Nonthoracotomy- Versus Thoracotomy-Implantable Defibrillators

Intention-to-Treat Comparison of Clinical Outcomes

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Background Nonthoracotomy-implantable cardioverter/defibrillator (ICD) systems may represent a significant advance in the treatment of patients with life-threatening ventricular arrhythmias, but their merits relative to those of the well-established thoracotomy systems remain largely unknown. The objective of this study was to compare the short- and long-term clinical outcomes after attempted ICD implantation via a nonthoracotomy versus thoracotomy approach in similar groups of patients.

Methods and Results Between September 1990 and December 1992, 212 consecutive patients underwent attempted ICD system implantation without concomitant cardiac surgery at a single institution. Approach selection was not randomized but rather was based primarily on hardware availability. Primary comparisons of short- and long-term outcome were performed according to the "intention-to-treat" principle. Implantation was attempted via a nonthoracotomy approach in 120 patients (57%) and via a thoracotomy approach in 92 patients (43%). Prior cardiac surgery was more prevalent in the nonthoracotomy patients; otherwise, groups did not differ significantly in terms of prognostically relevant clinical characteristics. Nonthoracotomy implantation was successful in 101 patients (84%). After crossover to thoracotomy implantation (14 patients), the eventual success rate for ICD system implantation was 96% in the nonthoracotomy group. Thoracotomy implantation was successful in 89 patients (97%). Operative mortality was 3.3% in the nonthoracotomy and 4.3% in the thoracotomy groups (P=.73). Nonthoracotomy group patients were less likely to experience postoperative congestive heart failure (6% versus 16%; P=.02) or supraventricular arrhythmia (6% versus 18%; P=.004) and had significantly shorter postoperative intensive care and total hospitalization. Total hospital costs were significantly lower in the nonthoracotomy group ($32,205 versus $37,265; P=.001). After a follow-up of 16±9 months, there were 17 deaths in the nonthoracotomy group (none sudden) and 12 deaths in the thoracotomy group (1 sudden). One- and 2-year Kaplan-Meier survival probabilities were .87 (95% CI, .78 to .91) and .80 (95% CI, .68 to .88) in the nonthoracotomy group and .90 (95% CI, .82 to .95) and .87 (95% CI, .77 to .93) in the thoracotomy group (P=.56; log-rank test).

Conclusions Nonthoracotomy ICD implantation is associated with reduced surgical morbidity, postoperative hospital care requirement, and hospital costs and has similar efficacy in preventing sudden death relative to the thoracotomy approach. From these nonrandomized data, it appears that a nonthoracotomy approach should be considered preferable in most patients requiring ICD therapy. (Circulation. 1994;90: 2833-2842.)

Key Words • electric stimulation • defibrillation • arrhythmia • tachycardia

The implantable cardioverter/defibrillator (ICD) has dramatically reduced the incidence of sudden cardiac death in patients with life-threatening ventricular tachyarrhythmias.1-3 Since its initial clinical use in 1980,4 ICD system technology has evolved significantly. New tiered-therapy ICDs not only are capable of defibrillation but also can provide low-energy cardioversion and antitachycardia and antibradycardia pacing.5-8 The lead systems used in interfacing the generator to the heart have evolved similarly. Early experiences with nonthoracotomy defibrillating lead systems9,10 were fraught with problems of poor lead reliability,11 but continued research and development in this area resulted in the availability of several promising nonthoracotomy lead systems for clinical application.12-15 It has been suggested that, compared with the conventional thoracotomy approach, the emerging nonthoracotomy lead technology decreases operative morbidity and mortality16-18 without compromising the long-term efficacy of defibrillator therapy. However, the relative merits of the two approaches have not been assessed in a large series of consecutive patients. In this study, we compare the short- and long-term clinical results of ICD systems implanted via a nonthoracotomy or a thoracotomy approach in similar groups of patients using an "intention-to-treat" principle.19 This pragmatic form of analysis provides the practitioner with information on outcomes that can be readily integrated into the clinical decision-making process.

Methods

Patient Population

The study population is composed of 212 consecutive patients who underwent an initial attempt at ICD implantation without concomitant cardiac surgery between September 11, 1990, and December 31, 1992. Ten previously reported patients who underwent implantation of an earlier, no longer available, nonthoracotomy lead system are not included in this analysis.20 Indications for ICD implantation agreed with those...
generally accepted.20 Patients gave informed written consent before implantation. Protocols for the implantation and follow-up of investigational ICD systems were approved by the Institutional Review Board of the Cleveland Clinic Foundation.

ICD System Selection

Epicardial defibrillating patches and sutureless epimyocardial rate-counting/pacing leads were supplied by various manufacturers (Cardiac Pacemakers, Inc; DAIG Corp; Intermedics, Inc; Medtronic, Inc; Telectronics Pacing Systems; and Ventritex, Inc). Three investigational nonthoracotomy lead systems were used during the course of the study. The Endotak C lead system (Cardiac Pacemakers) consists of a tripolar, passive-fixation, dual-coil lead that can perform defibrillating, morphology and rate sensing, and pacing functions. An extrathoracic (subcutaneous or submuscular) defibrillating patch may also be added to provide for a bidirectional defibrillating current pathway.13 The Transvene lead system (Medtronic) is composed of a tripolar, active-fixation, single-coil, right ventricular lead that provides pacing and sensing functions and serves as one electrode in the defibrillating pathway. A transvenous, single-coil lead (positioned in the superior vena cava or coronary sinus) and an extrathoracic patch electrode complete the defibrillating pathway.15 The Transvenous model 497-05 implantable defibrillator pacing lead (Intermedics) is a bipolar, active-fixation, single-coil lead providing sensing, pacing, and when used in combination with an extrathoracic patch electrode, defibrillating capability.

