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Quality of Life with Defibrillator Therapy or Amiodarone in Heart Failure

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ABSTRACT

BACKGROUND

Implantable cardioverter–defibrillator (ICD) therapy significantly prolongs life in patients at increased risk for sudden death from depressed left ventricular function. However, whether this increased longevity is accompanied by deterioration in the quality of life is unclear.

METHODS

In a randomized trial, we compared ICD therapy or amiodarone with state-of-the-art medical therapy alone in 2521 patients who had stable heart failure with depressed left ventricular function. We prospectively measured quality of life at baseline and at months 3, 12, and 30; data collection was 93 to 98% complete. The Duke Activity Status Index (which measures cardiac physical functioning) and the Medical Outcomes Study 36-Item Short-Form Mental Health Inventory 5 (which measures psychological well-being) were prespecified primary outcomes. Multiple additional quality-of-life outcomes were also examined.

RESULTS

Psychological well-being in the ICD group, as compared with medical therapy alone, was significantly improved at 3 months ($P=0.01$) and at 12 months ($P=0.003$) but not at 30 months. No clinically or statistically significant differences in physical functioning among the study groups were observed. Additional quality-of-life measures were improved in the ICD group at 3 months, 12 months, or both, but there was no significant difference at 30 months. ICD shocks in the month preceding a scheduled assessment were associated with a decreased quality of life in multiple domains. The use of amiodarone had no significant effects on the primary quality-of-life outcomes.

CONCLUSIONS

In a large primary-prevention population with moderately symptomatic heart failure, single-lead ICD therapy was not associated with any detectable adverse quality-of-life effects during 30 months of follow-up.

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IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS (ICDs) significantly extend survival among patients who are at high risk for sudden death because of the severity of their underlying heart disease.^{1,2} However, concern has emerged about the effects of ICD therapy on the quality of life. One concern is that the use of ICD therapy could trade a quick, relatively painless (albeit premature) death for a more unpleasant death from progressive deterioration of the underlying heart disease or a coexisting illness.³ Furthermore, in some previous studies, receipt of multiple ICD shocks has been associated with a reduced quality of life, although the causality of this relationship is unclear.

To date, two secondary-prevention trials (in which an ICD was implanted after a life-threatening arrhythmia to prevent future events) and one primary-prevention trial (in which an ICD was implanted in patients who were at increased risk for life-threatening arrhythmia but had not had such an event) have reported quality-of-life outcomes.⁴⁻⁶ Although data from these trials have not shown any consistent evidence of a worse quality of life with ICD therapy, the conclusions that could be derived from these studies were limited by methodologic problems and relatively short follow-up.

The issue of long-term quality of life is particularly important in primary prevention, in which the willingness to accept a potentially unpleasant therapy for an uncertain future benefit may be low. We therefore examined the effects of primary-prevention ICD therapy on health-related quality of life in the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) (ClinicalTrials.gov number, NCT00000609).

Although amiodarone did not improve survival in our trial, findings from earlier studies suggested that it might improve functional status.^{7,8} Thus, we also report on the quality-of-life outcomes from the comparison between the use of amiodarone and placebo in this trial.

METHODS

PATIENT POPULATION AND STUDY OVERVIEW

Between September 16, 1997, and July 18, 2001, SCD-HeFT enrolled 2521 patients who were at least 18 years of age and who had New York Heart Association chronic, stable class II or III congestive heart failure and a left ventricular ejection

fraction of 35% or less. The study design, methods, and primary results of SCD-HeFT have been reported previously.¹ The cause of heart failure was ischemic in 52% of the patients and nonischemic in 48%. Ninety percent of the study patients were enrolled in the United States, with the remainder in Canada and New Zealand.

Patients were randomly assigned to receive state-of-the-art medical therapy plus amiodarone (Cordarone, Wyeth-Ayerst Pharmaceuticals), an amiodarone placebo, or a conservatively programmed, single-chamber ICD (Medtronic, model 7223). Therapy was initiated on an outpatient basis according to the protocol. After a median follow-up of 45.5 months (range, 24 to 72), ICD therapy was associated with a 23% reduction in mortality, as compared with medical therapy, whereas amiodarone therapy was not associated with a significant effect on mortality.

