therapy has continuously evolved, including better selection of patients (eg, excluding NYHA functional class II HF patients with RBBB and QRS 120−149 ms), improved lead technology, greater experience in lead placement with reduced implantation time,[28] improved targeting of lead location,[29] pacemaker optimization,[30,31] novel pacing algorithms,[32] improved delivery of therapy with greater percentage biventricular pacing (via better rate control of atrial fibrillation, reduction in AV delay, or treatment of ventricular ectopy),[33−36] increased remote monitoring of HF diagnostics,[27] and increased collaboration among cardiology subspecialists with development of CRT clinics[37] Evidence supporting the progressive improvement in CRT comes from the ALTITUDE Registry, where median survival for CRT-D recipients improved by 14 months from 2003 through 2006 and mortality decreased every year from 2003 through 2010.[38]

Finally, the benefits of treatment early in the disease process of HF may be underappreciated. Whereas the long-term value of CRT in mild HF patients is uncertain (most trials last only ∼2 years), improvements in left ventricular function and size in trials of less advanced HF patients have been substantial.[4−6] Improvements in left ventricular size and function in a real-world clinical scenario were greater in NYHA functional class I/II HF patients than in class III/IV patients, suggesting that earlier intervention with CRT may lead to greater long-term benefit.[39] Calculation of lifespan gained by modeling survival data from 5 landmark CRT trials demonstrated that lifespan gained across all trials increased nonlinearly with time and was 65 times higher at 5 years than at 1 year.[40] Whereas higher-mortality (sicker) patients had a greater lifespan gain in the short term (eg, 2 years), this scenario was reversed at 15 years, with greater lifespan gain in the lower-mortality (less sick) patients. This initially surprising finding occurs because the lower-risk group has more survivors each year than the higher-risk group, so as time goes on, the lower-risk group increasingly benefits to a greater extent.

Risks

The third most common reason mentioned for not considering CRT was that the patient was too ill, suggesting that physicians are concerned that the risks do not outweigh the benefits. The patients referred to in the survey were likely not NYHA functional class IV, because they were receiving ICDs. In-hospital mortality from registry data of HF patients undergoing CRT implantation is low and has been decreasing significantly from 2002 (1.07%) to 2009 (0.76%).[41] Retrospective meta-analysis of 11 ICD and 7 CRT trials found in-hospital mortality to be similar and low in patients receiving an ICD (0.2%) versus a CRT-D (0.3%).[42] The risk of serious early complications from placement of a device varies based on the definitions and

time from implantation. Analysis of >161,000 patients in the National Cardiovascular Data Registry ICD Registry receiving a first-time ICD or CRT-D showed an in-hospital adverse event rate of 3.6% that was no different in patients treated with CRT-D versus ICD.[43] Similarly, a study of almost 31,000 patients from the Medicare Provider Analysis and Review showed no significant difference in overall complication rates for CRT-D versus ICD implantations.[44] In contrast, the prospective Ontario ICD Database demonstrated a major complication rate of 4.1% in first-time implants, with highest risk in patients receiving CRT-D compared with those receiving single- or dual-chamber ICDs.[45] In studies where CRT-D patients have higher adverse event rates compared with other device patients, the majority of this difference is due to lead dislodgement or replacement.[45] Therefore, in assessing the risk of CRT-D versus ICD, the physician should weigh the additional risk of lead dislodgement (with possible need for replacement) and phrenic nerve stimulation against the potential benefit of CRT and the competing risk of a second procedure if upgrade is needed.

Lack of Physician Interest, Knowledge or Skill in Lead Placement

One reason cited for not placing a CRT device in a patient receiving an ICD was difficult coronary venous anatomy. Although it is a well recognized problem, the rate of unsuccessful left ventricular lead implantation is ≤10% and lower in centers with extensive experience.[28] Two of the top 4 reasons cited were lack of documentation of QRS or NYHA functional class. Obtaining this information is simple, and the authors are dismayed that this would be considered as a reason. Perhaps these reasons were cited because ''some physicians do not want to implant CRT,'' the 5th most common reason mentioned in the survey. Reluctance to implant CRT could be due to inexperience or inadequate training in left ventricular lead placement or simply a long time lag for translation of research into clinical practice. Approximately 29% of ICDs are implanted by nonelectrophysiologists.[15] Although CRT is appropriately placed by electrophysiologists in 83.1% of ICD cases, it is used less often when ICDs are implanted by nonelectrophysiologist cardiologists (75.8%), thoracic surgeons (57.8%), or different specialists (74.8%).[15]

Reimbursement and Costs

Hospital reimbursement from the Centers for Medicare and Medicaid Services is similar for ICD and CRT-D implantation despite increased complexity, time, and experience required for CRT. Although physician reimbursement is about $300 higher for a CRT-D versus ICD, this may not be seen as adequate additional reimbursement. Whether reimbursement issues overtly or subtly influence the implant selection is unknown.

