European Journal of Heart Failure (2012) **14**, 696–702
doi:10.1093/eurjhf/hfs062

REVIEW

Use of implantable cardioverter defibrillators in patients with left ventricular assist devices

Stephen J. Pettit*, Mark C. Petrie, Derek T. Connelly, Alan G. Japp, John R. Payne, Saleem Haj-Yahia, and Roy S. Gardner

Scottish National Advanced Heart Failure Service, Golden Jubilee National Hospital, Clydebank, Glasgow G81 4DY, UK

Received 6 March 2012; revised 23 March 2012; accepted 30 March 2012; online publish-ahead-of-print 29 April 2012

Patients with left ventricular assist devices (LVADs) are at high risk of sustained ventricular arrhythmias, but these may be remarkably well tolerated and the association with sudden death is unclear. Many patients who receive an LVAD already have an implantable cardioverter defibrillator (ICD). While it is standard practice to reactivate a previously implanted ICD in an LVAD recipient, this should include discussion of the revised risks and benefits of ICD therapy following LVAD implantation. In particular, patients should be warned that they might receive a significant number of ICD shocks that may not be life saving. When ICDs are reactivated, device programming should minimize the risk of repeated shocks for non-sustained or well-tolerated ventricular arrhythmias. Implantation of a primary prevention ICD after implantation of an LVAD is not supported by current evidence, poses potential risks, and should be the subject of a clinical trial before it becomes standard practice.

Keywords Implantable cardioverter defibrillator • Left ventricular assist device • Ventricular fibrillation • Ventricular tachycardia

Should patients with left ventricular assist devices have implantable cardioverter defibrillators?

A patient with chronic heart failure and severe left ventricular (LV) systolic dysfunction caused by coronary artery disease received a HeartMate II left ventricular assist device (LVAD) as a bridge to transplantation. A primary prevention implantable cardioverter defibrillator (ICD) had been implanted 8 months prior to the LVAD. He has never required antitachycardia pacing (ATP) or shock therapy. These functions were deactivated before surgery. Should the ICD be reactivated after LVAD implantation and, if so, how should the ICD be programmed?

Are patients with left ventricular assist devices at risk of ventricular arrhythmias?

Ventricular tachycardia (VT) and ventricular fibrillation (VF) are common in patients with LVADs; case series, clinical trial data, and registry data are summarized in *Table 1*.[1–12] Comparison is limited by considerable variation in the definition of VT/VF. Most studies are small (only two include > 150 individuals) and the duration of follow-up is short. In the largest study, the Interagency Registry for Mechanical Circulatory Support (INTERMACS), cardiac arrhythmias were the third most common adverse event in LVAD patients (0.9 events per patient-year), after infection (2.1 events per patient-year) and bleeding (2.0 events per patient-year).[10] The risk of VT/VF is greatest in the early post-operative period. In the HeartMate II registry; the incidence of VT/VF was 10-fold higher in the first 30 days after LVAD implantation (1.89 events per patient-year) compared with subsequent follow-up (0.19 events per patient-year).[9] Similar findings were seen in two case series.[4,7] In the HeartMate II trial, arrhythmias were less common with continuous-flow devices (0.69 events per patient year) than pulsatile-flow devices (1.31 events per patient-year).[8]

What causes ventricular arrhythmias in left ventricular assist device patients?

In 32 patients with a pulsatile-flow LVAD and ventricular arrhythmias, 72% had monomorphic VT, 53% had polymorphic VT or VF,

*Corresponding author. Tel: +44 141 951 5000, Fax: +44 141 951 5859, Email: S.J.Pettit@doctors.org.uk

