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ELECTROPHYSIOLOGIC STUDIES

Comparison of Ventricular Arrhythmia Induction With Use of an Indwelling Electrode Catheter and a Newly Inserted Catheter

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Two methods of serial electrophysiologic testing are in widespread use. Most commonly, the electrode catheter is removed after each study and a new catheter reinserted through the femoral vein for every subsequent test. An alternative method employs an electrode catheter that remains in place during several days of serial testing. Little is known about differences between these two methods with respect to the likelihood of induction of arrhythmia or the frequency of complications.

To determine whether inducibility of sustained arrhythmia is altered or if the frequency of complications is unacceptably high with use of an indwelling catheter, a prospective randomized study was conducted in 78 patients. Each patient underwent baseline testing, several days of electropharmacologic testing with an indwelling catheter, a 24 h drug elimination period and placement of a new electrode catheter. Ventricular stimulation studies were then performed in each patient with both the indwelling and new electrode catheters.

No differences were found between the indwelling and new catheter tests with respect to induction of arrhythmia, number of extrastimuli required to induce arrhythmia, rate of arrhythmia or requirement for cardioversion. Ventricular pacing thresholds were higher and effective refractory periods were slightly longer when measured with the indwelling catheter. Complications related to the 156 catheter insertions included two that may have been related to the indwelling catheter (one episode of staphylococcal sepsis and one presumed pulmonary embolism) and four that were related to invasive procedures (pneumothorax in all). There were no long-term adverse sequelae of these complications.

An indwelling pacing catheter has induction characteristics identical to those of a newly placed catheter and complications of the indwelling catheter are infrequent. This approach may have advantages for patients and physicians.

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Serial electrophysiologic testing is usually performed by removing the electrode catheter at the end of each study and reinserting it through the femoral vein immediately before the next study. An alternative method employs an indwelling electrode catheter that remains in place for several days of testing. The latter method could be inferior to repeated catheter replacement if inducibility of arrhythmia is altered or complications are more frequent. Although a high complication rate and decreased inducibility of ventricular arrhythmia have been reported (1) with use of an indwelling catheter, these concerns have not been addressed in a controlled, prospective fashion in a large group of patients. The purposes of this study were to evaluate differences in induction of ventricular arrhythmia between studies performed with an indwelling pacing catheter and those performed with a newly inserted catheter and to monitor complications associated with an indwelling catheter.

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Methods

Study patients. Patients seen at Oregon Health Sciences University Hospital for electrophysiologic evaluation of ventricular arrhythmia were considered eligible if serial electrophysiologic testing was expected to require >4 days. Before initiation of the study, it was determined that 75 patients would be required to detect a clinically important difference in arrhythmia induction (see Statistical methods). Seventy-eight patients consented to enter the study. Their clinical characteristics are described in Table 1. Informed

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Table 1. Clinical Characteristics of 78 Patients

Mean age (yr)	60 ± 13
Ejection fraction	0.43 ± 0.15
Presentation (No.)	
Sustained ventricular tachycardia	45
Ventricular fibrillation	20
Symptomatic nonsustained ventricular tachycardia	13
Underlying heart disease (No.)	
Coronary artery disease	55
Valvular heart disease	2
Cardiomyopathy	12
Congenital	1
No identifiable heart disease	8

consent was obtained from all patients. The study was approved by the Institutional Human Research Committee.

Definitions. The following definitions were used in this study.

Initial catheter: The electrode catheter inserted at the time of the initial ventricular stimulation test.

Indwelling catheter: The initial catheter when used for approximately 4 days after insertion, during the concurrent indwelling and new catheter ventricular stimulation tests.

New catheter: The electrode catheter inserted approximately 4 days after the placement of the initial catheter, immediately before the indwelling and new catheter ventricular stimulation tests.

Initial test: The initial ventricular stimulation test.

Indwelling test: The ventricular stimulation test performed using the indwelling catheter, approximately 4 days after the initial test.

New test: The ventricular stimulation test utilizing the new catheter and performed concurrently with the indwelling catheter test.

Sustained ventricular tachycardia: Ventricular tachycardia lasting ≥30 s or requiring intervention as a result of hemodynamic instability.

Ventricular fibrillation: A ventricular tachyarrhythmia with the absence of clearly defined QRS complexes in the body surface electrocardiogram (ECG), requiring cardioversion.