QUALITY-OF-LIFE STUDY

The quality-of-life portion of the trial was funded by the National Heart, Lung, and Blood Institute. The authors designed the study, collected and analyzed the data, and prepared the manuscript. The corporate sponsors who contributed to the support of the trial (Wyeth-Ayerst Laboratories, Knoll Pharmaceuticals, and Medtronic) had no role in the design, analysis, or interpretation of the quality-of-life study.

All patients provided written informed consent, and the study was conducted in cooperation with the National Heart, Lung, and Blood Institute. The institutional review board or ethics committee at each site approved the study protocol.

Data-Collection Methods

Quality of life was measured by means of structured interviews at baseline, at months 3 and 12, and at 30 months or at the end of the study follow-up. At each site, the study coordinator conducted interviews at the time of a scheduled clinic visit or by telephone if a clinic visit was missed. Specific training was provided to each site coordinator to ensure standardization of data collection. According to the protocol, baseline quality-of-life assessments were to be conducted after informed consent had been obtained and before randomization. Follow-up quality-of-life assessments were to be performed within 1 month before or after the scheduled contact. For patients

who were too ill to complete the full questionnaire, had a language barrier, or were otherwise unable to participate in the full interview, a short proxy form was collected.

Quality-of-Life Measures

Two measures were prespecified as primary outcomes for the quality-of-life portion of the trial: the Duke Activity Status Index (DASI), reflecting cardiac-specific physical functioning, and the Medical Outcomes Study 36-Item Short-Form (SF-36) Mental Health Inventory 5 (MHI-5), reflecting psychological well-being. DASI was constructed to be a questionnaire-based analogue of the maximal exercise stress test used for patients with cardiac disease; it is scored from 0 to 58, with higher scores indicating better function and a difference of 4 points or more considered to be clinically significant.⁹ The MHI-5, used to assess psychological well-being, is scored from 0 to 100, with higher scores indicating better function.¹⁰ A clinically significant difference in the MHI-5 has not been formally defined but can be approximated as one quarter of 1 SD (5 points in this study).

Other scales from the SF-36 were used to assess role functioning (both physical and emotional limitations), general health perceptions, bodily pain, social functioning, and vitality. Like the MHI-5, these scales are scored from 0 to 100, with higher scores indicating better function and with one quarter of 1 SD representing a reasonable indication of a clinically significant difference.

The quality-of-life interviews also collected information on total numbers of "bed days," which were defined as the number of days out of the last 42 days in which a patient was at home in bed for all or most of the day for health reasons, and "disability days," which were defined as the number of days out of the last 42 days (not counting "bed days") in which the patient had to cut down on usual activities for health reasons. Additional questions were asked to determine whether a patient could currently drive a car (yes or no) and manage money independently (yes or no). Employment details were obtained with the use of an abbreviated series of questions adapted from the Bypass Angioplasty Revascularization Investigation Substudy on Economics and Quality of Life.¹¹

We assessed the effect of heart failure on the quality of life, using the Minnesota Living with

Heart Failure scale.¹² This scale is scored from 0 to 105, with higher scores indicating worse function, and a clinically significant difference considered to be approximately 5 points.¹³