Table 1 Ventricular arrhythmias in left ventricular assist device patients

Source	Patients	Follow-up	Type of LVAD (*n*)	Incidence	Definition
Arai[1] 1991	28	Mean 35.3 days	Thoratec LVAD (22), Novacor LVAS (6)	VT/VF in 5 (18%) patients	VF and sustained VT
Oz[2] 1994	21	Range 1–186 days	Thermocardiosystems HeartMate (21)	VT/VF in 9 (43%) patients	Sustained VT (>190 b.p.m.) or VF
REMATCH[3] 2001	68	Median 408 days	HeartMate XVE (68)	0.25 VT/VF per patient-year	Ventricular arrhythmias which threatened life, necessitated admission, or prolonged admission
Ziv[4] 2005	91	Range 1–126 days	HeartMate XVE (91)	179 VT/VF in 32 (35%) patients	VT/VF lasting > 30 s, or requiring ICD therapy, DC cardioversion, or defibrillation
Bedi[5] 2007	111	Mean 98 days	Novocor LVAS (72), Thoratec LVAD (28), HeartMate XVE (11)	VT/VF in 24 (22%) patients	VF, VT, or non-sustained VT with symptoms which required antiarrhythmic therapy
Refaat[6] 2008	42	Not stated	Unspecified	VT/VF in 15 (36%) patients	VF, VT, or non-sustained VT
Andersen[7] 2009	23	Mean 341 days	HeartMate II (23)	37 VT/VF in 12 (52%) patients	VT/VF lasting > 30 s
HeartMate II[8] 2009	200	Median 0.6 years (HeartMate XVE), median 1.7 years (HeartMate II)	HeartMate XVE (66), HeartMate II (134)	1.31 arrhythmias per patient-year (HeartMate XVE), 0.69 arrhythmias per patient year (HeartMate II)	All arrhythmias
Pagani[9] 2009	281	Median 155 days	HeartMate II (281)	72 VT/VF in 56 (20%) patients, 0.4 VT/VF per patient-year	VT/VF requiring DC cardioversion or defibrillation
INTERMACS[10] 2010	1092	Not stated	Unspecified; pulsatile flow (528) continuous flow (564)	0.92 arrhythmias per patient-year	All arrhythmias
Kuhne[11] 2010	76	Median 156 days	HeartMate VE (15), HeartMate XVE (34), HeartMate IP-1000 (1), Thoratec IVAD (3), HeartMate II (22), Micromed DeBakey (1)	VT/VF in 22 (29%) patients	VT/VF requiring cardioversion or defibrillation
Brenyo[12] 2011	61	Mean 622 days	HeartMate II (58), Jarvik 2000 (3)	VF/VT in 19 (31%) patients	VT/VF detected and treated by ICD

ICD, implantable cardioverter defibrillator; LVAD, left ventricular assist device; VF, ventricular fibrillation; VT, ventricular tachycardia.

and 25% had both. Monomorphic VT was most frequently localized to the LV apex by electrocardiogram (ECG) criteria and was fast (mean cycle length 308 ± 88 ms, rate 195 ± 44 b.p.m.).[4] In 61 patients with a continuous-flow LVAD who received ICD therapy, 52% had monomorphic VT, 13% had polymorphic VT, and 35% had VF.[13]

The VT/VF may be attributable to the underlying cardiac pathology or the LVAD itself. Placement of the LVAD inflow cannula at the LV apex may create a re-entrant circuit for VT. Suction events, due to acute LV underfilling or high pump speed, may be arrhythmogenic.[14] Acute unloading of the LV after LVAD implantation may prolong the QT interval, increasing the risk of postoperative VT/VF.[15] At a cellular level, LVAD support is associated with changes in the beta-adrenergic system and calcium handling which may alter the risk of VT/VF.[16] The relative importance of these mechanisms is uncertain; the high incidence of early postoperative VT/VF could suggest a transient proarrhythmic effect of surgery or a longer term antiarrhythmic effect of LVAD support. Randomized data from the HeartMate trial suggests that long-term LVAD support may be antiarrhythmic; a pulsatile-flow LVAD reduced the incidence of VT/VF compared with medical therapy [rate ratio 0.45, 95% confidence interval (CI) 0.22–0.90].[3]

What are the consequences of ventricular arrhythmias in left ventricular assist device patients?