Sustained ventricular arrhythmia: Ventricular tachycardia or ventricular fibrillation.

Study design. Patients underwent our standard electrophysiologic testing protocol during the first several days of the study. This protocol has been described in detail elsewhere (2). A 105 cm 7F hexapolar catheter bonded with an antithrombogenic polyurethane coating (Bard) was positioned at the right ventricular apex with use of a right subclavian vein approach. A 7F peelaway sheath (Cook) was used in conjunction with this catheter. A tripolar His catheter, quadripolar coronary sinus catheter and a 4F arterial pressure catheter were inserted (when indicated) through the right femoral vein, left basilic vein and right femoral artery, respectively.

Pacing impulses 2 ms in duration were delivered at twice diastolic threshold with use of two paced cycle lengths (600 and 400 ms), two right ventricular pacing sites and up to four extrastimuli during the initial test. In all subsequent tests, only one pacing site was used. For statistical purposes, only the results obtained from the apical pacing sites were compared; arrhythmias induced from the second site were not considered. If a sustained arrhythmia was induced, overdrive pacing or appropriately timed extrastimuli were used to restore sinus rhythm; if this was unsuccessful, the patient received sedation and cardioversion.

After the initial ventricular stimulation study, all catheters were removed except the right subclavian vein hexapolar catheter. The subclavian peelaway sheath was removed, the position of the catheter confirmed, bactericidal ointment applied to the skin, the catheter affixed using sterile adhesive strips and a sterile occlusive dressing applied. The dressing remained intact throughout testing and was removed only if infection was suspected. This catheter was not manipulated during several days of serial electropharmacologic testing. It was subsequently used as the indwelling catheter approximately 4 days later, during the concurrent indwelling and new catheter ventricular stimulation studies. The patient was monitored in the "step-down" area of the coronary care unit, where patients remain during administration and testing of antiarrhythmic agents. Patients were allowed to walk with the catheter in place between ventricular stimulation tests.

After several days of serial drug testing with use of the indwelling electrode catheter, patients entered a drug elimination period of at least 24 h. A new electrode catheter was then inserted through the left subclavian vein and positioned at the right ventricular apex in preparation for simultaneous testing using both the indwelling and new catheters. Serum levels of antiarrhythmic agents most recently administered were measured in 27 consecutive cases.

Programmed electrical stimulation was performed with the two catheters in an alternating fashion an average of 86 ± 26 h after the initial test. Patients were randomly assigned to be stimulated with either the indwelling catheter (n = 40) or the new catheter (n = 38) first. Programmed stimuli were delivered from this catheter to scan diastole until ventricular refractoriness was reached with use of a drive cycle length of 600 ms. Programmed stimuli were then delivered from the other catheter at the same cycle length until ventricular refractoriness was reached. On return to the first catheter, extrastimuli were delivered with use of a drive cycle length of 400 ms until ventricular refractoriness was reached; this alternating sequence continued until an end point was attained. End points included the induction of sustained arrhythmia with both catheters, completion of the stimulation protocol through four extrastimuli or cardioversion. If a

Table 2. Induction of Sustained Arrhythmia Among the Three Tests in 78 Patients

	Catheter Used		
	Initial*	New	Indwelling
Sustained arrhythmia induced*	37	38	36
Cardioversion required*	9	6	8

*p = NS between catheters used.

rhythm that required cardioversion was induced with one of the catheters, testing was halted.

A chest X-ray study was performed after invasive procedures. Each patient's temperature was recorded every 8 h and evaluation for source of fever was undertaken if a patient's temperature increased to 38.5°C or if otherwise clinically indicated. Evaluation for venous thrombosis or pulmonary embolism was undertaken if clinical suspicion was raised.

Statistical methods. The Student's *t* test or the paired *t* test was used to compare interval data. Ordered categoric data were analyzed using the Mann-Whitney-Wilcoxon or Kruskal-Wallis test. The chi-square test was used for nominal data. The least squares fit method of linear regression was used to analyze the effects of increasing numbers of extrastimuli on the ventricular effective refractory period. When appropriate, unpaired and pairwise comparisons were made. No statistical adjustments were made for multiple comparisons because this would have resulted in reduced sensitivity to differences between the catheters. A standard power calculation, with use of a change in frequency of induction from 60% to 40%, a beta error of 0.20 and an alpha error of 0.10, was used to determine the number of patients required for this study (3).

