Quality of Life in the Antiarrhythmics Versus Implantable Defibrillators Trial

Impact of Therapy and Influence of Adverse Symptoms and Defibrillator Shocks

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Background—Implantable cardioverter defibrillator (ICD) use reduces mortality in patients with serious ventricular arrhythmias compared with antiarrhythmic drug (AAD) use. However, the relative impact of these therapies on self-perceived quality of life (QoL) is unknown.

Methods and Results—Three self-administered instruments were used to measure generic and disease-specific QoL in Antiarrhythmics Versus Implantable Defibrillators trial participants. Generalized linear models were used to assess the relationships between self-perceived QoL and treatment (AAD versus ICD) and adverse symptoms and ICD shocks. To minimize the impact of missing data, only patients surviving 1 year were included in the primary analyses. Baseline characteristics among QoL participants (n=905) and nonparticipants (n=111) were similar, but participants who survived 1 year (n=800) were healthier at baseline than nonsurvivors (n=105). Of the 800 patients in the primary analysis, characteristics of those randomized to AAD (n=384) versus ICD (n=416) were similar. Overall, ICD and AAD use were associated with similar alterations in QoL. The development of sporadic shocks and adverse symptoms were each associated with reduced physical functioning and mental well-being and increased concerns among ICD recipients, whereas development of adverse symptoms was associated with reduced physical functioning and increased concerns among AAD recipients.

Conclusions—ICD and AAD therapy are associated with similar alterations in self-perceived QoL over 1-year follow-up. Adverse symptoms were associated with reduced self-perceived QoL in both groups, and sporadic shocks were associated with reduced QoL in ICD recipients. (Circulation. 2002;105:589-594.)

Key Words: quality of life ■ antiarrhythmia agents ■ heart arrest ■ tachyarrhythmias ■ defibrillation

Although the assessment of survival is vital to evaluating the efficacy of therapeutic strategies, quality of life (QoL) measurement is important for understanding how these strategies impact the daily lives of patients.1-4 Comprehensive QoL assessment includes the evaluation of physical, psychosocial, and emotional factors that contribute to an individual’s self-perceived QoL.5-10 To date, there is no randomized, prospective information regarding the impact of implantable cardioverter defibrillator (ICD) versus antiarrhythmic drug (AAD) therapy on the QoL of persons with serious ventricular arrhythmias. Moreover, although adverse symptoms related to either therapy would be anticipated to influence QoL, this has not been confirmed nor quantified. Likewise, the impact of shocks on the QoL of ICD recipients is an important aspect of the long-term care that merits additional study.

The Antiarrhythmics Versus Implantable Defibrillators (AVID) trial demonstrated improved survival with ICD compared with AAD therapy, primarily empiric amiodarone, in patients with ventricular fibrillation (VF) or symptomatic ventricular tachycardia (VT).11 Self-perceived QoL assessment was a predefined, secondary endpoint in the AVID trial. This analysis describes and contrasts temporal changes in QoL among AVID participants randomized to an ICD versus

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AVID and evaluates the impact of adverse symptoms and ICD shocks on self-perceived QoL.

**Methods**

**AVID Trial**
AVID was a multicenter, randomized trial that compared ICD with AAD therapy in patients with VF or symptomatic VT. Symptomatic VT included sustained VT resulting in syncope or sustained VT in the setting of a left ventricular ejection fraction \( \leq 0.40 \) and clinically important symptoms of hemodynamic compromise. A total of 1,016 patients were randomized before the early termination of AVID, when participants randomized to an ICD were shown to have significantly improved survival.11

**QoL Measurement**
In AVID, QoL was defined as a multidimensional construct that is individually perceived, dynamic, and quantifiable by self-report.12 Assessment of QoL began in June of 1993, concurrent with the onset of the overall trial. The initial year was used to evaluate instrument reliability,13 whereas the latter portion used a reduced set of 3 questionnaires to assess both generic and disease-specific QoL. Data were censored as of April 7, 1997, the date the main trial was terminated. Participants were encouraged to enroll in the QoL substudy; however, participation was not mandatory. Measurements were obtained at baseline (before randomization) and at 3, 6, and 12 months after randomization.