Ventricular arrhythmias may have life-threatening haemodynamic consequences in patients with LVADs. In a series of 42 patients over 24 months with an unspecified type of LVAD, five patients experienced syncope during VT and one patient died of shock-refractory VF.[6] In a series of 23 patients supported with a continuous-flow LVAD for a mean of 341 days, three patients experienced haemodynamic compromise during VT/VF.[7] Three studies have reported an association between VT/VF during LVAD support and increased mortality, although this does not indicate a causal relationship.[4,5,12]

In contrast, there are reports of LVAD patients who tolerate VT/VF remarkably well. In nine patients with a pulsatile-flow LVAD, VT/VF lasting up to 12 days caused weakness and palpitations but no syncope. There was a reduction in device flow, but no thrombo-embolic events or end-organ dysfunction.[2] In 32 patients with a pulsatile-flow LVAD, laboratory markers of inadequate systemic perfusion or right-sided heart failure were unchanged after termination of VT/VF.[4] In a remarkable case report, a 24-year-old female with a pulsatile-flow LVAD was in sustained VF for 15 months before cardiac transplantation.[17] Despite concern that continuous-flow LVADs may be less effective at supporting circulation in patients without an intrinsic rhythm, HeartMate II LVADs have supported a patient in VF for 12 h before defibrillation[18] and a patient in asystole for 2 months before cardiac transplantation.[19] In such cases, a low pulmonary vascular resistance is thought to be necessary to allow a Fontan-like circulation.

Clinical trial data suggest that sudden arrhythmic death in LVAD patients is rare. In REMATCH, there were 41 deaths in the LVAD group. The incidence of fatal VT/VF was not detailed, although 37 of 41 deaths were clearly attributable to a non-arrhythmic cause.[3] Similar findings were reported in the HeartMate II registry. There were 56 deaths during LVAD support in 18 months of follow-up, of which 50 deaths were clearly attributable to a non-arrhythmic cause.[9] Importantly, these trials do not describe the extent to which patients may have been protected from sudden death by an ICD.

How many patients with left ventricular assist devices have an implantable cardioverter defibrillator?

LVAD support may be used as a bridge to recovery, a bridge to transplantation, or destination therapy in patients with severe heart failure, impending cardiogenic shock, and/or multiorgan failure.[20] Many of these patients have longstanding chronic heart failure and have previously received an ICD for primary or secondary prevention, leading to a significant overlap in device use. An ICD was present at baseline in 163 of 200 (82%) patients in the HeartMate II trial[8] and 213 of 281 (75%) patients in the HeartMate II registry.[9] There appears to be an evolving trend to implant primary prevention ICDs in patients who already have an LVAD. Two European centres have described 78 patients with ICDs and continuous-flow LVADs; 50 (64%) of these patients received an ICD after LVAD implantation.[7,13] A single American centre described 61 patients with ICDs and continuous-flow LVADs; 12 (20%) of these patients received an ICD after LVAD implantation.[21]

How much implantable cardioverter defibrillator therapy do left ventricular assist device patients receive?

The burden of ICD therapy has been described in six series of LVAD patients (*Table 2*)[7,11–13,22,23] and one series of patients with either left, right, or biventricular assist devices.[24] There was considerable variation in the burden of ICD therapy, with appropriate therapy in 12–41% of patients and inappropriate therapy in 4–25% of patients, despite short periods of follow-up. Many patients had multiple shocks. ATP was successful in treating 25–50% of VT/VF.[7,24] There was no difference in the burden of ICD therapy between continuous-flow and pulsatile-flow LVADs.[11] LVAD patients with previous VT/VF and secondary prevention ICDs were twice as likely to receive ICD shocks than those with primary prevention ICDs.[12,13,24] ICD therapy is normally considered 'appropriate' when delivered for a sustained VT/VF, although 'appropriateness' is questionable in the context of LVAD patients, given the uncertain association between sustained VT/VF and sudden death.