Non-tiered-therapy ICD generators implanted during the study period included Ventak AICD (Cardiac Pacemakers) 1550 (n=46) and 1555 (n=14), Ventak P AICD 1600 (Cardiac Pacemakers) (n=34), and Guardian 4203 (Telectronics) (n=1). Tiered-therapy generators included Ventak PRx AICD 1700/1705 (Cardiac Pacemakers) (n=17), PCD 7216A/7217B (Medtronic) (n=64), Cadence V100 (Ventritex) (n=17), Res-Q ACD 101-01 (Intermedics) (n=8), and Guardian ATP 4210 (Telectronics) (n=3). Characteristics of the devices have been reviewed recently.21

No attempt was made to randomize patients to undergo a thoracotomy or nonthoracotomy approach or to receive lead systems or generators from the different manufacturers. The selection of the operative approach was generally based on hardware availability. However, a nonthoracotomy approach was preferred in patients with a history of prior cardiac surgery. Tiered-therapy generators were preferentially implanted in patients who presented with sustained monomorphic ventricular tachycardia, clinically significant bradyarrhythmias, or both.

Implant Procedures

Antiarrhythmic drug therapy was discontinued before implantation if it was anticipated to be unnecessary afterward. All procedures were performed under general anesthesia administered by cardiac anesthesiologists. Standard techniques were used for implantation and testing of epicardial lead systems.22 A limited thoracotomy via a subxiphoid approach was generally used in patients without prior cardiac surgery. A lateral thoracotomy was preferred in patients with previous cardiac surgery.

Nonthoracotomy ICD systems were implanted by cardiac electrophysiologists. Techniques for insertion of the various lead systems have been reported.10,12,15 Access to the venous system was via subclavian vein puncture. A retained guide wire technique24 was used when needed to insert a second lead. Testing of defibrillation capabilities was performed according to the different investigational protocols, which generally required the demonstration of a margin of safety of ≥10 J between the defibrillation threshold and the maximal generator output. In an effort to obtain reliable defibrillation with nonthoracotomy systems, changes in electrode number and position, energy-pulsing method, and defibrillation shock pulse width were tested as clinically appropriate.25 Patients in whom reliable defibrillation was not achieved with the nonthoracotomy lead system were offered thoracotomy ICD system implantation. This crossover procedure was performed on the same day in the initial two patients. Thereafter, it was performed at a later time (range, 1 to 13 days).

Postoperatively, patients undergoing thoracotomy ICD implant were observed in a surgical intensive care unit at least overnight. Patients with uncomplicated nonthoracotomy ICD implant were generally observed ≤6 hours in a postanesthesia recovery unit or surgical intensive care unit before transfer to a telemetry ward. Of patients discharged alive, 96% underwent a predischARGE electrophysological evaluation of their ICD systems to ensure appropriate function, including, when necessary, the design of an effective antitachycardia pacing “prescription.”

Definitions

Definitions used are in accord with the recommendations of the North American Society of Pacing and Electrophysiology.26 Death was classified as operative (death within 30 days of attempted implant or before hospital discharge or the direct result of an ICD-related complication), sudden cardiac (death within 1 hour after the onset of acute symptoms or an unexpected, unwitnessed death), nonsudden cardiac, or noncardiac.

Postoperative exacerbation of congestive heart failure was defined by the need for the initiation of or increase in diuretic therapy, inotropic therapy, or both. Postoperative supraventricular arrhythmias were defined by their sustained occurrence (requiring treatment) in patients who were in sinus rhythm before surgery. Postoperative ventricular arrhythmias were defined by the occurrence of sustained ventricular tachyarrhythmia or frequent, nonsustained ventricular tachycardia requiring therapy. ICD system infection was defined by erythema, tenderness, and swelling at surgical wounds and the recovery of a causative organism(s) from wound drainage or blood.27

ICD interventions were considered spurious when documented electrocardiographically28,29 or by analysis of RR interval data of stored events30 to have been delivered for supraventricular rhythms or when they occurred in an asymptomatic patient in whom ICD oversensing could be demonstrated shortly thereafter. No attempt was made to further classify nonspurious interventions as appropriate or indeterminate.28

Patient Follow-up

Patients were followed up for 16±9 months (mean±SD). Periodic follow-up was conducted at the Cleveland Clinic Foundation in 71% of patients. The remaining patients were followed up by phone contact with them or their physicians. Follow-up was complete in 99.5% of patients through April 15, 1993. One nonthoracotomy ICD system recipient was lost to follow-up after 26 months and was censored from analysis at time of last contact.

