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Conscious Sedation With Combined Hypnotic Agents for Implantation of Implantable Cardioverter-Defibrillators

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Objectives. **The objective of this study was to evaluate the feasibility, safety and efficacy of placing implantable cardioverter-defibrillators (ICDs) in the electrophysiology laboratory using conscious sedation with combined hypnotic agents and deep sedation with etomidate.**

Background. **Implantable cardioverter-defibrillators with transvenous leads permit the use of simplified implantation techniques similar to those used for the insertion of permanent pacemakers. However, implantation of ICDs without general anesthesia has thus far gained limited acceptance.**

Methods. **In 162 patients, conscious sedation during ICD placement was achieved with combined intravenous midazolam, morphine and promethazine (Phenergan). Intravenous etomidate was administered to induce deep sedation for defibrillation threshold testing. First-time implantations were in the prepectoral position (n = 142), but some patients with preexisting devices received abdominal implants (n = 20). The results were compared with those of concurrent patients (n = 56) who received prepectoral implants under propofol anesthesia administered by an attending anesthesiologist.**

Results. **The anesthetic protocol was implemented without major intraoperative complications. During deep sedation with etomidate, episodes of apnea, hypoxia or arterial hypotension requiring therapeutic intervention did not occur. During a mean (±SD) follow-up period of 257 ± 140 days (median 227, range 14 to 482), there were, among the 162 patients, a total of two nonsudden cardiac deaths—one 71 days and the other 157 days after the operation. There were two nonsudden deaths in the concurrent control subjects (n = 56)—one 13 days and the other 110 days after the operation.**

Conclusions. **Implantation of ICDs under conscious sedation with combined hypnotic agents and deep sedation with etomidate is a safe and effective procedure with low perioperative morbidity and low long-term complication rates.**

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The development of implantable cardioverter-defibrillators (ICDs) with transvenous lead systems has simplified their implantation. It is now possible to place ICDs under local anesthesia in electrophysiology laboratories with techniques similar to those used for the insertion of permanent pacemakers (1–5). However, recent reports indicate that most electrophysiologists still prefer to place ICDs in operating rooms under general anesthesia (6–14). This preference may reflect the fact that patients receiving ICDs are often critically ill, that the devices remain bulkier and heavier than pacemakers and that some form of general anesthesia or deep sedation is necessary for intraoperative testing of defibrillation thresholds (DFTs). Also, recently recommended submuscular or subpectoral implantation procedures require sufficient surgical dissection to warrant general anesthesia (4,12–14). Although reports from few centers suggest the feasibility of placing ICDs without general anesthesia (3,5), the risk and long-term outcome of simplified implantation procedures remain to be assessed.

We prospectively evaluated the feasibility and safety of placing ICDs in the electrophysiology laboratory using anesthetic methods that can be implemented without the assistance of an anesthesiologist.

Methods

Study patients. During the period from November 1995 to April 1997, consecutive nonselected adult patients of either gender admitted to university-affiliated hospitals (The Methodist Hospital, St. Luke's Hospital and St. Joseph Hospital) were entered in the study. Patients were treated with ICDs if they had survived at least one episode of aborted sudden cardiac death due to a ventricular tachyarrhythmia or if they had sustained episodes of hemodynamically unstable ventricular tachycardia. First-time placement of ICDs was performed in the prepectoral position as previously reported (15). Placement of ICDs in the abdominal position was restricted to patients requiring revision of a preexisting device. All patients received coronary arteriography; an estimation of left ventricular ejection fraction either by contrast angiography, radionuclide ventriculography or echocardiography; and baseline elec-

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Abbreviations and Acronyms
DFT = defibrillation threshold
ICD = implantable cardioverter-defibrillator
IV = intravenously

trophysiologic testing according to a standard protocol (16). Written informed consent was obtained from all patients.

Conscious and deep sedation. One hour before the operation, prophylactic antibiotics (usually vancomycin in combination with gentamicin or a fourth-generation cephalosporin) were administered intravenously (IV). A radial arterial catheter was inserted, and electrocardiographic leads and a finger pulse oximeter were attached to monitor hemodynamic variables, rhythm and oxygenation. Supplemental oxygen was delivered by nasal cannula or mask.