Results

Induction of sustained arrhythmia during the initial, new and indwelling tests (Table 2). Neither the number of patients in whom sustained ventricular tachycardia was induced nor the number of these patients who required cardioversion was different between the patient groups ($p > 0.5$). Rates of induced arrhythmia grouped into categories were not distributed differently between the new, indwelling and initial catheter tests ($p > 0.45$) (Table 3). Differences between tests with respect to the number of extrastimuli required to induce sustained arrhythmia were determined by subtracting the number of extrastimuli required to induce sustained arrhythmia during one test from the number required during the other test in the same patient (Table 4). The distributions of these differences were not significantly different from one another ($p > 0.55$).

Reproducibility of arrhythmia induction (Table 5). Because each patient underwent three similar ventricular stimulation studies (initial, indwelling and new catheter), reproducibility of the test results could be determined. New catheter tests were compared with indwelling catheter tests, initial catheter tests compared with indwelling catheter tests and initial catheter tests compared with new catheter tests. Reproducibility was calculated as the number of patients in whom the two test results were the same (that is, in whom sustained arrhythmia was induced during both tests or in neither test) divided by the total number of patients. Reproducibility of induction of sustained arrhythmia ranged from 0.69 to 0.74. For example, when indwelling and new catheter tests were compared, outcomes were the same in 54 (69%) of 78 patients; in 25, sustained arrhythmia was induced during both tests and in 29 during neither test. In 13 patients, sustained arrhythmia was induced with use of the new catheter only, whereas in 11 patients sustained arrhythmia was induced with only the indwelling catheter. Results were

Table 3. Distribution of Differences in Number of Extrastimuli Required for the Induction of Sustained Arrhythmia

Difference in No. of Extrastimuli Required for Induction of Sustained Arrhythmia	Catheters Compared		
	Indwelling-New	Initial-Indwelling	Initial-New
−2	0	1	3
−1	5	3	4
0	14	16	15
1	5	6	3
2	1	0	1

p = NS (by Kruskal-Wallis test).

Table 3. Rate of Sustained Ventricular Arrhythmia Among the Three Tests

Rate of Arrhythmia (beats/min)	Catheter Used		
	Initial (n = 37)	New (n = 38)	Indwelling (n = 36)
100–160	7	9	7
160–200	14	10	13
200–300	17	14	12
>300 or VF	4	5	4

p = NS (by Kruskal-Wallis test). VF = ventricular fibrillation.

Table 5. Reproducibility of Induction of Sustained Arrhythmia in 78 Patients

Catheters Compared	+/+	+/−	−/+	−/−	Reproducibility
New-indwelling	25	13	11	29	0.69
Initial-indwelling	26	11	9	31	0.74
Initial-new	26	11	11	29	0.71

+/+ = sustained arrhythmia induced during both tests; +/− = sustained arrhythmia induced only during the first of the two tests; −/+ = sustained arrhythmia induced only during the second of the two tests; −/− = sustained arrhythmia induced during neither test.

similar for comparisons between the initial and indwelling catheter tests and the initial and new catheter tests.

Ventricular effective refractory periods (Fig. 1). Effective refractory periods determined with use of the indwelling catheter were slightly but significantly longer than those determined with the new catheter and the difference between these measurements increased linearly with the number of extrastimuli delivered. A least squares fit linear regression demonstrates the following relation:

$$\Delta VERP = 0.34 \text{ ms} + 5.6 \text{ ms (number of extrastimuli)} \; (r = 0.97),$$

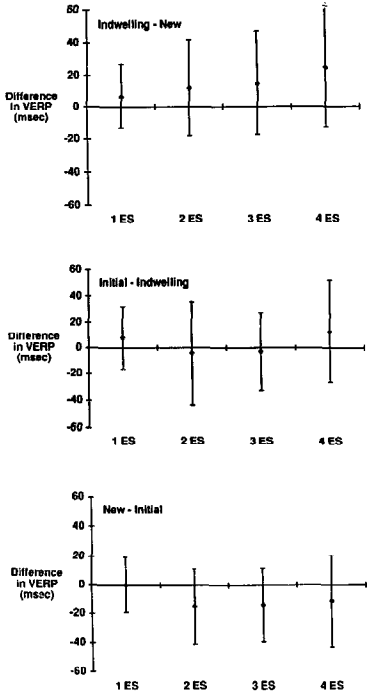
where ΔVERP represents the difference in ventricular effective refractory periods between the indwelling and new catheters in the same patient. Refractory periods were comparable between the initial and indwelling catheter tests, whereas refractory periods measured with the new catheter were significantly shorter than those measured with the initial catheter in the same patient.