Cost Measurements

Hospital costs for the entire initial admission were downloaded from a commercially available data management system (Transition Systems, Inc), which consists of a detailed accounting system linked to a computerized database. A “bottom-up”31 approach is used to estimate all costs incurred during a hospital admission. Costs are measured by a combination of “microcosting” techniques, including time-motion studies. Costs are categorized as technical or professional, with each category subdivided into direct and indirect. Direct costs included those directly linked to the production of a given service (defibrillator hardware, disposable supplies, pharmaceuticals). Indirect (overhead) costs included those that cannot be directly traced to a given output (eg, electricity, laundry, maintenance, etc).
TABLE 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=212)</th>
<th>Nonthoracotomy (n=120)</th>
<th>Thoracotomy (n=92)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Age, y (median/upper quartile/lower quartile)</td>
<td>64.5/58/71</td>
<td>63.5/58/70</td>
<td>66/59/73</td>
<td>.11*</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>172 (81)</td>
<td>97 (81)</td>
<td>75 (82)</td>
<td>.89†</td>
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<tr>
<td>Coronary artery disease, n (%)</td>
<td>163 (77)</td>
<td>97 (81)</td>
<td>66 (72)</td>
<td>.12†</td>
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<td>NYHA functional class, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>91 (43)</td>
<td>46 (38)</td>
<td>45 (49)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>89 (42)</td>
<td>53 (44)</td>
<td>36 (39)</td>
<td>.09*</td>
</tr>
<tr>
<td>III</td>
<td>28 (13)</td>
<td>17 (14)</td>
<td>11 (12)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>4 (2)</td>
<td>4 (3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest, n (%)</td>
<td>81 (38)</td>
<td>44 (37)</td>
<td>37 (40)</td>
<td>.68†</td>
</tr>
<tr>
<td>SMVT, n (%)</td>
<td>94 (44)</td>
<td>54 (45)</td>
<td>40 (43)</td>
<td>.55†</td>
</tr>
<tr>
<td>Syncope with inducible SMVT, n (%)</td>
<td>16 (8)</td>
<td>10 (8)</td>
<td>6 (7)</td>
<td>.81†</td>
</tr>
<tr>
<td>NSVT with inducible SMVT, n (%)</td>
<td>21 (10)</td>
<td>12 (10)</td>
<td>9 (10)</td>
<td>.93†</td>
</tr>
<tr>
<td>Previous cardiac surgery, n (%)</td>
<td>108 (51)</td>
<td>75 (63)</td>
<td>33 (36)</td>
<td>&lt;.001†</td>
</tr>
<tr>
<td>LV ejection fraction, median/upper quartile/lower quartile</td>
<td>0.30/0.23/0.44</td>
<td>0.30/0.21/0.44</td>
<td>0.30/0.24/0.44</td>
<td>.37*</td>
</tr>
<tr>
<td>Tiered-therapy ICD, n (%)</td>
<td>109 (51)</td>
<td>67 (56)</td>
<td>42 (46)</td>
<td>.13†</td>
</tr>
</tbody>
</table>

NYHA indicates New York Heart Association; SMVT, sustained monomorphic ventricular tachycardia; NSVT, nonsustained ventricular tachycardia; LV, left ventricular; and ICD, implantable cardioverter/defibrillator.

*Mann-Whitney U test; †Fisher’s exact test; *n=82; †n=165; and ‡n=157.

Statistical Analysis

All primary analyses were conducted according to the “intention-to-treat” principle.19 Patients were assigned to the initial approach attempted regardless of success or failure in implanting the ICD system with that approach and regardless of subsequent crossover to the alternative approach or ICD explant. Secondary analyses were performed according to actual treatment received. These analyses differed from the primary “intention-to-treat” analyses in that (1) patients were censored from the initial approach group at time of crossover and were thereafter assigned to the alternative group; (2) patients who did not have an ICD implanted were censored from follow-up after 30 days (to account only for operative morbidity and mortality); and (3) patients who underwent ICD system explantation without system replacement by the end of the study because of infection (1 patient), cardiac transplant (3 patients), or lead fracture secondary to generator “twiddling” with impossibility of regaining access to the central venous system and refusal of thoracotomy (1 patient) had their follow-up censored at the time of ICD explant.

Continuous variables were tested for normal distribution with the Kolmogorov-Smirnov goodness-of-fit test for normality. Because in all cases their observed frequencies differed significantly from the normal distribution, continuous variables were expressed as median, lower, and upper quartiles and were compared by the nonparametric Mann-Whitney U test. Ordered categories (ie, New York Heart Association functional class) were also compared by the Mann-Whitney U test. Discrete variables were compared by Fisher’s exact test. Kaplan-Meier actuarial curves for survival were constructed for patients in each group. Differences in mortality curves were assessed by the log-rank test. A two-tailed value of P≤.05 was considered significant.

Results

Patient Characteristics

The 120 patients (57%) who underwent initial implant attempt via a nonthoracotomy approach compose the nonthoracotomy group. The remaining 92 patients (43%) compose the thoracotomy group. Baseline clinical characteristics are compared in Table 1. Patients in each group did not differ significantly in age, sex, presence of coronary artery disease, New York Heart Association functional class for heart failure, clinical presentation, left ventricular ejection fraction, or use of tiered-therapy ICDs. As expected from the selection criteria, patients in the nonthoracotomy group were significantly more likely to have had prior cardiac surgery.

Operative Results

ICD system implantation was successful with the initial approach in 101 nonthoracotomy patients (84%). Implant failures were the result of high defibrillation thresholds in 18 patients and the presence of a clinically unsuspected left subclavian vein thrombosis in 1 patient. Fourteen of these patients elected to undergo subsequent thoracotomy ICD implantation (crossover), which was successful in all of them. Five patients underwent no further implant attempt: 4 declined additional surgical intervention, and 1 suffered an early operative death. Ultimately, 115 patients (96%) undergoing an initial nonthoracotomy attempt received a successful ICD system.