Table 2 Appropriate and inappropriate therapy received by left ventricular assist device patients with implantable cardioverter defibrillators

Source	Patients	Follow-up	LVAD (*n*)	ICD (*n*)	Appropriate ICD therapy	Inappropriate ICD therapy
Andersen[7] 2009	17	Mean 326 days	HeartMate II (17)	Unspecified	7 (41%) patients received unknown number of appropriate therapies	1 (6%) patient received unknown number of inappropriate shocks
Kuhne[11] 2010	76	Median 156 days	HeartMate VE (15), HeartMate XVE (34), HeartMate IP-1000 (1), Thoratec IVAD (3), HeartMate II (22), Micromed DeBakey (1)	Medtronic (28), Boston (42), Biotronik (3), St Jude (3)	9 (12%) patients received 43 appropriate therapies	3 (4%) patients received 11 inappropriate therapies
Ambardekar[22] 2010	33	Mean 238 days	HeartMate XVE (16), HeartMate II (15), unspecified (2)	Medtronic (18), Boston (11), Biotronik (3), St Jude (1)	8 (24%) patients received unknown number of appropriate shocks	6 (18%) patients received unknown number of inappropriate shocks
Oswald[13] 2010	61	Median 12 months	HeartMate II (44), Heartware (17)	Unspecified	21 (34%) patients received 144 appropriate therapies (102 ATP and 42 shocks)	15 (25%) patients received unknown number of inappropriate therapies
Brenyo[12] 2011	61	Mean 622 days	HeartMate II (58), Jarvik 2000 (3)	Medtronic (38), Boston (17), St Jude (6)	19 (31%) patients received unknown number of appropriate therapies	4 (7%) patients received unknown number of inappropriate shocks
Refaat[23] 2012	33	Mean 119 days	Thoratec LVAD (7), Novacor LVAD (14), HeartMate XVE (12)	Unspecified	7 (21%) patients received unknown number of appropriate shocks	Not described

ICD therapy refers to the combination of ATP and shocks; the specific type of ICD therapy is detailed when known.
ATP, antitachycardia pacing; ICD, implantable cardioverter defibrillator; LVAD, left ventricular assist device; VF, ventricular fibrillation; VT, ventricular tachycardia.

Do implantable cardioverter defibrillators reduce mortality in left ventricular assist device patients?

This critical question has not been addressed in a prospective, randomized controlled trial. Limited observational data are available. Two studies suggest that a pre-existing ICD may confer a survival benefit after LVAD implantation. An ICD was associated with increased survival in a multivariable analysis of 144 LVAD patients, 45 of whom had an ICD (odds ratio 2.72, 95% CI 1.03–7.16; $P = 0.04$).[23] In a similar study that included both a multivariable and a propensity-matched analysis, an ICD was associated with lower all-cause mortality in 478 VAD patients, 90 of whom had an ICD (hazard ratio 0.55, 95% CI 0.32–0.94; $P = 0.028$).[24] However, this study combined patients with left, right, and biventricular assist devices despite potentially important differences in their ability to support patients without an intrinsic rhythm. Both studies are susceptible to selection bias; ICDs may be more likely to be implanted in subjects with a better prognosis.

What are the risks of implantable cardioverter defibrillator use in patients with left ventricular assist devices?

Adverse effects with ICDs have been reported in three series of consecutive LVAD patients. In a series of 15 patients with a VentrAssist LVAD and a pre-existing ICD, LVAD placement caused a significant increase in right ventricular (RV) stimulation threshold and a reduction in R-wave sensing, but no VT/VF undersensing. The need for ICD revision was not described. During follow-up, two patients had shock-refractory VT/VF due to high defibrillation thresholds and one patient had an inappropriate shock due to electromagnetic interference.[25] In a series of 61 patients with a HeartMate II or Heartware LVAD, 14 (23%) patients required ICD revision for problems including loss of ICD telemetry ($n = 4$), ICD generator depletion ($n = 4$), RV lead failure ($n = 3$), and haematoma ($n = 3$).[13] In a series of 76 patients with several types of LVAD, two patients required ICD revision for loss of telemetry after implantation of a HeartMate II LVAD and six patients were hospitalized for ICD-related problems including generator depletion ($n = 4$) and haematoma ($n = 2$).[11] Loss of telemetry appears to be confined to ICDs which use an 8 kHz operating frequency, close to the 7.2 kHz frequency of the HeartMate II pulse width modulator; details of this interaction are described on the manufacturer's website.[26]

ICD revision procedures are associated with a risk of infection.[27] This is a particular concern for LVAD patients, for whom system infection represents one of the most frequent and serious complications.[9] The incidence of infection in LVAD patients after ICD revision has not been described in the published case series.

Should primary prevention implantable cardioverter defibrillators be implanted in left ventricular assist device patients?