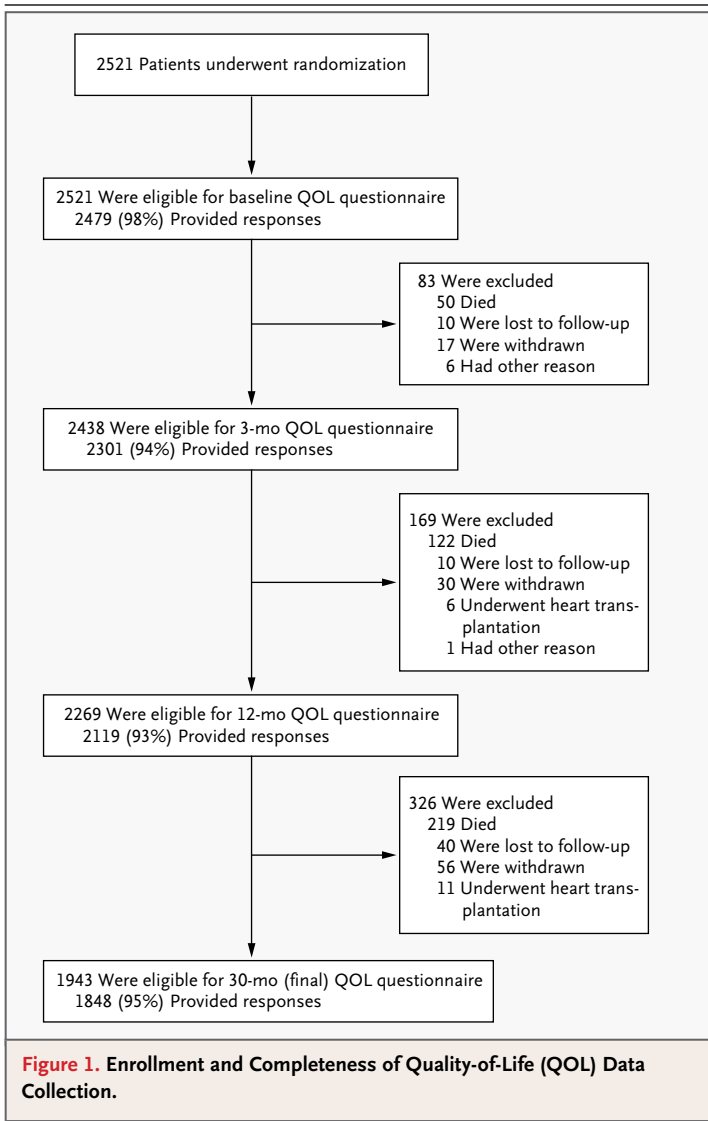
The relative desirability (utility) of each patient's health status, on a scale from 0 (a state of health equivalent to being dead) to 1 (excellent health), was assessed with the time-trade-off technique.¹⁴ Patients were asked to assume that they would have a life expectancy of 5 years in their current state of health and then were asked in a series of questions to decide how many of those 5 years they would be willing to trade for excellent health in the remaining time. As a second, more intuitive global measure, patients were also asked to rate their health on a scale of 0 to 100, with 100 indicating excellent health and 0 a state of health equivalent to being dead. A 5-point difference in this scale (one quarter of 1 SD) approximated clinical significance.

STATISTICAL ANALYSIS

We used means and standard deviations, medians and 25th to 75th percentiles, or both to describe the distributions of continuous variables. Percentages were used to describe categorical variables. Univariate comparisons were performed with the use of Pearson's chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Each active treatment was compared pairwise with the placebo group.

Patients with an ICD who received a shock from the device within the month preceding a scheduled quality-of-life assessment were compared with patients in the ICD group who did not receive a shock during the same period. These comparisons were based on the Wilcoxon rank-sum test for changes in the scores from the most recent quality-of-life measurements before the shock occurred. This analysis was repeated with the use of 2-month and 12-month time frames.

The primary outcome of the trial — death from any cause — differed significantly between the ICD group and the placebo group. This mortality difference resulted in a nonrandom subgroup of survivors whose quality of life could be compared according to the assigned treatments. To account for this potential bias, we applied an estimator for the survival average causal effect as a sensitivity analysis.^{15,16} These estimates are based on weighted averages of the observed



quality-of-life data multiplied by survival estimates specific to the study group, with P values and 95% confidence intervals for the estimated survival average causal effect based on a non-parametric bootstrap procedure.¹⁷

All reported P values are two-sided. No adjustments were made for multiple testing.

RESULTS

PATIENTS AND BASELINE CHARACTERISTICS

Of 2521 patients who underwent randomization, 2479 (98%) completed quality-of-life questionnaires at baseline (Fig. 1). The initial demographic and clinical characteristics of the patients were well balanced among the study groups (Table 1).¹

At each follow-up interval, questionnaires were collected from 93 to 95% of eligible patients. Overall, from a total of 9171 expected contacts with patients, 8747 quality-of-life questionnaires (95%) were collected. Only 1.2% of patients declined to complete the questionnaires, and only 1.4% of forms were judged to be incomplete. In 69 of 6268 follow-up interviews (1.1%), proxy forms were substituted for the full questionnaire.