Ventricular stimulation thresholds (Fig. 2). The mean threshold determined with the indwelling catheter was 1.05 mA, whereas mean thresholds determined with the initial and new catheters were both 0.58 mA. The initial and new catheter mean thresholds were not different ($p > 0.9$), whereas the mean threshold determined with the indwelling catheter was significantly different from both the initial and new catheter mean thresholds ($p < 0.01$).

Serum levels of antiarrhythmic agents. Serum levels of the most recently administered antiarrhythmic agents were determined in 27 consecutive patients. Levels of quinidine, procainamide and disopyramide were universally low or unmeasurable. Five of 16 patients who had most recently been tested during mexiletine therapy had measurable levels; levels in 2 patients were therapeutic (both 1 μg/ml).

Complications. Four complications occurred in the 78 patients during the 156 invasive procedures. All were pneumothoraces and two required placement of a chest tube; the latter two were noted immediately, whereas the others were detected radiographically. Two of the pneumothoraces occurred during insertion of the initial catheter and two during insertion of the new catheter. Two additional complications may have been related to the length of time that the indwelling catheter was in place (one episode of staphylococcal bacteremia and one episode of unexplained dyspnea and hypoxemia requiring intubation). In investigating the cause of the bacteremia, a breakdown of sterile procedure was discovered that had resulted in the loss of catheter sterility before its insertion. Investigation of the episode of sudden dyspnea and hypoxemia failed to identify the cause. Noninvasive evaluation of the limbs and a ventilation/perfusion lung scan were inconclusive and a pulmonary angiogram was not performed. Therapy was directed at congestive heart failure and presumed pulmonary embolism and the patient recovered uneventfully. No patient had long-term sequelae from a complication.

Figure 1. Pairwise differences in ventricular effective refractory periods (VERP) measured with use of the initial, indwelling and new catheters (mean differences ± 1 SD). Values were calculated for each patient by subtracting the effective refractory period determined during one test at a particular cycle length and number of extrastimuli (ES) from the effective refractory period determined during the other test under the same conditions. Although the error bars span zero, many of these paired differences are significantly different from zero because of a large sample and the paired nature of the data. **Top panel,** Refractory periods are approximately 5.6 ms longer per extrastimulus delivered when measured with use of the indwelling catheter compared with the new catheter; all four values are significantly different from zero ($p < 0.05$). **Middle panels,** Refractory periods are similar when measured with the initial and indwelling catheters ($p < 0.05$ for one extrastimulus; $p > 0.05$ in other cases). **Bottom panel,** Refractory periods are shorter when measured with the new catheter compared with the initial catheter ($p > 0.05$ for one extrastimulus; $p < 0.05$ in other cases).



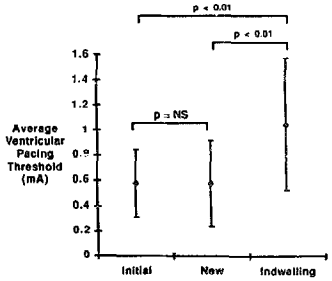


Figure 2. Average ventricular pacing thresholds determined during the three tests (mean ± 1 SD). Thresholds were significantly higher during the indwelling catheter test than during the other catheter tests ($p < 0.01$); thresholds during the initial and new catheter tests were not different ($p > 0.9$).

Discussion

The primary finding of this study is that there is no difference in frequency of induction of sustained ventricular arrhythmia between tests performed immediately after placement of a pacing catheter and tests performed simultaneously using a catheter that has remained in place for 3 to 4 days. The rate of induced tachycardia and the number of extrastimuli required to induce sustained arrhythmia are not different. Small but statistically significant changes in ventricular pacing threshold and effective refractory periods occur. Two complications may have been related to the length of time that the catheter remained in place and four others were related to invasive procedures.