In the thoracotomy group, surgical access was subxiphoid in 56 patients, lateral thoracotomy in 32, "partial" median sternotomy in 2, and standard median sternotomy in 2. ICD system implantation was successful in 89 patients (97%). In 8 thoracotomy patients (9%), implantation of the complete ICD system required an additional surgical procedure: 5 patients with high defibrillation thresholds required delayed implantation of a high-energy or biphasic waveform–capable generator, 2 patients with inadequate epicardial sensing required the placement of an endocardial sensing lead, and 1 patient experienced incessant ventricular tachyarrhythmia at defibrillation threshold testing, prompting
an aborted procedure. In all cases, the epicardial electrodes were implanted during the initial attempt and buried subcutaneously in the left upper abdominal region. During the second surgical procedure, the appropriate generator or the transvenous lead was implanted. Three patients (3%) in the thoracotomy group did not receive an ICD. In 2, high defibrillation thresholds persisted at the time of attempted delayed implant using the previously implanted epicardial electrodes. In another patient who developed incessant ventricular tachyarrhythmias during the initial implant attempt, further attempts were thought to be unwarranted.

Four operative deaths occurred in each group, resulting in a 3.3% operative mortality in the nonthoracotomy group and 4.3% in the thoracotomy group (P=.73). Two of the deaths in the nonthoracotomy group occurred in patients who did not receive a nonthoracotomy ICD system. Operative deaths are described in Table 2.

Operative Morbidity

Patients in the nonthoracotomy group required a significantly shorter postoperative intensive care unit stay (median, 0 days; lower quartile, 0 days; upper quartile, 1 day) than patients in the thoracotomy group (median, 1 day; lower quartile, 1 day; upper quartile, 1 day) (P<.001, Mann-Whitney U test). Likewise, patients in the nonthoracotomy group required shorter postoperative total hospital stays (median, 5 days; lower quartile, 4 days; upper quartile, 8 days) than patients in the thoracotomy group (median, 7 days; lower quartile, 5 days; upper quartile, 10 days) (P<.001, Mann-Whitney U test). Operative complications are compared in Table 3. Significantly lower incidences of postoperative congestive heart failure and supraventricular arrhythmias were observed in the nonthoracotomy group. These differences persisted in the secondary analysis.

In the nonthoracotomy group, 3 of the patients in the pulmonary complications group had small pneumothoraces that did not require intervention. One patient experienced a hemopneumothorax that required transfusion and thoracoscopic evacuation, 2 patients developed pneumonia (1 after crossover to the thoracotomy approach), and 1 patient developed adult respiratory distress syndrome, also after crossover. All 3 required prolonged mechanical ventilatory support.

### Table 2. Operative Mortality

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>LVEF</th>
<th>POD</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonthoracotomy group (n=4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>68</td>
<td>63</td>
<td>0.35</td>
<td>38</td>
<td>ARDS</td>
<td>After crossover to thoracotomy due to high DFT</td>
</tr>
<tr>
<td>83</td>
<td>56</td>
<td>0.25</td>
<td>20</td>
<td>Pneumonia/sepsis</td>
<td>Severe COPD; no ICD implanted due to high DFT</td>
</tr>
<tr>
<td>93</td>
<td>72</td>
<td>0.28</td>
<td>26</td>
<td>Multigener failure</td>
<td>Repair of aorto-innominate fistula</td>
</tr>
<tr>
<td>101</td>
<td>57</td>
<td>0.42</td>
<td>17</td>
<td>Bradycardia, failure of dual-chamber PPM</td>
<td>Autopsy: no acute findings; device not interrogated</td>
</tr>
</tbody>
</table>

| Thoracotomy group (n=4) | | | | | |
| 22 | 76 | 0.27 | 4 | Pulmonary embolism | Autopsy: multiple acute pulmonary emboli |
| 31 | 79 | 0.30 | 20 | Low-output syndrome/ARF | |
| 45 | 70 | 0.23 | 5 | Asystolic arrest, recurrent VT, ICD discharge, EMD | Internal and external defibrillation ineffective |
| 66 | 69 | 0.23 | 20 | Incessant ventricular tachycardia | Probable drug-induced proarrhythmia |

LVEF indicates left ventricular ejection fraction; POD, postoperative day; ARDS, adult respiratory distress syndrome; DFT, defibrillation threshold; COPD, chronic obstructive pulmonary disease; ICD, implantable cardioverter/defibrillator; PPM, permanent pacemaker; ARF, acute renal failure; VT, ventricular tachycardia; and EMD, electromechanical dissociation.