Patients with an LVAD were not represented in randomized controlled trials of primary prevention ICDs. No study has prospectively investigated whether or not patients who do not have an ICD before LVAD implantation should have an ICD implanted subsequently. Implantation of a primary prevention ICD after LVAD implantation is not addressed by European Society of Cardiology guidelines on device use.[28] Any potential benefit must be balanced against the uncertain risk of complications. Infection is a particular concern and could be a catastrophic in LVAD patients. We believe that the risk–benefit ratio should be examined in a prospective, randomized controlled trial before implantation of primary prevention ICDs can be recommended after LVAD implantation.

How should implantable cardioverter defibrillators be programmed in left ventricular assist device patients?

Where an ICD is already *in situ*, there is little evidence to guide programming after LVAD implantation. Most ICDs detect VT/VF and deliver shock therapy before loss of consciousness. Consequently, ICD shocks are painful and associated with reduced quality of life.[29] LVAD patients may have a high burden of non-sustained VT, especially in the early post-operative period. Sustained VT/VF may be well tolerated, at least in the short term, and refractory to ICD therapy. Frequent ICD shocks will contribute to premature generator depletion.

One group suggested that LVAD patients who develop VT/VF should be assessed for haemodynamic compromise and those with decreased LVAD flow or acute right heart failure should be treated with cardioversion.[4] This approach is incompatible with an ICD that will make decisions solely on the basis of heart rate and supraventricular tachycardia discriminators. Two groups have reported ICD programming in their LVAD patients; one used standard programming and one used long detection periods of 10 s for VT and 3 s for VF to reduce the chance of ICD therapy for non-sustained VT.[11,13] Longer detection periods reduced ICD shocks without altering clinical outcome in two trials of ICD programming for patients that did not have LVADs.[30,31] However, these detection periods are still shorter than the programmable maximum for many ICDs.

We believe that ICD therapy should be tailored to individual patients. We considered electrophysiological (EP) testing to assess the haemodynamic consequences of VT/VF and ensure a safe defibrillation threshold, but decided against this due to the absence of evidence to support EP testing in this situation and concern about potential adverse events. We elected empirically to program high zone boundaries, the longest programmable

detection times, ATP as sole therapy within a single VT zone, and ATP before shocks in the VF zone.

Conclusions

Patients receiving LVAD support are at high risk of sustained ventricular arrhythmias but these may not cause sudden death. Whilst it is standard practice to reactivate a previously implanted ICD in an LVAD recipient, this should include discussion of the revised risks and benefits of ICD therapy following LVAD implantation. In particular, patients should be warned that they might receive a significant number of ICD shocks that may not be life saving. When ICDs are reactivated, device programming should minimize the risk of repeated shocks for non-sustained or well-tolerated ventricular arrhythmias. Implantation of a primary prevention ICD after implantation of an LVAD is not supported by current evidence, poses potential risks, and should be the subject of a clinical trial before it becomes standard practice.

Conflict of interest: none declared.