**Instruments**
The Medical Outcomes Short Form 36-item questionnaire (SF-36) measures generic health status.14,15 It evaluates several health dimensions, including limitations in physical, emotional, or social functioning because of health or emotional problems, bodily pain, general health perceptions, vitality (energy and fatigue), and general mental health (psychological distress and well-being). Four subscales measure physical health, whereas 4 others evaluate the impact of disease or treatment on an individual’s mental health. Each set of subscales can be reduced to a summary measure, a physical component summary (PCS) score, and a mental component summary (MCS) score.14,15 Overall SF-36 scores, PCS scores, and MCS scores each range from 0 to 100 points, with higher scores indicating superior QoL. The patient concerns checklist evaluates disease-specific aspects of QoL relevant to patients with VF or symptomatic VT. The 46-item checklist used in the present analysis16 was adapted from a 63-item assessment. Scores range from 0 to 46 points, with higher scores indicating increased concern and poorer QoL. The cardiac version of the QoL index (QL index) assesses issues relevant to persons with heart disease,17 including satisfaction and health perception, functioning, socioeconomic factors, psychological and spiritual well-being, and family life. Scores range from 0 to 30 points, with higher scores indicating superior QoL. The SF-36 and patient concerns checklist were administered at baseline and 3, 6, and 12 months, whereas the QL index was administered at baseline and 12 months after randomization.

**Adverse Symptoms**
Symptoms were assessed and recorded at baseline and at follow-up. Data were collected at each visit and when a long-term change in therapy occurred (eg, crossover, ICD reprogramming, or AAD dose alteration). Symptoms were labeled as cardiovascular, pulmonary, neurological, ocular, dermatological, gastrointestinal, genitourinary, musculoskeletal, endocrine, or infectious. Some prespecified ECG abnormalities were considered adverse symptoms (bradyarrhythmias causing a prompt change in therapy, advanced heart block, a QRS duration \( \geq 200 \) ms or \( \geq 2 \) times the baseline value, or a corrected QT interval \( \geq 500 \) ms), as were ICD complications or heart failure requiring the initiation of or a change in treatment. Local investigators categorized symptoms as mild to moderate or severe on the basis of prespecified descriptions. Noticeable, bothersome, or uncomfortable symptoms that resulted in minor change of study therapy or a

**Results**
**Study Population**
Of the 1,016 patients randomized to ICD or AAD therapy, 905 patients (89%) completed at least one QoL assessment in the first year of follow-up (Figure 1). QoL substudy participants were younger on average (65 versus 68 years) and more likely to be male (81% versus 70%), be white (88% versus 70%), be living with a spouse or partner (71% versus 51%), and have graduated from high school (73% versus 42%) compared with the 111 nonparticipants. Most (800 of 905 [88%]) QoL substudy participants survived 1 year. As a group, those who survived were more likely to live with a
spouse or partner (72% versus 62%) and to have graduated from high school (74% versus 65%) compared with the 105 participants who died in the first year after randomization. The 800 participants who survived 1 year had higher mean left ventricular ejection values (0.32 versus 0.27), were less likely to have a history of heart failure (43% versus 70%), were more likely to receive an ICD (52% versus 37%), and were more often discharged with a β-blocker (30% versus 17%) compared with the 105 participants who died in the first year. Of the 800 patients included in the present analysis, 416 were randomized to an ICD and 384 were randomized to AAD therapy. Baseline characteristics of these groups were similar, except that the patients assigned to ICD therapy were more often discharged from hospital with β-blocker therapy (Table 1).

Incomplete Data
Complete QoL data were available for most patients at each of the specified time points (Table 2). A larger amount of information was missing at later compared with earlier assessments. Most (49%) incomplete data were considered missing because of their collection outside of specified time periods.

Baseline Scores
Self-perceived physical functioning (PCS) and mental well-being (MCS) were significantly impaired in both treatment groups (Figure 2). Participants randomized to an ICD had mean PCS and MCS scores of 37.4±10.9 and 45.9±11.8, respectively, whereas those randomized to AAD therapy had scores of 36.5±11.2 and 47.5±11.5, respectively. High baseline patient concerns checklist (15.9±8.6 versus 16.2±8.9) and low QL index (22.1±4.9 versus 21.9±5.0) scores were also observed in patients randomized to ICD versus AAD therapy, respectively.