QUALITY-OF-LIFE OUTCOMES

In unadjusted comparisons, cardiac-specific physical functioning on DASI did not differ significantly between the ICD group and the placebo group at baseline (median score of 23 in both groups, $P=0.76$) and at months 3, 12, and 30 (median score of 24 in both groups for all three intervals, $P>0.10$) (Table 2 and Fig. 2A). There were also no significant differences at any point between the amiodarone group and the placebo group on cardiac-specific physical functioning.

Psychological well-being did not differ significantly between the ICD group and the placebo group at baseline on MHI-5 (median scores of 76 in both groups, $P=0.17$) but was better in the ICD group than in the placebo group at 3 months (median scores, 80 and 76, respectively; $P=0.01$) and at 12 months (median scores, 80 and 76, respectively; $P=0.003$). At 30 months, there was no significant difference between the two study groups (median score of 76 in both groups, $P=0.79$) (Table 2 and Fig. 2B). In the comparison between the amiodarone and placebo groups, we did not observe significant differences at any point during follow-up on the basis of MHI-5.

For each of the six other SF-36 scales, at least one interval comparison (i.e., at 3 months, 12 months, or both) showed significantly better scores in the ICD group. However, values were clinically similar and did not differ significantly at baseline or at 30 months on any of these scales (Table 1 of the Supplementary Appendix, available with the full text of this article at www.nejm.org). As compared with patients in the placebo group, those in the amiodarone group had significantly higher scores on the SF-36 pain index at all four time points.

At baseline, patients reported a mean of approximately 2 bed days and 8 to 9 disability days during the preceding 42 days. In addition, 86% of patients were able to drive a car, 92% could manage their finances independently, and 27%

Table 1. Baseline Characteristics of the Patients.*

Variable	Amiodarone (N=830)	Placebo (N=833)	ICD (N=816)
Age — yr	59.6±11.9	59.1±11.9	59.9±11.9
Female sex — no. (%)	204 (24.6)	190 (22.8)	187 (22.9)
Nonwhite race — no. (%)†	188 (22.7)	197 (23.6)	184 (22.5)
New York Heart Association class II — no. (%)	592 (71.3)	583 (70.0)	556 (68.1)
Ischemic cause of heart failure — no. (%)	420 (50.6)	449 (53.9)	425 (52.1)
Ejection fraction — %	23.9±7.0	24.0±6.8	23.6±7.0
Current smoker — no. (%)	123 (14.8)	139 (16.7)	141 (17.3)
Other conditions — no. (%)			
Diabetes	238 (28.7)	263 (31.6)	250 (30.6)
Hypertension	457 (55.1)	474 (56.9)	448 (54.9)
Pulmonary disease	145 (17.5)	158 (19.0)	174 (21.3)
Atrial fibrillation or flutter	129 (15.5)	114 (13.7)	139 (17.0)
Previous stroke	53 (6.4)	64 (7.7)	43 (5.3)

* Plus–minus values are means ±SD. ICD denotes implantable cardioverter–defibrillator.

† Race was self-reported.

were employed outside the home. We were not able to detect an effect of ICD therapy as compared with placebo on the number of bed days or disability days or on the proportion of patients who were able to drive a car, manage their finances, or maintain employment during the follow-up period.

The Minnesota Living with Heart Failure scores were similar at baseline in the ICD group and the placebo group (median scores, 41 and 43, respectively; $P=0.77$). Scores were generally better (i.e., lower) in the ICD group than in the placebo group at 3 months (median scores, 30 and 36, respectively; $P=0.006$), at 12 months (median scores, 32 and 36, respectively; $P=0.07$), and at 30 months (median scores, 32 and 36, respectively; $P=0.05$).

The time–trade-off utility measure averaged 0.80 at baseline in all three study groups; there was a significant improvement in the ICD group over the placebo group at 3 months but not at any of the other time points. On a scale of 0 (worst) to 100 (best), the patients in the ICD group rated their overall health more highly than did those in the placebo group at 3 months (median scores, 75 and 70, respectively; $P=0.002$) and at 12 months (median scores, 75 and 70, respectively; $P=0.05$), but there was no significant difference at 30 months (median score of 70 in both groups, $P=0.18$).