### Table 3. Operative Morbidity

| Complication | Intention to Treat | | Actual Treatment |
|--------------|-------------------| |ругерозиврач | | |
| Mortality, n (%) | Nonthoracotomy (n=120) | Thoracotomy (n=92) | P | Nonthoracotomy (n=120) | Thoracotomy (n=106) | P |
| Heart failure, n (%) | 4 (4.4) | 4 (4.3) | .73 | 3 (2.5) | 5 (4.7) | .48 |
| SVT, n (%) | 7 (6) | 15 (16) | .02 | 7 (6) | 15 (14) | .026 |
| VT, n (%) | 17 (14) | 12 (13) | .95 | 13 (11) | 17 (16) | .32 |
| Pulmonary, n (%) | 7 (6) | 9 (10) | .30 | 5 (4) | 11 (10) | .11 |
| Bleeding/vascular, n (%) | 5 (4) | 3 (3) | .51 | 5 (4) | 3 (3) | .43 |
| Miscellaneous, n (%) | 2 (2) | 6 (7) | .07 | 2 (2) | 6 (6) | .10 |
| Infection, n (%) | 3 (2) | 5 (5) | .22 | 3 (2) | 5 (5) | .29 |
| Reoperation, n (%) | 28 (23) | 19 (21) | .74 | 28 (23) | 21 (20) | .62 |

SVT indicates supraventricular tachycardia; VT, ventricular tachycardia.
In the thoracotomy group, 1 of the pulmonary complications was a pneumothorax after subxiphoid access requiring chest tube placement, 3 patients experienced pulmonary embolism, 2 patients developed pneumonia, 2 patients developed sepsis-associated adult respiratory distress syndrome, and 1 patient with severe preexisting lung disease developed ventilatory failure. The latter 5 patients required prolonged mechanical ventilatory support.

Vascular complications in the nonthoracotomy group included the creation of an aorto-innominate fistula during vascular sheath/lead placement in 1 patient; the development of axillary, subclavian, cephalic, and jugular venous thrombosis after a failed nonthoracotomy attempt in 1 patient; and the development of hematomas in 3 patients, all of them on warfarin (1 at the subcutaneous patch site and 2 at the generator site).

Vascular complications in the thoracotomy group included two episodes of postoperative mediastinal bleeding requiring reoperation and repair (in one patient, the circumflex artery had been eroded by the epicardial patch) and the development of lower extremity deep venous thrombosis in 1 patient.

Two patients in the nonthoracotomy group experienced miscellaneous surgical complications. One patient with preexisting complete left bundle branch block developed transient complete heart block during placement of the right ventricular defibrillating/sensing lead and required temporary pacing for 24 hours. One patient developed cutaneous erosion at the generator site without infection that required surgical revision. Miscellaneous surgical complications in the thoracotomy group were more severe. One patient experienced perforation of the right ventricle during epicardial lead placement that required emergent median sternotomy for control of bleeding. Two patients suffered postoperative cerebrovascular accidents and 1 patient, a myocardial infarction. Two patients developed sepsis without evidence of ICD infection.

Two of the 3 patients in the nonthoracotomy group who developed ICD system infection required system explantation, which was easily performed without the need for specialized extraction tools, and prolonged parenteral antibiotic therapy for successful management. Both underwent successful ICD system reimplantation after infection was cleared. One patient was managed with long-term antibiotic therapy alone.

Four of the 5 patients in the thoracotomy group who developed ICD infection had deep-seated infection and were managed with system explantation and prolonged parenteral antibiotic therapy. Three of these patients underwent successful ICD system reimplantation. Another patient with a superficial wound infection was successfully managed with a short course of oral antibiotics.

Lead Complications and Reoperations

Lead complications and their remedial actions are presented in Table 4. Nine patients (8%) in the nonthoracotomy group experienced lead complications. Intra-cardiac lead or extrathoracic patch migration were responsible for 6 of these. Five patients (5%) in the thoracotomy group experienced lead complications. Similarly, the majority of lead complications in the thoracotomy group were the result of the migration of an epicardial patch. There was no significant difference in the proportion of patients with lead complications in each group (P = .28).

Twenty-eight (23%) of the nonthoracotomy group patients required a total of 31 reoperative procedures during the follow-up period. This includes 16 reoperations for 14 patients undergoing crossover implantation of a thoracotomy system, 7 for lead complications, 3 for vascular/bleeding complications, 1 for generator pocket erosion, and 4 for the management of 2 ICD system infections. Nineteen patients (21%) in the thoracotomy group required a total of 23 reoperative procedures during the follow-up period. This includes 10 "delayed" attempted implants after failure to achieve a working system at initial implant (8 of them successful), 3 related to lead complications, 2 for mediastinal bleeding, and 8 for the management of four ICD system infections (1 patient required 2 operations to reimplant a functioning system, and 1 patient underwent system explantation without reimplant). There was no significant difference in the proportion of patients requiring reoperations in each group (P = .74).

Hospital Costs for the Initial Admission

True hospital costs for the initial admission using the "intention-to-treat" approach are presented in Table 5. Technical direct costs (composed mainly of the ICD pulse generator and lead system costs) were similar in the two groups. Indirect technical costs, professional costs, and total costs were significantly lower in the nonthoracotomy group. Median total hospital costs were $5420 lower in the nonthoracotomy group.

Learning Curve Effect for the Nonthoracotomy Approach

There were no significant differences in any of the baseline clinical variables between the first and second half of patients in the nonthoracotomy group. Likewise, there were no significant differences in the implant success rate, operative mortality, and incidence of complications. Postoperative hospital stay was significantly shorter for patients in the second half (median, 5 days; lower quartile, 3 days; upper quartile, 6 days versus median, 5 days; lower quartile, 4 days; upper quartile, 10 days; P = .02).

Device Intervention and Long-term Survival

Nonspurious device intervention occurred in 64 (66%) of the nonthoracotomy and 55 (62%) of the thoracotomy patients. There was no significant difference in the proportion of patients undergoing nonspurious ICD intervention in the two groups (P = .39).