The etomidate protocol was implemented at only one of the institutions (The Methodist Hospital), where approval had been obtained. Conscious sedation was produced with a combination of midazolam (Versed [Roche Laboratories], 15 to 30 μg/kg body weight IV within 20 s), promethazine (Phenergan, 180 to 360 μg/kg IV) and morphine (30 to 90 μg/kg IV). To induce deep sedation for DFT testing, a bolus of etomidate (Amidate [Abbot Pharmaceuticals], 80 to 120 μg/kg within 20 s) was administered. A single maintenance dose of the same magnitude was administered to 42% of the patients, and 6% (10 patients) received a third dose. The etomidate protocol was implemented in the absence of an anesthesiologist or anesthesiology staff member. During the period of evaluation of the etomidate protocol, we continued to use propofol at the other institutions for conscious and deep sedation, as previously reported (15). In brief, conscious sedation was achieved by giving midazolam (15 to 30 μg/kg IV) and a continuous infusion of propofol (Diprivan [Stuart Pharmaceuticals], 20 to 50 μg/kg per min IV) to ensure patient comfort without inducing loss of consciousness. To produce brief deep sedation for the testing of DFTs, a propofol bolus (400 to 500 μg/kg within 20 s) was given. According to institutional anesthesia guidelines, propofol was used only in the presence of an anesthesiologist. The concurrent patients receiving propofol served as nonhistoric control subjects for the patients receiving etomidate. With both the etomidate and propofol protocols, the aim of deep sedation was to produce a brief loss of responsiveness to glabellar tap and loud auditory stimulation (Ramsey sedation score 5 or 6 [17] or Adenbrooke sedation score 4 or 5 [18]). The speed of recovery from deep sedation was assessed by recording the interval from the time of the last anesthetic bolus injection to the time when patients were first able to respond to simple commands (opening of eyes on verbal command [19]). For comparison with other studies (20–22), the percentage of patients responding to simple command after 10 and 15 min was recorded. After full recovery from sedation, patients were questioned to assess the degree of amnesia for operative and postoperative events.

Local anesthesia. For prepectoral implantation, generators and their transvenous leads were inserted through single left infraclavicular incisions after local anesthesia of the skin with 1% lidocaine. The subcutaneous space requiring dissection for the creation of a prepectoral pocket was infiltrated with small amounts of 1% lidocaine. Similar infiltrations were performed at the site of abdominal ICDs undergoing revision. The cumulative dose of lidocaine did not exceed the recommended maximal dose of 4.5 mg/kg. Subcutaneous tunneling of the leads from their venous insertion site to the abdominal pocket was performed during deep sedation immediately after DFT testing.

Placement of ICDs. Models from different manufacturers included Jewel models 7219B (n = 1), 7219C (n = 17), 7220C (n = 1) and 7220E (n = 3) and Micro-Jewel models 7221B (n = 1), 7221E (n = 11) and 7221Cx (n = 93) from Medtronic; Cadet models V-115C (n = 2) and V-115AC (n = 56) and Contour model V-145 AC (n = 7) from Ventritex; Ventak Mini models 1741 (n = 14), 1743 (n = 1) and 1763 (n = 7) from Cardiac Pacemaker Incorporated (Guidant-CPI); Sentinel model 2010 (n = 2) from Angeion; and Res-Q Micron model 101-09 (n = 2) from Sulzer-Intermedics. The weight and volume of the devices ranged between 109 and 139 g and between 57 and 89 ml.

In patients receiving first-time implants (142 patients receiving etomidate, 56 control subjects), ICDs were placed in the prepectoral position as previously reported (15). However, among the patients receiving etomidate, 20 had abdominal implants for the replacement of preexisting units. Defibrillation threshold testing was performed according to a simplified step-down scheme (3,15).

Outpatient follow-up. Follow-up care consisted of a wound examination at 1 week and a visit at 1 and 3 months, when long-term DFTs were tested. Subsequent visits with routine ICD examinations were at 3-month intervals, but additional visits were scheduled when patients reported shocks or other ICD-related events.

Data analysis. Data storage and statistical analysis were performed using a desk computer installed with Windows versions D-Base 5.0 and GB-STAT 6.0 programs. Demographic and outcome data were recorded for the entire cohort (n = 218), the patients receiving etomidate (n = 162) and the concurrent control subjects receiving propofol (n = 56). Intergroup differences for continuous and ordinal (scaled) variables were assessed using the Kruskal-Wallis test (one-way analysis of variance by rank). The chi-square test was applied to assess differences in event rates. Total deaths, sudden cardiac deaths (within 1 h from symptom onset) and nonsudden cardiac deaths were recorded for the 30-day perioperative period, the first year and the entire follow-up. Because of the small number of deaths recorded, survival (actuarial) analyses were not performed (23). The significance level selected was $p < 0.05$. Data are expressed as mean value ± SD.

Table 1. Patient Characteristics

	All Patients (n = 218)	Etomidate Group (n = 162)	Concurrent Propofol Group (n = 56)
Men	179 (82%)	134 (83%)	46 (82%)
Age (yr)	64 ± 12	64 ± 12	62 ± 15
Body mass index (kg/m^2)			
Men	27 ± 7	27 ± 8	28 ± 6
Women	27 ± 7	27 ± 9	27 ± 5
Aborted arrhythmic sudden death	76 (36%)	57 (35%)	20 (35%)
NYHA functional class			
I	72 (33%)	53 (33%)	18 (32%)
II	118 (54%)	86 (53%)	31 (55%)
III	28 (13%)	23 (14%)	7 (13%)
Left ventricular ejection fraction	33 ± 12	33 ± 12	34 ± 11
Coronary artery disease	177 (81%)	133 (82%)	45 (80%)

Data presented are mean value ± SD or number (%) of patients. NYHA = New York Heart Association.