EFFECT OF ICD SHOCKS ON QUALITY OF LIFE

In the ICD group, 49 patients received a shock within 1 month before a scheduled quality-of-life assessment. As compared with patients in the ICD group who did not receive a shock, the quality of life of patients in the month after a shock was characterized by a significant decrease in perceived general health, physical and emotional functioning, social functioning, and self-rated health (all comparisons unadjusted) (Fig. 3).

For the 66 patients who had received a shock within 2 months before a scheduled quality-of-life assessment, the pattern was the same but with smaller differences. When we compared the quality of life of 100 surviving patients who had received an ICD shock at any time during the first year of the study with that of 638 patients who did not receive a shock, no significant differences were evident. In addition, the number of ICD discharges above an arbitrary number, ranging from 2 to 5 or more, did not have a significant effect on the subsequent quality of life.

SURVIVAL-ADJUSTED ANALYSES

To account for the improved survival of the patients in the ICD group, we estimated the survival average causal effect for each quality-of-life variable. Overall, the results were not materially different from the unadjusted comparisons described above (Table 3).

Table 2. Primary Quality-of-Life Measures.*

Measure	Amiodarone	ICD	Placebo	Difference between Amiodarone and Placebo (95% CI)	Difference between ICD and Placebo (95% CI)
Duke Activity Status Index†					
Baseline					
No. of patients	825	814	829		
Median (interquartile range)	23 (14 to 35)	23 (13 to 33)	23 (13 to 34)		
Mean	25.3±14.1	24.6±13.6	24.9±14.1	0.44 (-0.92 to 1.80)	-0.34 (-1.68 to 1.00)
3 mo					
No. of patients	756	766	768		
Median (interquartile range)	23 (15 to 37)	24 (16 to 37)	24 (15 to 37)		
Mean	26.2±14.7	26.9±14.1	26.2±14.3	-0.01 (-1.47 to 1.45)	0.69 (-0.73 to 2.11)
12 mo					
No. of patients	676	734	697		
Median (interquartile range)	23 (15 to 37)	24 (16 to 37)	24 (15 to 38)		
Mean	26.1±14.5	26.8±14.4	26.6±14.8	-0.58 (-2.14 to 0.97)	0.16 (-1.35 to 1.68)
30 mo					
No. of patients	575	665	585		
Median (interquartile range)	24 (15 to 38)	24 (16 to 37)	24 (13 to 37)		
Mean	27.1±15.3	26.8±14.3	25.9±15.3	1.20 (-0.56 to 2.96)	0.89 (-0.75 to 2.53)
Mental Health Inventory 5†					
Baseline					
No. of patients	827	814	830		
Median (interquartile range)	76 (60 to 88)	76 (60 to 88)	76 (56 to 88)		
Mean	72.1±20.1	71.7±20.5	70.0±21.4	2.11 (0.11 to 4.11)‡	1.64 (-0.39 to 3.67)
3 mo					
No. of patients	759	764	767		
Median (interquartile range)	76 (60 to 88)	80 (64 to 88)	76 (60 to 88)		
Mean	72.9±20.6	74.4±19.3	71.3±21.5	1.60 (-0.51 to 3.72)	3.15 (1.10 to 5.19)‡

12 mo				
No. of patients	674	734	693	
Median (interquartile range)	76 (60 to 88)	80 (60 to 90)	76 (56 to 88)	
Mean	72.9±20.5	74.5±18.9	70.9±21.5	1.99 (-0.24 to 4.22)
30 mo				
No. of patients	560	654	564	
Median (interquartile range)	76 (60 to 91)	76 (60 to 88)	76 (56 to 88)	
Mean	73.2±20.3	72.2±19.1	71.0±21.7	2.22 (-0.24 to 4.68)
				1.24 (-1.06 to 3.53)

* Plus-minus values are means ±SD. ICD denotes implantable cardioverter-defibrillator.

† Primary quality-of-life measures were scores on the Duke Activity Status Index, which range from 0 to 58, with higher scores indicating better function, and scores on the Medical Outcomes Study 36-Item Short-Form Mental Health Inventory 5, which range from 0 to 100, with higher scores indicating better function.

‡ P≤0.05, uncorrected for multiple comparisons.