Change in Scores Over Time
Baseline PCS scores were alike in the 2 treatment groups (P=0.3) and increased over time (P=0.01) similarly (P=0.3). When patients who died in the first year of follow-up were included, similar results in baseline scores (P=0.1), alteration in scores over time (P=0.01), and change in 2 treatment groups over time (P=0.3) were observed. Participants randomized to an ICD had lower mean MCS scores at baseline compared with AAD patients (P=0.006). No significant time trend in MCS scores was observed during follow-up (P=0.7). When participants who died in the first year were included, similar results in baseline scores (P=0.04) and temporal changes in MCS were observed

| TABLE 1. Characteristics of Eligible Patients by Treatment Group |
|-------------------|-------------------|------------------|
| Characteristic    | ICD (n=416)       | AAD (n=384)      | P     |
| Age, mean±SD      | 64.3±10.5         | 64.7±10.1        | 0.5   |
| Male, %           | 81.3              | 80.5             | 0.8   |
| White race, %     | 89.7              | 88.0             | 0.5   |
| Live with spouse/partner, % | 72.6 | 70.6 | 0.5 |
| High school graduate, % | 74.0 | 74.5 | 0.9 |
| VF index arrhythmia, % | 43.5 | 42.4 | 0.8 |
| Ejection fraction, mean±SD | 0.33±0.13 | 0.32±0.14 | 0.6 |
| History of heart failure, % | 44.5 | 41.1 | 0.3 |
| Discharge β-blocker use, % | 43.0 | 16.4<0.001 |

| TABLE 2. Complete Versus Incomplete Information Among Eligible Patients (n=800) |
|-------------------|-------------------|-------------------|-------------------|
| Visit             | Baseline          | 3-Month           | 6-Month           | 12-Month          |
| Form completed    | 667 (83%)         | 630 (79%)         | 575 (72%)         | 491 (61%)         |
| Form not completed| 133 (17%)         | 170 (21%)         | 225 (28%)         | 309 (39%)         |
| Outside of specified collection time point | 48 | 46 | 104 | 210 |
| Physical limitation, too ill | 28 | 10 | 17 | 16 |
| Patient refusal   | 19                | 24                | 21                | 24                |
| Patient forgot    | 2                 | 43                | 34                | 25                |
| Cannot read English | 9 | 4 | 3 | 2 |
| Missing           | 0                 | 18                | 27                | 13                |
| Other reason      | 27                | 25                | 19                | 19                |
Patients who received an ICD and were discharged from hospital on β-blocker therapy had similar MCS (P=0.9) and PCS (P=0.9) scores compared with patients who received an ICD and were not receiving β-blockers at the time of hospital discharge. No significant differences in patient concerns checklist scores at baseline (P=0.6) or during follow-up (P=0.1) were observed between groups, but scores declined over time in the group as a whole (P<0.001). When participants who died in the first year were included, similar results in baseline (P=0.6) and follow-up (P=0.2) scores were observed. Similar mean baseline and follow-up QL index scores were observed in the 2 groups, and scores did not significantly change over time.

### Adverse Symptoms

Adverse symptoms were reported in 49% of patients during the first 3 months, among 36% of patients at 6 months, and in 54% of patients at 1 year. The proportion of patients with adverse symptoms was similar in the 2 treatment groups (P=0.8). Most adverse symptoms (62%) were categorized as cardiovascular (34%) or relating to worsening heart failure (28%). Severe adverse symptoms were reported in 17% of patients at 3 months, 7% of patients at 6 months, and 14% of patients at 1 year. Most of these (69%) were categorized as ICD complication (35%), cardiovascular (18%), or related to worsening heart failure (16%). The occurrence of adverse symptoms was associated with significant reductions in PCS and MCS scores in patients randomized to ICD implantation and reduced PCS scores in patients randomized to AAD therapy on multivariate analysis. A similar relationship between severe adverse symptoms and alterations in QoL scores was observed. Significant increases in patient concerns were observed, independent of the randomized therapy (Table 3).

### ICD Shocks

Among the 416 ICD recipients, 373 (90%) had complete data on the development of shocks. Of these 373 patients, 144 (39%) experienced ≥1 shock during the initial year of follow-up. The majority of shocks (94%) were categorized as appropriate. Similar numbers of ICD recipients who experienced shocks had 1 or 2 shocks (n=71; 49%) versus ≥3 shocks (n=73; 51%). In the initial 3 months of follow-up, 85 patients experienced ≥1 shocks, whereas 52 patients suffered shocks between 3 to 6 months and 55 experienced shocks in the final 6 months of follow-up. The occurrence of ≥1 versus no shocks during these time periods was independently associated with significant reductions in mental well-being and physical functioning and an increase in patient concerns (Table 3). The development of more frequent shocks (≥3 versus <3) was associated with similar alterations in self-perceived QoL.