Inducibility and reproducibility. These findings differ from those of a previous report (1) in which ventricular stimulation studies in 11 patients whose catheter was replaced daily (the "replacement" group) were compared with studies in 13 patients with an indwelling catheter (the "indwelling" group). It was found that arrhythmia was invariably induced in the 31 follow-up tests in the replacement group (100% reproducibility), whereas it was induced in only 28 of 36 follow-up tests in the indwelling group (78% reproducibility). The authors (1) postulated that the lower inducibility and reproducibility in the indwelling group may have been related to the indwelling nature of the catheter, but this degree of reproducibility is well within the 50% to 93% range reported in other published series (2,4–11). The unusually high 100% reproducibility and inducibility in the replacement group is not as easily understood. The results of our current study may differ from those of Duff et al. (1) because of the use of a larger study group and the considerable differences in study design. In particular, the design of the current study allowed each patient to serve as his or her own control and for the newly placed and indwelling catheters to be tested concurrently.

Changes in measured electrophysiologic variables. *Ventricular effective refractory periods.* Refractory periods measured during the indwelling catheter test were longer than those determined during the new catheter test (Fig. 1). Because these two tests were performed simultaneously, differences in refractory periods cannot be attributed to differences in heart rate or systemic factors such as residual antiarrhythmic medication levels, catecholamine levels or electrolytes; rather, they must be attributed to local (presumably time-dependent) factors such as edema, fibrin formation and tissue injury. Interestingly, refractory periods measured during the new catheter test were significantly shorter than those during the initial catheter test. These differences cannot be attributed to local time-dependent factors because these catheters had been in place for similar periods of time before the measurements were made; rather, they must be attributed to differences in systemic factors. It is unclear precisely which local and systemic factors may be involved in these subtle but statistically significant differences. Residual antiarrhythmic agents present during the initial catheter test or differences in anesthetic technique may contribute to the differences in effective refractory periods between new and initial catheter tests.

Ventricular stimulation thresholds. Change in ventricular stimulation thresholds over time is a well described phenomenon attributed to local factors; this study confirms previous findings (12).

Complications. Electrophysiologic testing is a safe procedure: the incidence of all complications in 8,548 studies at six university centers (13) has been reported to be <1%. It is unfortunate that complications during this trial occurred to a greater degree than in our overall experience; the episode of sepsis was the second such episode in >800 patients studied to date and the episode of probable pulmonary embolism was the first. To date, no study has specifically compared the incidence of complications associated with different techniques of electrophysiologic testing.

Infection. Infectious complications of central venous catheterizations have been very thoroughly investigated (14), although no study has specifically evaluated infectious risk in a large group of patients with an indwelling electrode catheter. Important determinants of the risk of infection after subclavian vein catheterization include the patient group, catheter material, presence of antithrombogenic coating, catheter size, number of lumens and type of infusate (14–19); the length of time that the catheter remains in place is not universally accepted as a risk factor. If time is a factor, it is unlikely to be significant until at least the fifth day (15,20). A prospective study (15) of 2,431 indwelling subclavian vein catheters revealed no infection before the fifth day

after insertion. In the subgroup of 1,291 patients who had a Swan-Ganz catheter inserted electively and left in place for 3 to 5 days (conditions similar to our study in many regards), there was no infection at any time. Because electrode catheters used at most institutions are small, antithrombogenically coated, without a lumen, without a port or sheath and without a requirement for manipulation, they may be expected to have a very low infection rate.

Thrombosis and pulmonary embolism. Many factors that are important for the development of infection are also important determinants of thrombosis, including catheter material, antithrombogenic bonding, catheter size, number of lumens and type of infusate. Multiple venipunctures (21) and the bed rest after femoral procedures (13) may also be important. Small gauge catheters, especially those with no lumen or a single lumen, are associated with a very low incidence of thrombosis; a review (21) of complications of subclavian vein catheterizations reported that thromboses were found exclusively in association with multilumen or large-bore catheters, constant infusion delivery systems or implanted silicone rubber venous access systems; no thromboses were related to small gauge single lumen catheters. In those studies (13,22) that addressed electrophysiologic testing in particular, thromboses were femoral, with a single exception. Small gauge antithrombogenically coated catheters such as those commonly used for electrophysiologic testing should be expected to have a particularly low risk of clinically important thrombosis and embolization and the decreased requirement for femoral venipuncture and subsequent bed rest may further decrease the incidence of this complication.

Pneumothorax. Pneumothorax is a well documented complication of subclavian vein catheterization; its incidence ranges from 0% to 6% (23). In practice, because the indwelling catheter may not be replaced during serial electropharmacologic testing, many patients undergo a single subclavian vein procedure at our institution, which could result in a lower incidence of pneumothorax. The insertion of this catheter rather than complications related to its indwelling nature have accounted for nearly all of the catheter-related morbidity in >800 patients studied at this institution.