DISCUSSION

In our trial, single-lead ICD therapy enhanced survival and did not detectably diminish health-related quality of life for up to 30 months in patients with stable but moderately symptomatic heart failure. Although ICD therapy for primary prevention of sudden death was not expected to improve the quality of life, the possibility of harm from either psychological or physical complications of the therapy was of concern. In our overall comparisons, we found no statistically or clinically significant evidence of either psychological or physical harm. In a double-blind comparison of amiodarone with placebo, we did not detect an effect of amiodarone on either of the two primary quality-of-life measures.

Among patients in the ICD group who had received an ICD shock within the month preceding a scheduled follow-up visit, as compared with patients who had not received a shock, the quality of life was diminished in multiple domains. An analysis that included patients who had received shocks within 2 months before a quality-of-life assessment showed the same trends but with reductions in the magnitude and statistical significance of the differences. These trends were eliminated altogether when the window between the ICD shock and subsequent assessment was extended to 1 year. Although it may be plausible to assume that this association was causal, our analyses did not have sufficient statistical power to examine the relative contributions of the ICD shocks and concomitant deterioration in clinical status to these observations.

Among other primary-prevention trials of ICD therapy, only the Coronary Artery Bypass Graft (CABG)-Patch trial has reported on quality-of-life outcomes.¹⁸ At 6 months, the ICD group had significantly lower levels of psychological well-being than the control group. Furthermore, patients who had received at least one ICD shock had a reduced quality of life on several measures. Important differences between the CABG-Patch quality-of-life study and our study include the ICD technology (a large, bulky ICD in the CABG-Patch study vs. a small, low-profile ICD in our study), the method of ICD implantation (open-chest implantation with an abdominal pocket vs. outpatient transvenous implantation with a pectoral pocket), and the target population (patients referred for CABG who had an ejection fraction

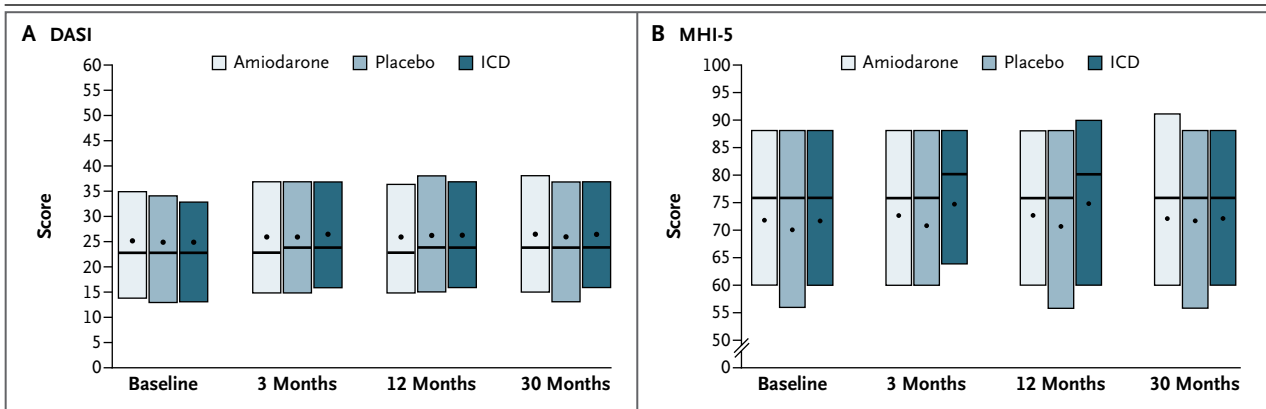


Figure 2. Scores on the DASI and MHI-5 in the Three Study Groups.

Panel A shows scores for cardiac physical function on the Duke Activity Status Index (DASI) on a scale ranging from 0 to 58, with higher scores indicating better function. Panel B shows scores for psychological well-being on the Medical Outcomes Study 36-Item Short-Form Mental Health Inventory 5 (MHI-5) on a scale ranging from 0 to 100, with higher scores indicating better function. The top lines of the box plots represent 75th percentiles, the bottom lines represent 25th percentiles, horizontal lines within the boxes represent medians, and dots represent means. ICD denotes implantable cardioverter–defibrillator.