References

1. Arai H, Swartz MT, Pennington DG, Moriyama Y, Miller L, Peigh P, McBride L. Importance of ventricular arrhythmias in bridge patients with ventricular assist devices. *ASAIO Trans* 1991;**37**:M427–M428.
2. Oz MC, Rose EA, Slater J, Kuiper JJ, Catanese KA, Levin HR. Malignant ventricular arrhythmias are well tolerated in patients receiving long-term left ventricular assist devices. *J Am Coll Cardiol* 1994;**24**:1688–1691.
3. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL, Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;**345**:1435–1443.
4. Ziv O, Dizon J, Thosani A, Naka Y, Magnano AR, Garan H. Effects of left ventricular assist device therapy on ventricular arrhythmias. *J Am Coll Cardiol* 2005;**45**:1428–1434.
5. Bedi M, Kormos R, Winowich S, McNamara DM, Mathier MA, Murali S. Ventricular arrhythmias during left ventricular assist device support. *Am J Cardiol* 2007;**99**:1151–1153.
6. Refaat M, Chemaly E, Lebeche D, Gwathmey JK, Hajjar RJ. Ventricular arrhythmias after left ventricular assist device implantation. *Pacing Clin Electrophysiol* 2008;**31**:1246–1252.
7. Andersen M, Videbaek R, Boesgaard S, Sander K, Hansen PB, Gustafsson F. Incidence of ventricular arrhythmias in patients on long-term support with a continuous-flow assist device (HeartMate II). *J Heart Lung Transplant* 2009;**28**:733–735.
8. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatooles AJ, Delgado RM, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH, HeartMate II Investigators. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009;**361**:2241–2251.
9. Pagani FD, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ, Conte JV, Bogaev RC, MacGillivray TE, Naka Y, Mancini D, Massey HT, Chen L, Klodell CT, Aranda JM, Moazami N, Ewald GA, Farrar DJ, Frazier OH, HeartMate II Investigators. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. *J Am Coll Cardiol* 2009;**54**:312–321.
10. Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA, Ulisney KL, Baldwin JT, Young JB. Second INTERMACS annual report: more than 1,000 primary left ventricular assist device implants. *J Heart Lung Transplant* 2010;**29**:1–10.
11. Kühne M, Sakumura M, Reich SS, Sarrazin J-F, Wells D, Chalfoun N, Crawford T, Boonyapisit W, Horwood L, Chugh A, Good E, Jongnarangsin K, Bogun F, Oral H, Morady F, Pagani F, Pelosi F. Simultaneous use of implantable cardioverter-defibrillators left ventricular assist devices in patients with severe heart failure. *Am J Cardiol* 2010;**105**:378–382.
12. Brenyo A, Rao M, Koneru S, Hallinan W, Shah S, Massey HT, Chen L, Polonsky B, McNitt S, Huang DT, Goldenberg I, Aktas M. Risk of Mortality for Ventricular Arrhythmia in Ambulatory LVAD Patients. *J Cardiovasc Electrophysiol*;in press.
13. Oswald H, Schultz-Wildelau C, Gardiwal A, Lüsebrink U, König T, Meyer A, Duncker D, Pichlmaier MA, Klein G, Strüber M. Implantable defibrillator therapy for ventricular tachyarrhythmia in left ventricular assist device patients. *Eur J Heart Fail* 2010;**12**:593–599.
14. Boyle A. Arrhythmias in patients with ventricular assist devices. *Curr Opin Cardiol* 2012;**27**:13–18.
15. Harding JD, Piacentino V, Rothman S, Chambers S, Jessup M, Margulies KB. Prolonged repolarization after ventricular assist device support is associated with arrhythmias in humans with congestive heart failure. *J Card Fail* 2005;**11**:227–232.
16. Ambardekar AV, Buttrick PM. Reverse remodeling with left ventricular assist devices: a review of clinical, cellular, and molecular effects. *Circ Heart Fail* 2011;**4**:224–233.
17. Nishimura M, Ogiwara M, Ishikawa M, Yatsu S, Masuoka A, Okamura N, Imanaka K, Kato M, Asano H, Kyo S. Fifteen-month circulatory support for sustained ventricular fibrillation by left ventricular assist device. *J Thorac Cardiov Sur* 2003;**126**:1190–1192.
18. Sims DB, Rosner G, Uriel N, Gonzalez-Costello J, Ehlert FA, Jorde UP. Twelve hours of sustained ventricular fibrillation supported by a continuous-flow left ventricular assist device. *Pacing Clin Electrophysiol*;in press.