CRT-D therapy is expensive, with costs heavily weighted up front. However, CRT can reduce costs by reducing health care utilization. Heart failure hospitalization is the

major cost determinant for this disease, with each hospitalization costing ~$10,000. Several papers have demonstrated the cost-benefit and cost-effectiveness of CRT versus optimal medical therapy or ICD.[46-48] In COMPANION, hospitalization costs were reduced by 29% (CRT-D) and 37% (CRT-P), with acceptable cost-effectiveness ratios.[47] In MADIT-CRT 4-year health care expenditures in CRT-D patients were only $5,550 more than in ICD patients ($62,600 vs $57,050) and the incremental cost-effectiveness ratio was $7,320 per quality-adjusted life-year when assessed over a longer time horizon in LBBB patients.[48]

Concern About Retribution/Reprisal for Using Clinical Judgment Rather Than Guidelines for Decision Making

Several recent developments have raised concern among physicians referring patients for implantable devices. The first is the publication of 2 papers assessing the use of CRT and/or ICDs in the US.[49,50] Fein et al evaluated >45,000 CRT-D implants from January 2006 to June 2008.[50] They argued that 23.7% of devices implanted were "off-label," predominantly because of NYHA functional class <III or narrow QRS. The authors stated that placement of CRT-Ds in patients not meeting guideline-based indications requires careful scrutiny. That study, along with a study by Al-Khatib et al on ICD use, has been interpreted as showing that many ICD implants (with and without CRT) are not "evidence based."[49] An alternative explanation is that many of these "off-label" procedures are "borderline cases where the experts made an intelligent choice to implant a device informed by trial evidence and the guidelines that they know are likely to change in the future."[51]

The second event has been the investigation of cardiology sites by the Department of Justice to determine whether implanted ICDs were not medically indicated or violated coverage policies. Of 227 cases initially flagged at 1 center as not indicated, only 34 (1.3% of all implants) were ultimately considered to be not indicated after careful review.[52] Reasons for a change in interpretation from inappropriate to appropriate included syncope in the presence of HF, trivial myocardial enzyme leak coded inappropriately as myocardial infarction, bradycardia requiring pacing, percutaneous revascularization not expected to affect chronic left ventricular dysfunction, and implantation during an HF admission (near, but not yet at, the required waiting period after revascularization). While a wide range of interpretations are possible, a large gray zone exists. This experience, among others, highlights the complexity of applying guidelines or coverage decision criteria to real-world clinical practice.

Not Anticipating Future Problems

For HF patients receiving a device, the correct device should be implanted initially. Although an ICD can be upgraded to a CRT-D, risks and costs are substantial. Complications for repeated procedures are substantially greater than for initial implantations, with infection rates 2.5 times higher.[42] The cost of upgrade from ICD to CRT-D is high (~$25,000-$35,000). Therefore, in addition to assessing the patient's current condition, the astute clinician should use judgment to determine if the patient is likely to need CRT in the near future. If a patient is likely to require ventricular pacing due to conduction system disease or need to increase beta-blocker medication, then CRT should be considered because of the high risk of worsening HF and increased mortality from right ventricular pacing.[17] The incremental time, cost, and risk of adding a left ventricular lead to an ICD procedure is not very high compared with the time, cost, and risk of upgrade. Based on these and other arguments, Cleland et al favor an aggressive approach where the majority of patients who require an ICD have an attempt at left ventricular lead placement with abandonment of this component of the procedure if it is excessively complex, time consuming, or not a crucial need.[53]

Additional Potential Reasons for CRT Underutilization

Because most CRT recipients receive a concomitant ICD, any factors that affect ICD utilization should affect CRT utilization. ICD underutilization is well documented,[12,54-57] and yearly ICD implantations in the US (with or without a CRT) have decreased substantially since peaking in 2006 (Fig. 3). Much has been written about device safety and device recalls.[58] Negative publicity around ICDs and device therapy for HF has likely contributed to the underutilization of CRT. Although the flattening in CRT-D use since 2005 corresponded with a major device recall, the impact of safety concerns on utilization is uncertain and difficult to quantify.