There were 17 deaths in the nonthoracotomy group. Fourteen of them were considered cardiac deaths (4 operative, 9 from progressive congestive heart failure, and 1 from incessant ventricular arrhythmia). The 3 noncardiac deaths were consequent to malignancy, end-stage renal disease in a renal transplant recipient, and suicide. There were 12 deaths in the thoracotomy group. Nine of them were considered cardiac deaths (4 operative, 3 from progressive congestive heart failure, 1 from acute myocardial infarction, and 1 sudden). The 3 noncardiac deaths were consequent to chronic respiratory insufficiency, abdominal sepsis after colon surgery,
TABLE 4. Lead Complications

<table>
<thead>
<tr>
<th>Patient</th>
<th>Complication Description</th>
<th>POD</th>
<th>Clinical Presentation</th>
<th>Remedial Action</th>
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<td>Nonthoracotomy group (n=9)</td>
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<tr>
<td>15</td>
<td>Multiple lead fractures close to header</td>
<td>376</td>
<td>&quot;Twiddler,&quot; spurious shocks</td>
<td>Explant ICD system</td>
</tr>
<tr>
<td>27</td>
<td>Migration of CS lead to IVC</td>
<td>4</td>
<td>Asymptomatic, CXR</td>
<td>Reoperation to reposition</td>
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<tr>
<td>50</td>
<td>Ventricular lead dislodgment</td>
<td>69</td>
<td>Asymptomatic, CXR</td>
<td>Reoperation to reposition</td>
</tr>
<tr>
<td>54</td>
<td>Migration of CS lead to RVOT</td>
<td>42</td>
<td>Asymptomatic, CXR</td>
<td>None; satisfactory safety margin for defibrillation preserved</td>
</tr>
<tr>
<td>58</td>
<td>Loose set screw</td>
<td>46</td>
<td>Spurious shocks</td>
<td>Reoperation</td>
</tr>
<tr>
<td>60</td>
<td>Migration of CS lead to SVC</td>
<td>31</td>
<td>Asymptomatic, CXR</td>
<td>Reprogram current delivery pathway</td>
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<tr>
<td>75</td>
<td>Axillary patch migration</td>
<td>78</td>
<td>&quot;Twiddler,&quot; asymptomatic, increased DFT</td>
<td>Reoperation to reposition</td>
</tr>
<tr>
<td>110</td>
<td>Loose set screw</td>
<td>1</td>
<td>Spurious shocks</td>
<td>Reoperation</td>
</tr>
<tr>
<td>111</td>
<td>Axillary patch migration</td>
<td>72</td>
<td>Axillary discomfort</td>
<td>Reoperation to reposition</td>
</tr>
<tr>
<td>Thoracotomy group (n=5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Epicardial patch migration</td>
<td>78</td>
<td>Asymptomatic, CXR</td>
<td>None; satisfactory safety margin for defibrillation preserved</td>
</tr>
<tr>
<td>19</td>
<td>Epimyocardial lead fracture</td>
<td>593</td>
<td>Spurious shocks</td>
<td>Reoperation, TV sensing lead placed</td>
</tr>
<tr>
<td>25</td>
<td>Sensing lead adapter fracture</td>
<td>17</td>
<td>Spurious shocks</td>
<td>Reoperation to replace</td>
</tr>
<tr>
<td>28</td>
<td>Epicardial patch migration</td>
<td>333</td>
<td>Asymptomatic, CXR</td>
<td>None; satisfactory safety margin for defibrillation preserved</td>
</tr>
<tr>
<td>60</td>
<td>Epicardial patch migration</td>
<td>170</td>
<td>Asymptomatic, CXR, increased DFT</td>
<td>Reoperation to reposition</td>
</tr>
</tbody>
</table>

POD indicates postoperative day; CS, coronary sinus; IVC, inferior vena cava; RVOT, right ventricular outflow tract; SVC, superior vena cava; ICD, implantable cardioverter/defibrillator; CXR, finding on routine chest radiography; DFT, defibrillation threshold; and TV, transvenous.

and pneumonia. Based on intention to treat, 1- and 2-year actuarial survival probabilities were .87 (95% CI, .78 to .91) and .80 (95% CI, .68 to .88) in the nonthoracotomy group and .90 (95% CI, .82 to .95) and .87 (95% CI, .77 to .93) in the thoracotomy group (P=.56; log-rank test) (Figure). One- and 2-year probabilities of freedom from cardiac death were .89 (95% CI, .81 to .93) and .85 (95% CI, .74 to .91) in the nonthoracotomy group and .90 (95% CI, .82 to .95) and .90 (95% CI, .81 to .95) in the thoracotomy group (P=.56; log-rank test).

TABLE 5. Cost Comparisons

<table>
<thead>
<tr>
<th>Type of Costs</th>
<th>Nonthoracotomy, $ (min, max)</th>
<th>Thoracotomy, $ (min, max)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical direct</td>
<td>19 446 (16 704, 25 453)</td>
<td>20 534 (17 417, 29 411)</td>
<td>.18</td>
</tr>
<tr>
<td>Technical indirect</td>
<td>7006 (5090, 10 301)</td>
<td>9512 (7488, 13 010)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Technical total</td>
<td>27 893 (22 502, 35 560)</td>
<td>29 232 (25 961, 42 672)</td>
<td>.025</td>
</tr>
<tr>
<td>Professional direct</td>
<td>2354 (1523, 4012)</td>
<td>4250 (3062, 5545)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Professional indirect</td>
<td>1780 (1163, 2829)</td>
<td>2906 (2172, 4114)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Professional total</td>
<td>4192 (2837, 6955)</td>
<td>7093 (5432, 9550)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total costs</td>
<td>32 205 (25 305, 43 458)</td>
<td>37 265 (32 707, 51 261)</td>
<td>.001</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test.
Results were similar when analyses were performed according to treatment actually received.