19. Felix SEA, Martina JR, Kirkels JH, Klopping C, Nathoe H, Sukkel E, Hulstein N, Ramjankhan FZ, Doevendans PAFM, Lahpor JR, de Jonge N. Continuous-flow left ventricular assist device support in patients with advanced heart failure: points of interest for the daily management. *Eur J Heart Fail* 2012;**14**:351–356.
20. Lund LH, Matthews J, Aaronson K. Patient selection for left ventricular assist devices. *Eur J Heart Fail* 2010;**12**:434–443.
21. Brenyo A, Link MS, Barsheshet A, Moss AJ, Zareba W, Wang PJ, McNitt S, Huang D, Foster E, Estes M, Solomon SD, Goldenberg I. Cardiac resynchronization therapy reduces left atrial volume and the risk of atrial tachyarrhythmias in MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). *J Am Coll Cardiol* 2011;**58**:1682–1689.
22. Ambardekar AV, Allen LA, Lindenfeld J, Lowery CM, Cannon AP, Cleveland JC, Brieke A, Sauer WH. Implantable cardioverter-defibrillator shocks in patients with a left ventricular assist device. *J Heart Lung Transplant* 2010;**29**:771–776.
23. Refaat MM, Tanaka T, Kormos RL, McNamara D, Teuteberg J, Winowich S, London B, Simon MA. Survival benefit of implantable cardioverter-defibrillators in left ventricular assist device-supported heart failure patients. *J Card Fail* 2012;**18**:140–145.
24. Cantillon DJ, Tarakji KG, Kumbhani DJ, Smedira NG, Starling RC, Wilkoff BL. Improved survival among ventricular assist device recipients with a concomitant implantable cardioverter-defibrillator. *Heart Rhythm* 2010;**7**:466–471.
25. Foo D, Walker BD, Kuchar DL, Thorburn CW, Tay A, Hayward CS, Macdonald P, Keogh A, Kotlyar E, Spratt P, Jansz P. Left ventricular mechanical assist devices and cardiac device interactions: an observational case series. *Pacing Clin Electrophysiol* 2009;**32**:879–887.
26. Thoratec Corporation. Reported ICD experience. http://www.thoratec.com/medical-professionals/reported-icd-experience.aspx (accessed 21 March 2012)
27. Johansen JB, Jørgensen OD, Møller M, Arnsbo P, Mortensen PT, Nielsen JC. Infection after pacemaker implantation: infection rates risk factors associated with infection in a population-based cohort study of 46299 consecutive patients. *Eur Heart J* 2011;**32**:991–998.
28. Authors/Task Force Members, Dickstein K, Vardas PE, Auricchio A, Daubert J-C, Linde C, McMurray J, Ponikowski P, Priori SG, Sutton R, Van Veldhuisen DJ, ESC Committee for Practice Guidelines (CPG), Vahanian A, Auricchio A, Bax J, Ceconi C, Dean V, Filippatos G, Funck-Brentano C, Hobbs R, Kearney P, McDonagh T, Popescu BA, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Vardas P, Widimsky P, Document Reviewers, Tendera M, Anker SD, Blanc JJ, Gasparini M, Hoes AW, Israel CW, Kalarus Z, Merkely B, Swedberg K, Camm AJ. 2010 Focused Update of ESC Guidelines on device therapy in heart failure: an update of the 2008 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. Developed with the special contribution of the Heart Failure Association and the European Heart Rhythm Association. *Eur Heart J* 2010;**31**:2677–2687.
29. Mark DB, Anstrom KJ, Sun JL, Clapp-Channing NE, Tsiatis AA, Davidson-Ray L, Lee KL, Bardy GH, Sudden Cardiac Death in Heart Failure Trial Investigators. Quality of life with defibrillator therapy or amiodarone in heart failure. *N Engl J Med* 2008;**359**:999–1008.
30. Wilkoff BL, Williamson BD, Stern RS, Moore SL, Lu F, Lee SW, Birgersdotter-Green UM, Wathen MS, Van Gelder IC, Heubner BM, Brown ML, Holloman KK, PREPARE Study Investigators. Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators

reduces shocks in primary prevention patients: results from the PREPARE (Primary Prevention Parameters Evaluation) study. *J Am Coll Cardiol* 2008;**52**: 541–550.
31. Gasparini M, Menozzi C, Proclemer A, Landolina M, Iacopino S, Carboni A, Lombardo E, Regoli F, Biffi M, Burrone V, Denaro A, Boriani G. A simplified biventricular defibrillator with fixed long detection intervals reduces implantable cardioverter defibrillator (ICD) interventions and heart failure hospitalizations in patients with non-ischaemic cardiomyopathy implanted for primary prevention: the RELEVANT [Role of long dEtection window programming in patients with LEft VentriculAr dysfunction, Non-ischemic eTiology in primary prevention treated with a biventricular ICD] study. *Eur Heart J* 2009;**30**:2758–2767.