### Discussion

This analysis demonstrates that ICD and AAD therapy are associated with similar effects on self-perceived QoL in patients with serious ventricular arrhythmias. The development of adverse symptoms is associated with significant impairment in QoL, regardless of the therapeutic strategy, and the occurrence of sporadic shocks in ICD recipients.

### Other Cardiac Populations

Data on QoL in patients with life-threatening arrhythmias are sparse. The data in the present analysis provide important information on baseline and serial QoL in a large group of patients with serious ventricular arrhythmias receiving contemporary therapy. Baseline physical function and mental well-being were lower than mean values (50.7±9.5 and 50.0±9.9, respectively) in the general adult population in the United States, indicating moderate to severe impairment in self-perceived QoL. Similar degrees of impairment have been reported in elderly patients with a recent myocardial infarction and in elderly persons with severe heart failure. These values are substantially lower than ambulatory patients with heart failure or hypertension, indicating that patients with serious ventricular arrhythmias have greater impairment in QoL when compared with patients with other forms of heart disease.

### Influence of Treatment

Self-perceived physical functioning was stable over time and did not differ between the 2 treatment groups. Stability in this aspect of QoL is not surprising given that neither therapy would be anticipated to alter physical functioning. Our results are consistent with smaller studies, which have demonstrated that physical functioning is frequently impaired in patients receiving an ICD. However, in contrast to smaller studies, which suggested that this impairment was a transient phenomenon, we found it to be relatively stable during follow-up. Thus, baseline physical functioning assessment seems to provide a reasonable measure of longer-term functioning. Self-perceived mental well-being scores were lower in patients randomized to ICD versus AAD therapy at baseline but were similar in the 2 groups at 1 year. This finding may reflect regression to the mean or simply a chance finding. The convergence of scores over time likely reflects regression to the mean rather than the influence of AAD.
versus ICD therapy, given that MCS scores were similar in the 2 groups by 3 months.

**Adverse Symptoms**

The development of adverse symptoms was associated with a significant reduction in physical functioning among participants randomized to AAD therapy and both physical functioning and mental well-being in participants randomized to an ICD. The development of severe adverse symptoms was also associated with significant reductions in physical functioning in both groups. Adverse symptoms were associated with a significant increase in patient concerns with both therapies. These data are not surprising given the presumed impact of adverse symptoms on patient’s daily lives.

**ICD Shocks**

The occurrence of ICD shocks is associated with increased psychological distress in both patients and their families. Past studies indicate that patients who experience frequent (>5) shocks have lower QoL compared with those who do not. The present analysis extends these findings by demonstrating that, independent of other markers of disease severity, the development of ≥1 shock in the initial year of follow-up is associated with significant declines in both physical functioning and mental well-being and increased patient concerns. This result has important implications, because the development of frequent ICD therapies is also associated with an increased risk of death, and therapies designed, in part, to reduce the frequency of recurrent VT and VF, such as sotalol, seem to reduce cardiovascular mortality. The present analysis raises the possibility that reducing ICD shock frequency may lead to an improvement in QoL as well. However, this remains to be prospectively evaluated.

**Limitations**

The primary results were based on excluding patients who died during the first year of follow-up and thus may provide a biased estimate of differences between ICD and AAD therapy. These patients were excluded because their QoL could not be reliably defined. It is unlikely that these deaths occurred independently of QoL. Arguably, QoL would be anticipated to be more significantly impaired in individuals who died before 1 year, and the QoL of these patients is likely to be lower than that of the overall group. By including only patients who survived 1 year, more reliable estimates of changes in QoL were obtained. Despite this, when all patients were analyzed, independent of their surviving 1 year, similar results were obtained. It is also important to note that QoL assessment was limited to the initial year of follow-up, and it is possible that long-term differences in QoL may exist because of more frequent ICD complications over time and higher rates of organ toxicity with long-term amiodarone usage.

**Clinical Significance**

This is the first large, prospective evaluation of the effect of ICD versus AAD therapy on the self-perceived QoL of patients with serious ventricular arrhythmias. Although ICD and AAD therapy are associated with similar self-perceived QoL, the development of adverse symptoms and the occurrence of sporadic ICD shocks are each associated with significant impairment in QoL. Whether interventions aimed at limiting adverse symptoms or reducing shocks will result in improved QoL in individuals with serious ventricular arrhythmias requires prospective confirmation.

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