Discussion

In this study we compared, according to an intention-to-treat principle, the clinical outcomes of a large, homogeneous group of intended recipients of nonthoracotomy and thoracotomy ICD systems at a single institution. We found similar results with both types of systems with regard to operative mortality and overall survival. However, recipients of nonthoracotomy ICDs experienced significantly lower surgical morbidity, shorter postoperative intensive care and total hospitalization, and lower hospital costs.

Recent reports have attempted to compare, explicitly or implicitly, the results of nonthoracotomy ICDs with those of conventional thoracotomy ICD systems.32-34 These studies suffered from several biases that limit the extraction of sound conclusions. Series have been relatively small and focused on a single generator or lead system.32 Other, larger studies have been based on manufacturers’ databases,32,34 which are generally oriented toward the assessment of hardware performance and not of patient outcome.35 Thoracotomy control groups have been historical34 or, if contemporary, inhomogeneous and including patients with concomitant cardiac surgery.32,34 Furthermore, previous studies have generally been based on the actual treatment received rather than the intended treatment.32,34

Several design features of our study attempt to minimize those previously mentioned biases. The primary analyses are based on the intended and not the actual treatment received. The majority of the clinically available lead systems and tiered-therapy generators have been used in this relatively large population. Although the two approaches were not prospectively randomized, the two groups were essentially comparable because selection of the implant approach was based primarily on hardware availability.

Our 84% initial nonthoracotomy implant success rate is similar to rates previously reported. Importantly, the majority of patients failing nonthoracotomy implantation received a successful thoracotomy ICD system. In those patients, initial high defibrillation thresholds did not preclude success after crossover. Therefore, the eventual implant success rates were almost identical (96% versus 97%) in the two groups.

Operative Mortality

Our finding of similar operative mortality with the two approaches contradicts previous reports that had suggested a lower operative mortality with nonthoracotomy ICD implantation.32-34 Several factors may explain the relatively high operative mortality in our nonthoracotomy patients. In previous studies, patients crossing over to a thoracotomy approach or not receiving an ICD have seldom been analyzed by the intention-to-treat principle, thus artificially lowering the operative death rate. However, even when analyzed according to intention to treat, operative mortality with nonthoracotomy ICDs has ranged between 0%9,12 and 2.7%.35 Discrepancies in outcomes may be the result of superior surgical techniques or of the random variation existent in small series.36 Alternatively, it is more likely that they are a reflection of different patient selection criteria for ICD implantation. Comparison of our nonthoracotomy population with those of Böcker et al9 and Bardy et al5 reveals that our patients were older and had poorer left ventricular function. For example, 9% of our nonthoracotomy patients were ≥75 years of age versus 2% in the study by Bardy et al. A lower operative mortality might have been achieved by a more restrictive process of patient selection. However, such a restriction would result in a decreased number of patients likely to benefit from ICD implantation.38

Operative Morbidity

Multiple factors have been implicated in the operative morbidity observed after thoracotomy ICD implantation. These include prolonged general anesthesia, irritation of the pericardium and epicardium,39 extensive defibrillation threshold testing,6,40 postoperative catecholamine surges,41 electrolyte and fluid imbalances, and the mechanical, nociceptive, and metabolic consequences of the thoracotomy incision itself. Some of these factors may be lessened or even eliminated by nonthoracotomy implantation, whereas others cannot. Current nonthoracotomy techniques introduce additional factors that may increase morbidity, such as the need for vascular instrumentation with large-bore sheaths, multiple surgical access sites, and the more extensive defibrillation testing frequently prompted by the many alternative configurations in a multilead system.15,25,33 Therefore, it is not surprising that some postoperative complications were significantly reduced in the nonthoracotomy group, while others were not. Less pain and a reduced systemic metabolic response could partially explain the shorter recovery with the nonthoracotomy approach. Likewise, the lack of pericardial inflammation may be responsible for the reduced incidence of supraventricular tachyarrhythmias with the nonthoracotomy approach.

The incidence of pulmonary complications was similar in the two groups, although they tended to be less severe in the nonthoracotomy group. In the nonthoracotomy group, longer anesthesia times and pneumothoraces may have counterbalanced the avoidance of the deleterious effects of the thoracotomy on the mechanics of respiratory function. As in a previous report,41 the incidence of postoperative ventricular arrhythmias did not depend on the operative approach, suggesting that the catecholamine responses to surgery may be more
important than the direct effects of the myocardial patches in their genesis. It is encouraging that no complication was significantly more frequent in the nonthoracotomy group, allowing for future refinements in lead design and energy delivery to further reduce surgical morbidity with nonthoracotomy ICD implantation.

The incidence of ICD system infection did not differ significantly between the two approaches. In all but one case, a combined strategy of system explantation and antibiotic therapy was required for the successful management of infection. However, while the explantation of a thoracotomy ICD system required a major surgical intervention, explantation of nonthoracotomy systems was easily achieved under local anesthesia without the need for specialized lead extraction tools.