Limitations. *Distribution of episodes of cardioversion.* This study was intended to compare results of tests in which the new and indwelling catheters were used under identical circumstances. When a rhythm requiring cardioversion was induced, such comparison was not strictly possible because testing was terminated after cardioversion. If cardioversion occurs before induction of sustained arrhythmia with both catheters, a bias is introduced that increases apparent inducibility by the catheter from which the rhythm was induced because stimulation is not continued with use of the other catheter. In the extreme example, if ventricular fibrillation had been induced with one extrastimulus with the catheter designated to be paced from first, the patient would undergo defibrillation, testing would be halted and stimulation would not be performed with the second catheter. In this circumstance, the first catheter would appear to be more capable of inducing arrhythmia than the second, whereas the second catheter may in fact have been equally capable of inducing arrhythmia had it been tested. If episodes of cardioversion were equally distributed between catheters, this would not be an issue. In this study, however, there was only one instance in which cardioversion was required for arrhythmia induced with the new catheter before the indwelling catheter could be tested with the same number of extrastimuli, whereas there were five instances in which arrhythmia that required cardioversion was induced with the indwelling catheter before the new catheter could be similarly tested. The greatest degree of bias that could arise from this effect would occur under hypothetical conditions in which all five of the "new" tests would have resulted in induction of sustained arrhythmia had testing continued after defibrillation in each of these studies. If this had been the case, the induction rate would have been 55% during the new catheter tests and 46% during the indwelling catheter tests; these induction rates are not significantly different.

Differences between the initial test and other tests. The initial ventricular stimulation test utilized two pacing sites, whereas other tests utilized only one. Although consideration of information from both sites could affect comparisons involving the initial catheter test, it cannot affect the main comparison of this study between the concurrent indwelling and new catheter tests, each of which used only one site. When results were reanalyzed after inclusion of arrhythmias induced from both sites during the initial catheter test, the findings of this study were unchanged. This was not unexpected because initial and subsequent catheter tests have previously been demonstrated to be functionally equivalent in our protocol despite different numbers of pacing sites (24). That few arrhythmias were induced at a second site confirms previous findings (25).

Residual antiarrhythmic medication. Despite a 24 h medication elimination period, antiarrhythmic medication was detectable in some patients at the time of the indwelling and new catheter tests. Because this residual medication affects the new and indwelling catheter tests equally, comparisons between these tests were not expected to be affected. Residual medication may, however, affect comparisons with the initial catheter test, including effective refractory periods and ventricular stimulation thresholds.

Practical implications. The use of an indwelling catheter allows great flexibility in the timing of bedside ventricular stimulation studies. Preparation of the patient and equipment can be performed by the nursing staff. Because no invasive procedures are performed, a stimulation study can be completed at the bedside usually in 15 to 20 min, and patients can undergo testing on weekends or weekday morn-

ings with little disruption of the routine of the patient, physician or laboratory. This may be particularly relevant for institutions without a dedicated electrophysiology laboratory, where scheduling requirements of others must be accommodated. In addition, patients may be out of bed with the electrode catheter in place; it is reasonable to infer that ambulation and fewer femoral procedures may in part be responsible for the low incidence of femoral thrombosis and embolic complications associated with the indwelling subclavian vein catheter. Because testing is expeditious, it is unusual for a patient at our institution to pass the weekend without testing; many patients undergo two tests during the weekend. This technique allows multiple serial studies to be readily performed in each patient, which may be particularly helpful in determining reproducibility of ventricular stimulation tests.

Conclusions. Serial electrophysiologic testing may be performed using an indwelling pacing catheter with neither a change in arrhythmia inducibility from baseline nor a difference in inducibility compared with that of a newly placed catheter that is tested simultaneously. Statistically significant changes in ventricular pacing threshold and effective refractory period are detectable, but appear to be clinically unimportant. Septic and clinically detectable thrombotic complications are uncommon. Although this study was not designed to compare complication rates between different methods of electrophysiologic testing, femoral and clinically important pulmonary embolic phenomena are infrequent with an indwelling electrode catheter. If these results can be applied to the setting of serial electropharmacologic testing, reductions in complications, discomfort and expenses related to invasive procedures may be realized. In addition, patient and physician time may be better utilized.

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