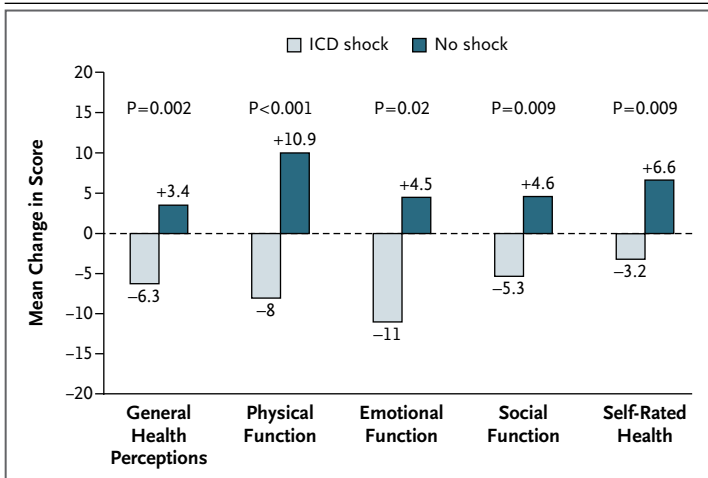


Figure 3. Effect of ICD Shocks on Patients' Quality of Life.

Patients in the implantable cardioverter–defibrillator (ICD) group who had received an ICD shock within 1 month before a scheduled quality-of-life follow-up assessment were compared with patients who had not received a shock. Changes in scores on the Medical Outcomes Study 36-Item Short-Form (SF-36) scale for patients who had received an ICD shock were calculated as the value after the shock was delivered minus the most recent value before the shock was delivered. Changes in scores for the comparison groups were the quality-of-life values at 3 months minus the values at baseline. The results were similar when other follow-up time points (i.e., 12 months and 30 months) were used to calculate the changes in scores in the no-shock subgroup. A positive change indicates better function.

of $\leq 35\%$ vs. those with stable heart failure and an ejection fraction of $\leq 35\%$, about 50% of whom had a nonischemic cause of heart failure).

Another large study of quality of life in pa-

tients who had undergone ICD therapy was the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial, a secondary-prevention study that was stopped prematurely by the data and safety monitoring board because of the improved survival in the ICD group.^{4,19} In that study, the ICD group and the antiarrhythmic-therapy group had similar changes in scores on both the physical and mental components of the SF-36 questionnaire. Among patients in the ICD group with complete data on ICD shocks and follow-up quality-of-life data, the occurrence of one or more ICD shocks was significantly associated with subsequent reductions in both physical functioning and psychological well-being. Major differences between the AVID trial and our study include differences in the study populations (patients with life-threatening arrhythmias in the AVID trial vs. those with stable heart failure in our study) and a significantly lower rate of quality-of-life data collection in the AVID trial (83% at baseline and 61% at 1 year). Nonetheless, a reasonable conclusion from the AVID analysis is that in the absence of administered shock therapy, ICDs were well tolerated and did not diminish the quality of life.

The Canadian Implantable Defibrillator Study (CIDS), another secondary-prevention ICD trial, obtained quality-of-life data at 6 and 12 months of follow-up.⁵ Scores for emotional and physical health improved in the ICD group, as compared with the amiodarone group. Patients in the ICD

