

Consider Deactivating ICD Near End of Life

BY SHERRY BOSCHERT
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SAN FRANCISCO — One reason that few implantable cardioverter defibrillators get shut off to prevent a painful, unnecessary shock near the end of a patient's life is that physicians disagree about who should begin the deactivation discussion, Dr. Amy S. Kelley said.

In addition, some physicians prefer further aggressive medical treatments and

postpone discussing deactivation of implantable cardioverter defibrillators (ICDs), according to a survey mailed to 4,876 physicians and completed by 558. Inadequate knowledge about or awareness of ICDs also contributed to physicians' lack of attention to the issue, Dr. Kelley reported in a poster presentation at the annual meeting of the Gerontological Society of America.

"People at the bedside caring for a dying patient—internists and palliative care physicians—may not be familiar with how the ICD works, and the fact that they are very easy to deactivate," said Dr. Kelley of the University of California, Los Angeles. "Even if it's functioning as a pacemaker, the shut-off function is entirely separate and could be deactivated in a moment's time at the bedside with a magnet and an electrophysiologist or even a nurse."

The 96 general internists, 106 cardiologists, 163 geriatricians, and 193 electrophysiologists surveyed were asked if they would discuss ICD deactivation, advance directives, and do not resuscitate (DNR) orders with terminally ill patients described in five vignettes. (See box.) The survey also solicited comments, and investigators analyzed 310 comments provided by 177 physicians to identify recurrent themes.

Of the 177 who commented, 6% said they had never thought about deactivating an ICD, 2% were unaware of the separate pacer and defibrillator functions, and 1% declared a lack of knowledge about defibrillators, reported Dr. Kelley and her associates. Overall, 21% of the commenters expressed a preference for further medical

treatments (including medications, devices, and procedures) over ICD deactivation.

Of the 177, 13% accepted primary responsibility for initiating discussions about deactivating pacemakers, 10% said another specialist should start the discussion, and 7% said the patient or family should bring it up first.

"As a geriatrician and a primary care provider, if I'm ready to discuss other end-of-life topics with a patient or with the family, this would be on my list of things to discuss," Dr. Kelley said. "I want them to know they have the option to possibly pass quietly from arrhythmia versus the possibility of being shocked."

Data from a previous retrospective study that surveyed next of kin after a patient's death suggest that fewer than a fourth of ICDs get deactivated near the end of life, and then only after the patient suffered a painful shock from the device, she said.

Informed consent for ICD implantation should include information about deactivation options, 77% of physicians in the current survey agreed. A majority (58%) said that guidance from experts regarding management of patients with ICDs would be helpful. There are no guidelines for managing the deactivation of ICDs.

The study has been accepted for publication in the *American Journal of Geriatric Cardiology*, Dr. Kelley said.

In two of the patient vignettes, physicians who said they had no religious affiliation were more likely to discuss ICD deactivation with patients. ■

Most Physicians Willing to Talk

In the following scenarios, the percentages indicate how many of 558 surveyed physicians would discuss ICD deactivation, advance directives, or DNR orders with patients.

► A man with severe chronic obstructive pulmonary disease who reports a poor quality of life:

ICD deactivation: 56%
Advance directives: 88%
DNR: 82%

► A man with advanced dementia who is agitated by medical tests:

ICD deactivation: 71%
Advance directives: 84%
DNR: 84%

► A woman with stage IV ovarian cancer who requests palliative care:

ICD deactivation: 79%
Advance directives: 94%
DNR: 93%

► A man with end-stage renal failure who declines dialysis:

ICD deactivation: 76%
Advance directives: 90%
DNR: 90%

► A woman with a massive stroke whose family requests ventilator withdrawal:

ICD deactivation: 83%
Advance directives: 80%
DNR: 83%

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(3% and <1%); Anorgasmia (2% and <1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo \geq Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflamed injury, anxiety. *Primarily ejaculatory delay. †Denominator used was for males only (N=225 Lexapro; N=188 placebo). ‡Denominator used was for females only (N=490 Lexapro; N=404 placebo). **Generalized Anxiety Disorder Table 3** enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see TABLE 3). **TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder (Lexapro (N=429) and Placebo (N=427)).** **Autonomic Nervous System Disorders:** Dry Mouth (3% and 5%); Sweating Increased (4% and 1%); **Central & Peripheral Nervous System Disorders:** Headache (24% and 17%); Paresthesia (2% and 1%); **Gastrointestinal Disorders:** Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Flatulence (2% and 1%); Toothache (2% and 0%); **General:** Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%); **Musculoskeletal:** Neck/Shoulder Pain (3% and 1%); **Psychiatric Disorders:** Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%); **Urogenital:** Ejaculation Disorder^{1,2} (14% and 2%); Anorgasmia (6% and <1%); Menstrual Disorder (2% and 1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo \geq Lexapro: inflamed injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=182 Lexapro; N=195 placebo). §Denominator used was for females only (N=247 Lexapro; N=232 placebo). **Dose Dependency of Adverse Events** The potential dose dependency of common adverse events (defined as an incidence rate of $\geq 5\%$ in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). **TABLE 4: Incidence of Common Adverse Events in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=310).** **Insomnia** (4%, 7%, 14%); **Diarrhea** (5%, 6%, 14%); **Dry Mouth** (3%, 4%, 9%); **Somnolence** (1%, 4%, 9%); **Dizziness** (2%, 4%, 7%); **Sweating Increased** (<1%, 3%, 8%); **Constipation** (1%, 3%, 6%); **Fatigue** (2%, 2%, 6%); **Indigestion** (1%, 2%, 6%). *Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. **Male and Female Sexual Dysfunction with SSRIs** Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experiences and performance cited in product labeling are likely to underestimate their actual incidence. **TABLE 5** shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. **TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials (In Males Only: Lexapro (N=407) and Placebo (N=383)); Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (6% and 2%); Impotence (2% and <1%). (In Females Only: Lexapro (N=737) and Placebo (N=639)); Libido Decreased (3% and 1%); Anorgasmia (3% and <1%).** There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priligis has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes** Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes** Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.2 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Events Observed During the Premarketing Evaluation of Lexapro** Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the **ADVERSE REACTIONS** section, reported by the 1429 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in **Tables 2 & 3**, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1000 patients; cardiovascular - frequent: palpitation, hypertension; infrequent: bradycardia, tachycardia, ECG abnormal, flushing, varicose vein; Central and Peripheral Nervous System Disorders - frequent: light-headed feeling, migraine; infrequent: tremor, vertigo, restless legs, shaking, twitching, dysequilibrium, tics, carpal tunnel syndrome, muscle contractions/involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased; Gastrointestinal Disorders - frequent: heartburn, abdominal cramp, gastroenteritis; infrequent: gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult; General - frequent: allergy, pain in limb, fever, hot flushes, chest pain; infrequent: edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall; Hematologic and Lymphatic Disorders - frequent: bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical; Metabolic and Nutritional Disorders - frequent: increased weight; infrequent: decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia; Musculoskeletal System Disorders - frequent: arthralgia, myalgia; infrequent: jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness; Psychiatric Disorders - frequent: appetite increased, lethargy, irritability, concentration impaired; infrequent: jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruising, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency; Reproductive Disorders/Female - frequent: menstrual cramps, menstrual disorder; infrequent: menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses; *% based on female subjects only; †N=305 Respiratory System Disorders - frequent: bronchitis, sinus congestion, coughing, nasal congestion, sinus headache; infrequent: asthma, breath shortness, laryngitis, pneumonia, tracheitis; Skin and Appendages Disorders - frequent: rash; infrequent: pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodule; Special Senses - frequent: vision blurred, tinnitus; infrequent: taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste; Urinary System Disorders - frequent: urinary frequency, urinary tract infection; infrequent: urinary urgency, kidney stone, dysuria, blood in urine. **Events Reported Subsequent to the Marketing of Escitalopram** - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post marketing experience and were not observed during the premarketing evaluation of escitalopram: abnormal gait, acute renal failure, aggression, akathisia, allergic reaction, anger, angioedema, atrial fibrillation, chorea-thetosis, delirium, delusion, diplopia, dysarthria, dyskinesia, dystonia, echymosis, erythema multiforme, extrapyramidal disorders, fulminant hepatitis, hepatic failure, hypoesthesia, hypocoercemia, hypokalemia, INR increased, gastrointestinal hemorrhage, glaucoma, grand mal seizures (or convulsions), hemolytic anemia, hepatic necrosis, hepatitis, hypotension, leucopenia, myocardial infarction, myoclonus, neuroleptic malignant syndrome, nightmare, nystagmus, orthostatic hypotension, pancreatitis, paranoia, photosensitivity reaction, priapism, prolactinemia, prothrombin decreased, pulmonary embolism, QT prolongation, rhabdomyolysis, seizures, serotonin syndrome, SIADH, spontaneous abortion, Stevens Johnson Syndrome, tardive dyskinesia, thrombocytopenia, thrombosis, torsade de pointes, toxic epidermal necrolysis, ventricular arrhythmia, ventricular tachycardia and visual hallucinations.