Table 2. Hemodynamic and Oxygenation Variables

	Etomidate Group (n = 162)	Concurrent Propofol Group (n = 56)
Arterial pressure (mm Hg)		
Before sedation		
Systolic	140 ± 28	145 ± 25
Diastolic	80 ± 10	78 ± 13
Max dev during sedation		
Systolic	120 ± 24	104 ± 31*
Diastolic	70 ± 11	61 ± 13*
Heart rate (beats/min)		
Before sedation	78 ± 14	78 ± 13
Max dev during sedation	79 ± 12	80 ± 14
Oximetric saturation (%)		
Before sedation	97 ± 2	98 ± 2
Max dev during sedation	94 ± 2	96 ± 3

*$p < 0.05$. Data presented are mean value ± SD. Max dev = maximal deviation.

Results

Clinical characteristics of patients. The demographic features of the entire cohort and of the two subgroups are summarized in Table 1. The groups exhibited a similar age, a marked dominance of male gender, a similar incidence of aborted sudden death preceding ICD placement, absence of severe heart failure (no patients in New York Heart Association functional class IV), a left ventricular ejection fraction slightly below 35% and a very high incidence of coronary artery disease documented by arteriography. There were no statistically significant differences between the entire cohort and the subgroups (Table 1).

Conscious and deep sedation. *Etomidate protocol.* During conscious sedation with combined midazolam, morphine and promethazine, the patients appeared relaxed and questioning failed to elicit complaints of pain. Bolus injection of etomidate for deep sedation evoked no episodes of arterial hypotension or hypoxia. The hypotensive effects of etomidate were significantly less than those of propofol (Table 2). In 11 (6.7%) of 162 patients, muscular fasciculations were noted (Table 3). Recovery of responsiveness at 10 and 15 min was observed in 95% and 99% of patients, respectively. Recollection of intraoperative events after full recovery was not elicited. In no patient was postoperative vomiting recorded (Table 3).

Propofol protocol for concurrent control subjects. During conscious sedation with midazolam and propofol, patient questioning elicited no complaint of pain at the sites of lead and generator insertion. Maximal effects of propofol on systolic and diastolic pressure occurred ~1 min after the onset of drug infusion (Table 2). No drop in oxygenation was observed. With the induction of deep sedation, no episodes of sustained apnea or arterial hypotension (systolic pressure <90 mm Hg) were recorded (Table 2). No patient required assisted ventilation by face mask or endotracheal intubation. Recovery of responsiveness to simple commands was noted in the majority of patients within 10 min after the propofol bolus (Table 3). After full recovery from sedation, all patients demonstrated amnesia for operative events (Table 3).

Placement of ICDs. Active can/right ventricle lead configurations were implanted in 186 of 198 pectoral implants. Other configurations included superior vena cava/right ventricle (n = 30) and subcutaneous patches (n = 2). Defibrillation thresholds were determined using on average 2.4 ± 2.5 and 2.5 ± 2.6 inductions per patient in the etomidate and propofol subgroups, respectively. A safety margin of 10 J was obtained in all cases.

In all first-time ICD recipients (n = 198), prepectoral subfascial implantation was accomplished without difficulty or operative complications. The mean length of the procedure measured from the time of the first injection of lidocaine to the time of completed skin closure averaged 79 ± 32 min and 78 ± 31 min in the etomidate and concurrent propofol subgroups, respectively.

Long-term follow-up. The mean and median follow-up times for all patients were 257 ± 140 days (range 14 to 482) and 227 days, respectively.

During the entire follow-up, seven lead revisions were required, but none of these were related to lead fractures. There was no case of prepectoral pocket erosion. There were

Table 3. Characteristics of Sedation

	Etomidate Group (n = 162)	Concurrent Propofol Group (n = 56)
Recovery from deep sedation		
At 10 min (mean ± SD)	95 ± 9	96 ± 9
At 15 min	>99	>99
Amnesia	100	100
Myoclonic movements	6.7	0
Vomiting	0	0

Data presented are percent of patients.

no in-hospital deaths. In the etomidate group, there were a total of two nonsudden cardiac deaths—one 71 and the other 157 days after implantation. In the control group, there were a total of two nonsudden cardiac deaths—one 13 and the other 110 days after implantation. Among the 218 patients, there were thus a total of four deaths, which occurred all during the first year. There was one perioperative death at 13 days after implantation.