What Can Be Done to Increase Appropriate Use of CRT?

Increased Education

Education on the indications, risks, and benefits of CRT may help to address underutilization. IMPROVE-HF assessed the effectiveness of a focused multifaceted performance improvement initiative.[59] Over 2 years, CRT utilization increased by >35%, to 85% of eligible patients, with a significant reduction in variation of CRT utilization across practice sites. Also, the intervention increased CRT use (1.9% to 20.8%) in NYHA functional class II patients with wide QRS complex and low LVEF when evidence supporting CRT use in these patients was accumulating but not yet reflected in guidelines.

The cost and risk of implanting a left ventricular lead in a patient undergoing ICD implantation is modest, whereas the potential benefit in appropriate candidates is large. All patients considered for ICD should be evaluated for CRT-D. It is important to make the correct decision at initial implantation to minimize risk and expense associated with need for a repeated (upgrade) procedure.

Perhaps, most importantly, this education should instruct how CRT can provide tremendous benefits for properly selected patients with HF: how it can improve quality of

life, improve ventricular remodeling and function, reduce need for expensive, complicated, prolonged, and risky hospitalization, reduce need for more aggressive therapies (eg, ventricular assist device), and even reduce the risk of dying.

Use of Clinical Judgment in Addition to Guidelines in Making Decisions for Individual Patients

Clinical guidelines are extremely valuable in educating physicians and improving the quality of health care. However, they are not mandates and are not expected to apply to all patients or clinical circumstances. Unfortunately, guidelines are increasingly considered to be mandates, with payment for services and assessment of care quality linked to adherence. The appropriate percentage of CRT-D devices that should be implanted outside current guidelines is unknown, but is likely not zero. We propose that if guidelines are used as templates and roadmaps rather than mandates, a modest number of HF patients (perhaps 10%−20%) should be expected to receive a CRT device ''off label'' yet still deemed to be appropriate.

One approach to enhance physician decision making, health care delivery, and reimbursement policy is the development of appropriate use criteria (AUC). Common clinical scenarios are evaluated and rated based on evidence and practical experience by multiple experts. AUC have been published for ICD/CRT, with clinical implantation scenarios categorized as appropriate, maybe appropriate, or rarely appropriate.[60] These AUC can help to improve decision making and fill gaps in guidelines while allowing for clinical judgment and individualized patient care. Combining evidence-based medicine and clinical guidelines with the ''art of medicine,'' free from fear of censure or recrimination, is, in our opinion, an important means to increase appropriate utilization of CRT and improve outcomes.

Study Limitations

This paper has focused predominantly on CRT-D implantation and not on CRT-P for several reasons. CRT-D patients make up the majority (84%) of those patients treated with CRT and offer the most readily accessible and complete data. CRT-P patients differ substantially from CRT-D patients (older and sicker), and these differences likely significantly affect estimates of mortality. Factors favoring implantation of CRT-P over CRT-D listed in the 2013 European Society of Cardiology guidelines include advanced HF, severe renal insufficiency, other major comorbidities, frailty, and cachexia.[61] The calculations of patients eligible for CRT-D and patients alive with CRT are only estimates. We recognize the limitations of a cascaded diagram and the fact that changes in assumptions can significantly affect the final estimate. We based most of our estimates on several sources, calculated conservative and aggressive models, and used different values of annual mortality to demonstrate a range of possible estimates of CRT-D underutilization.

Conclusion

CRT-D implantation rate in the US has changed little over the past few years, and CRT-D is likely substantially underutilized. CRT underutilization has many potential explanations. A better understanding of the factors impacting CRT utilization should help to increase appropriate CRT implantation, improve outcomes, and save lives.

Disclosures

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Appendix A

US Device Implant Data

Estimates of CRT-D and ICD initial implants used for Figs. 1, 3, and 5 were compiled from the following sources:

1. Morgan Stanley US ICD/CRT Market Model, 2011.
2. JP Morgan Cardiac Rhythm Management Market Model, 2012.
3. Goldman Sachs Cardiac Rhythm Disease Management Market, 2013.

The estimated number of new device implants was calculated by averaging data from the 3 sources.

Appendix B

Data Assumptions and Sources for Fig. 3

Heart failure prevalence: 5,800,000 in the United States.
Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics—2010 update. Circulation 2010;121:e46−215.