Medtronic Defibrillator Lead Recall Underway

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Medtronic Inc.'s decision to voluntarily recall all Sprint Fidelis defibrillator leads was announced "because of the potential for lead fractures," but recommended against replacing leads with no apparent problems.

The company identified five deaths "in which a Sprint Fidelis lead fracture may have been a possible or likely contributing factor," Medtronic said in a statement announcing the recall. The clinical signs of lead fractures can include audible alerts, inappropriate shocks, and/or loss of output.

The leads are used with defibrillators, including implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds). Patients with Medtronic pacemakers are not affected. About 268,000 of these leads (models 6930, 6931, 6948, and 6949) have been implanted worldwide, the company said.

Medtronic has data showing that at 30 months, the viability of the Sprint Fidelis lead is lower than that of the company's Sprint Quattro lead (97.7% vs. 99.1%), which is not statistically different. However, "if the current lead fracture rates become significant over time, the statement said.

The Medtronic statement explains that the company, its independent panel of physicians, and Dr. Bruce Lindsay, professor of medicine and director of cardiac electrophysiology at Washington University, St. Louis, who is also president of the Heart Rhythm Society, "do not recommend that patients seek prophylactic replacement of Sprint Fidelis leads, as the risks of removal or insertion of another lead exceed the small risk to patients of a lead fracture."

The letter to physicians points out that lead extraction carries risks "that should be considered in patient management," and that published literature "suggests major complications (death or surgical intervention) from lead extraction range from 1.4% [to] 7.3%. As always, with confirmed lead failure, the risk of extraction should be weighed against the risk of adding an additional lead."

In a statement issued by the Food and Drug Administration, Dr. Daniel Schultz, director of the FDA's Center for Devices and Radiological Health, said that based on the agency's initial review of reported adverse events, some deaths and major complications have occurred after the leads have fractured.

Although this can be frightening to patients, Dr. Schultz added that "patients can be assured that the likelihood of fracture is very low."

The currently available adverse event data for the leads indicate that fractures have occurred in less than 1% of the approximately 268,000 leads implanted, but whether the rate will increase or remain constant over the life of the leads is unknown, the FDA statement said.

The day after the Medtronic announcement, Sen. Chuck Grassley (R-Iowa) sent a letter to the FDA and Medtronic requesting more information about the recalled leads. And in another letter to the FDA, the public advocacy group, Public Citizen's Health Research Group, requested that the agency conduct an investigation into why the FDA did not compel Medtronic to recall the Sprint Fidelis defibrillator leads earlier this year, when the FDA was aware of "the rapidly mounting number of injury reports" associated with these leads, according to the letter.

The FDA statement says that Medtronic first notified physicians about the lead fracture rate and about the proper method of implantation of the leads in March, and that the decision to suspend marketing of the leads was prompted by "additional data on adverse events" that had accumulated since that time. ■

Medtronic has posted information for physicians and patients at www.medtronic.com/fidelis.