Lead Complications

The complex design of multielectrode nonthoracotomy defibrillators leads, their extended subcutaneous course, and the frequent positioning of the subcutaneous patch in a region subject to repetitive movement (ie, axilla) would appear to place these lead systems at a higher risk for dislodgment, migration, and conductor or insulation breakdown. The incidence of lead complications did not differ significantly between patients with nonthoracotomy and thoracotomy systems. With both approaches, the majority of them consisted of transvenous lead or defibrillation patch migration. However, epicardial patch migration was more often associated with preservation of defibrillation capabilities than was nonthoracotomy lead migration, with fewer reoperative procedures required for repair. Thus, the functional integrity of nonthoracotomy ICD systems appears more vulnerable to lead migration than does that of thoracotomy systems.

Our study underscores the frequent need for reoperative procedures in ICD recipients, a point that has not been emphasized previously. With both implant approaches, up to a 15% incidence of failure to achieve a functioning system at the initial implant attempt can be expected. However, the majority of these failures may be remedied with an additional procedure (ie, crossover to thoracotomy implantation or the creation of a “hybrid” system by combining epicardial and nonthoracotomy electrodes). Therefore, teamwork between cardiac electrophysiologists and cardiovascular surgeons is still needed to guarantee optimal defibrillator therapy.

Long-term Survival

The nearly complete prevention of sudden death in both groups reaffirms the efficacy of ICDs in terminating ventricular tachyarrhythmias and confirms the long-term reliability of current nonthoracotomy ICD systems. There were no significant differences in the 1- and 2-year actuarial survival between the two groups. Survival in the thoracotomy group is in agreement with previous reports, but survival in the nonthoracotomy group was poorer. For example, Bardy et al.\(^\text{15}\) reported a 98% survival rate over 11 months and Bocker et al.\(^\text{16}\) a 95% rate over 12 months. In our study, death was most frequently the result of progressive congestive heart failure. Again, differences in patient selection may have contributed to the observed disparities in survival, in view of the unexpectedly low incidence of cardiac nonarrhythmic death in the previously mentioned studies. Survival in patients with life-threatening ventricular tachyarrhythmias, including those undergoing ICD implantation, depends primarily on the severity of heart failure and left ventricular dysfunction.\(^\text{42-45}\) Because patients more likely to benefit from ICD therapy have concurrent competing risks of death from heart failure and acute myocardial ischemia, the benefits of ICD therapy on overall survival have been difficult to demonstrate in the absence of randomized trials.\(^\text{46,47}\)

Study Limitations

Because of the lack of randomization, the presence of hidden, subtle selection biases cannot be ruled out. Although there were no statistically significant differences in baseline prognostic variables between the two groups, 3% of the patients in the nonthoracotomy group were in functional class IV, whereas none in the thoracotomy group were in class IV. This could explain the trend toward more frequent incidence of death from heart failure in the nonthoracotomy group. Few patients in the nonthoracotomy group received devices with biphasic waveform capabilities. Early reports suggest that the efficiency of nonthoracotomy defibrillation lead systems can be greatly enhanced by a biphasic waveform.\(^\text{48}\) Dislodgment of a coronary sinus lead accounted for 50% of the lead dislodgments in the nonthoracotomy group. Recent reports do not suggest increased defibrillation efficiency for lead configurations including the coronary sinus, and we, like most investigators, have abandoned that practice. Because 100% of the nonthoracotomy systems and 47% of the thoracotomy systems were implanted within clinical research protocols, implantation procedures often required extensive testing to meet protocol criteria. This extensive testing may not reflect the patterns of clinical practice once such systems are available outside investigational protocol. We did not find a learning-curve effect by comparing results in the first versus the second half of the patients with attempted nonthoracotomy implantation. This could be the result of our earlier experience with another nonthoracotomy lead system\(^\text{10}\) or the use of different nonthoracotomy lead systems that were introduced at different times during the time frame of the study. Alternatively, the learning curve may be very steep, and stable results could have been achieved after few implants.

As a consequence of the relatively recent availability of the nonthoracotomy lead systems for investigational use, the follow-up period is necessarily short. As yet unanswered questions regarding the long-term stability, integrity, and clinical performance of such lead systems will require a longer duration of follow-up to satisfactorily address these issues.

Conclusions

Implantation of ICD systems via a nonthoracotomy approach can be achieved with a high degree of success in unselected patients with life-threatening ventricular tachyarrhythmias. The nonthoracotomy approach is associated with significant advantages with regard to surgical morbidity, hospitalization, and hospital costs compared with the well-established thoracotomy approach. Long-term outcome seems not to be compromised by the nonthoracotomy approach, which confers similar protection from sudden cardiac death. There-
fore, recommendations by federal regulatory agencies for the conduction of randomized studies comparing thoracotomy versus nonthoracotomy ICD systems do not seem justified. Likewise, current and future trials\textsuperscript{49,50} evaluating ICD therapy against alternative treatments should endorse nonthoracotomy as the initial approach to ICD implant. We conclude from these nonrandomized data that a nonthoracotomy approach should probably be considered as the procedure of choice for patients requiring ICD implantation without concomitant cardiac surgery. Anticipated advances in energy storage and delivery technology will soon make possible pectoral ICD implantation with a single transvenous lead.\textsuperscript{51} Therefore, optimistic expectations for improved ICD performance, less invasive implantation with lower morbidity, and further improvement in cost-effectiveness\textsuperscript{52,53} are realistic.

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