Table 3. Differences between Study Groups in Quality-of-Life Measures.*

Outcome	3 Months	12 Months <i>difference (95% CI)</i>	30 Months
Amiodarone versus placebo			
Primary measures†			
DASI	-0.06 (-1.42 to 1.31)	-0.72 (-2.29 to 0.84)	0.99 (-0.81 to 2.80)
MHI-5	1.57 (-0.51 to 3.65)	1.92 (-0.32 to 4.16)	2.05 (-0.55 to 4.64)
Secondary measures‡			
SF-36			
Pain	5.82 (3.07 to 8.58)§	4.12 (1.28 to 6.96)§	5.54 (2.71 to 8.37)§
General health	0.69 (-1.50 to 2.88)	0.83 (-1.56 to 3.23)	0.44 (-2.23 to 3.12)
Emotional function	3.66 (-0.37 to 7.69)	1.96 (-2.23 to 6.15)	1.14 (-4.01 to 6.29)
Physical function	1.99 (-1.71 to 5.69)	1.46 (-2.32 to 5.24)	3.44 (-1.21 to 8.09)
Social function	1.10 (-1.84 to 4.05)	0.36 (-2.32 to 3.03)	1.36 (-1.62 to 4.34)
Vitality	0.45 (-1.83 to 2.73)	1.17 (-1.35 to 3.69)	0.23 (-2.30 to 2.77)
Self-rating scale	-0.15 (-2.20 to 1.89)	1.01 (-1.30 to 3.32)	1.02 (-1.63 to 3.68)
Time trade-off	0.08 (-0.09 to 0.24)	-0.02 (-0.19 to 0.14)	0.00 (-0.18 to 0.17)
ICD versus placebo			
Primary measures†			
DASI	0.64 (-0.84 to 2.12)	0.01 (-1.55 to 1.58)	0.61 (-1.03 to 2.26)
MHI-5	3.13 (1.09 to 5.18)§	3.56 (1.43 to 5.69)§	1.02 (-1.38 to 3.41)
Secondary measures‡			
SF-36			
Pain	4.99 (2.18 to 7.81)§	4.48 (1.64 to 7.32)§	1.58 (-1.20 to 4.36)
General health	3.24 (0.84 to 5.64)§	2.97 (0.54 to 5.40)§	0.53 (-2.02 to 3.09)
Emotional function	5.38 (1.45 to 9.32)§	4.06 (-0.02 to 8.14)	-0.98 (-6.10 to 4.14)
Physical function	4.36 (0.50 to 8.22)§	3.48 (-0.61 to 7.57)	3.35 (-1.54 to 8.23)
Social function	3.43 (0.65 to 6.20)§	3.68 (1.21 to 6.14)§	0.79 (-2.07 to 3.64)
Vitality	2.50 (0.09 to 4.91)§	1.62 (-0.74 to 3.99)	0.03 (-2.62 to 2.67)
Self-rating scale	3.49 (1.49 to 5.50)§	2.83 (0.63 to 5.02)§	1.94 (-0.57 to 4.45)
Time trade-off	0.19 (0.03 to 0.34)§	-0.01 (-0.16 to 0.14)	0.00 (-0.16 to 0.16)

* Values are mean differences in scores on quality-of-life scales between study groups at each follow-up point, adjusted for differences in survival. Positive values indicate that either of the active treatments was better than placebo. ICD denotes implantable cardioverter-defibrillator.

† Primary measures were scores on the Duke Activity Status Index (DASI) and the Medical Outcomes Study 36-Item Short-Form Mental Health Inventory 5 (MHI-5).

‡ Secondary measures were scores on various domains of the SF-36 survey and on the self-rating scale and time trade-off.

§ P<0.05.

group who received five or more shocks did not have improvement in these quality-of-life scales, as compared with patients who received fewer than five shocks. However, the quality-of-life scores for patients in the ICD group who received one to four shocks during follow-up did not differ significantly from those for patients who received no shocks.

All studies of the effects of ICD therapy on

quality of life, including our study, are limited by an inability to mask the therapy. Thus, the perceived effects of ICDs that we show may reflect attitudes of the study doctors and nurses that were transmitted to the patients, as well as the beliefs and expectations of the patients themselves. Patients may view the ICD either as an electronic security blanket or as an unpredictable and uncontrollable source of physical and emo-

tional discomfort. In this unblinded comparison, we observed small improvements in some domains of quality of life during the first year of follow-up in the ICD group. We have no direct means of determining whether these improvements reflect the effects of such biases.

Caution should be exercised in interpreting significant differences in quality-of-life measures among the study groups, given the numerous statistical tests performed in this study. P values that are shown were uncorrected for multiple comparisons. Since the quality of life was a secondary outcome, the study was not constructed to test formally for the noninferiority of ICD therapy with respect to these outcomes.

Our evaluation of the effects of ICD shocks on subsequent quality of life was limited by the lack of quality-of-life data linked to the delivery of ICD shocks (collection of such data was judged to be logistically infeasible) and by the relatively small number of patients with a quality-of-life assessment shortly after a shock episode. We did not have enough patients with multiple shock

episodes during a 24-hour period ("ICD storm") to determine the effects of that phenomenon on subsequent quality of life.

In conclusion, we evaluated the quality of life of patients with moderately symptomatic, stable heart failure. Random assignment to the ICD group was not associated with adverse effects on health-related quality of life during the first 30 months of follow-up.

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