Left ventricular ejection fraction distribution: >35% in 60%.

Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J 2011;161:1024−30.

Fonarow GC, Stough WG, Abraham WT, Albert NM, Gheorghiade M, Greenberg BH, et al. Characteristics, treatments, and outcomes of patients with preserved stystolic function hospitalized for heart failure. J Am Coll Cardiol 2007;50:768−77.

Fonarow GC, Yancy CW, Heywood JT. Adherence to heart failure quality-of-care indicators in US hospitals. Arch Int Med 2005;165:1469−77.

QRS distribution: QRS < 120 ms in 48%.

Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, et al. Improving evidence-based care for heart failure in outpatient cardiology practices: primary results of the registry to improve the use of evidence-based heart failure therapies in the outpatient setting (IMPROVE HF). Circulation 2010;122:585−96.

Shamim W, Yousunfuddin M, Cicoria M, Gibson DG, Coats AJS, Henein MY. Incremental changes in QRS duration in serial ECGs over time identify high risk elderly patients with heart failure. Heart 2002;88:47−51.

Contraindicated for CRT: age >85 y; hospice/palliative care, nonambulatory class IV in 10%.

Kirklin JK, Naftel DC, Kormos RL, et al. The fourth IN-TERMACS annual report: 4,000 implants and counting. J Heart Lung Transplant 2012;31:117−26.

Weir R, McMurray J, Taylor J, Brady A. Heart failure in older patients. Br J Cardiol 2006;13:257−66.

US Census Bureau 2011. The older population: 2010. Available at: http://www.census.gov/prod/cen2010/briefs/c2010br-09.pdf.

Accessed April 10, 2013.

Conservative Use

NYHA distribution: NYHA functional class I in 30%.
Fonarow GC, Yancy CW, Hernandez AF, Peterson ED, Spertus JA, Heidenreich PA. Potential impact of optimal

implementation of evidence-based heart failure therapies on mortality. Am Heart J 2011;161:1024−30.

QRS duration and morphology: QRS <150 ms and non-LBBB morphology in 21%.

Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. Circulation 2012;126:1784−800.

Dupont M, Rickard J, Baranowski B, et al. Differential response to cardiac resynchronization therapy and clinical outcomes according to QRS morphology and QRS duration. J Am Coll Cardiol 2012;60:592−8.

Permanent atrial fibrillation prevalence: 25%.

Barold SS, Herweg B. Cardiac resynchronization and atrial fibrillation: what's new? Pacing Clin Electrophysiol 2012;35:1281−9.

Tolosana JM, Madrid AH, Brugada J, et al. Comparison of benefits and mortality in cardiac resynchronization therapy in patients with atrial fibrillation versus patients in sinus rhythm. Am J Cardiol 2008;102:444−9.

Maisel WH, Stevenson LW. Atrial fibrillation in heart failure: Epidemiology, pathophysiology, and rationale for therapy. Am J Cardiol 2003;91:2D-8D.

Aggressive Use

28% NYHA functional class I (except with LBBB, QRS ≥150 ms, EF ≤30%, and ischemic etiology).

Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. Circulation 2012;126:1784−800.

Appendix C

Methodology and Table for Estimating Number of CRT-D Patients Alive

The table below (same data as Fig. 1) presents estimated numbers of new CRT-D implantations per year from 2002 through 2012. For simplicity, all implantations each year were assumed to take place midyear. Using assumptions of 8%, 9%, and 10% annual mortality, the number of patients alive was thus determined for all 527,499 patients receiving implants during this 11-year period through mid-2013. The assumptions of 8%, 9%, and 10% annual mortality were based on data from the ALTITUDE CRT-D database of >130,000 CRT-D implants from 2003 to 2011, where annual mortality was ~10% in patients receiving implants in 2003 and ~8% in patients receiving implants in 2009.[38]

Year	CRT-D Implants	8% Mortality	9% Mortality	10% Mortality
2002	13,483	5,388	4,778	4,234
2003	30,840	13,397	12,010	10,732
2004	46,129	21,780	19,740	17,852
2005	55,084	28,270	25,903	23,692
2006	51,955	28,983	26,848	24,829
2007	51,847	31,438	29,442	27,531
2008	50,972	33,595	31,808	30,073
2009	55,388	39,680	37,982	36,340
2010	58,135	45,269	43,809	42,380
2011	59,100	50,022	48,941	47,871
2012	54,566	50,201	49,655	49,109
Total	527,499	348,022	330,917	314,644