Discussion

The development of reliable transvenous lead systems and down-sized generators has greatly facilitated the placement of ICDs (1–5). However, optimal anesthetic and surgical techniques for the implantation of these devices remain controversial (4,12–14). Although it has been suggested that ICDs could now be implanted in electrophysiology laboratories with little more surgical intervention than that needed for the insertion of simple pacemakers (3), review of the recent published reports reveals that the majority of electrophysiologists continue to place ICDs in operating rooms under general anesthesia (6–14). Arguing that intravenous sedation fails to ensure adequate ventilation in critically ill patients and that ventilatory difficulties may contribute to hemodynamic deterioration, Epstein and Kay (12) advocate routine elective endotracheal intubation and mechanical ventilation for the placement of ICDs. However, to our knowledge, the relative hazard of different anesthesia protocols in patients threatened by potentially lethal ventricular tachyarrhythmias has not been evaluated in controlled trials.

Etomidate protocol. The etomidate protocol was initiated in the fall of 1995 with the intent of prospectively evaluating a procedure that would preclude the need for general inhalation anesthesia. The regimen was based on the simultaneous use of combined intravenous drugs, which has been shown to be preferable to anesthesia with single agents (24–29). It was designed for use in the absence of an assisting anesthesiologist. Variable and evolving reimbursement schemes make cost analyses of anesthesia for ICD placement difficult, but our estimates suggest that operations without the assistance of an anesthesiologist may reduce cost by $1,550 to $2,000. We chose etomidate because this hypnotic agent exerts modest or no hypotensive and respiratory depressant effects compared with opioids (fentanyl), barbiturates and propofol administered in hypnotic dosages (20–22,25–27). Although etomidate was accepted with considerable enthusiasm after its introduction in 1972, it was subsequently relegated to a second-choice drug because of concerns about adrenocortical suppressant activity (25) and other side effects such as pain on injection, myoclonic movements and postoperative vomiting (27–29). However, critical reevaluation of the data suggested that the risk of adrenal suppression during short procedures was close to nonexistent (25). Although the adrenal suppressant effects of etomidate have been ascribed to its imidazole structure (24,25), it is important to recognize that such effects may also occur with structurally unrelated anesthetic agents (30). In the present study, the dosage of etomidate was only about one-third of the single dose for inducing general anesthesia (300 μg/kg), which helped minimize side effects. The adequacy of the low dosage probably reflects the potentiating effect of premedication with a benzodiazepine and an opiate (25). Our etomidate protocol was implemented without incident, and we believe that it can be safely administered by electrophysiologists without special training in anesthesiology. However, etomidate is not recommended for prolonged deep sedation (>30 min) because of the possibility of hypercapnia and adrenal suppression. Therefore, should prolonged deep sedation be required, we advise another IV agent (propofol) or inhalation anesthesia and monitoring of alveolar carbon dioxide tension.

In this study, we compared the etomidate regimen with propofol, a hypnotic agent frequently used for anesthesia during brief surgical procedures (26–29). For nonanesthesiologists, propofol may be less attractive because of its propensity to induce apnea. Hypnotic doses of propofol, as used for the induction of general anesthesia (2,000 to 2,500 μg/kg), induce apnea in ~20% of patients (26). Also, propofol exerts hypotensive effects (26–29). In contrast, propofol is known for rapid recovery after anesthesia and low side effects, including a low incidence of postoperative nausea and vomiting. However, in the present study, low dose etomidate compared with propofol did not yield more undesirable effects or appreciably slower awakening.

Submuscular implantation under general anesthesia. In our study, the use of prepectoral implantation in all patients receiving first implants facilitated the implementation of a simplified anesthesia protocol. Fearing that prepectoral implantation may be associated with inordinately high rates of pocket erosion and infection, elaborate subpectoral procedures under general anesthesia have been recommended (4,13,14). These operations involve medial peelback (4) or posterolateral mobilization (13,14) of the pectoralis major muscle with penetration of the subpectoral space in a region occupied by important neural and vascular structures. One report was based on the operation of six patients without follow-up (13). Another study described 23 patients with an undefined mean follow-up period (14). The third report was a theoretic methods paper without clinical data (4). These reports fail to characterize the long-term results of deep pectoral implantations on shoulder motion and integrity of upper limb neuromuscular function. Our results do not support the notion that prepectoral implantation is associated with a high risk of pocket erosion.

Conclusions. We report on the follow-up of nonselected patients who received ICDs with the use of a new anesthetic protocol. The results of our implantation method suggest that conscious and deep sedation with combined intravenous anesthetic agents is safe and can be administered without the attendance of an anesthesiologist. Results obtained with the new anesthetic regimen involving deep sedation with etomidate compare favorably with those for implantation procedures relying on general anesthesia (1,2,5–11,13,14).

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