

Impact of Descent and Stay at a Dead Sea Resort (Low Altitude) on Patients with Systolic Congestive Heart Failure and an Implantable Cardioverter Defibrillator

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ABSTRACT: **Background:** As the lowest natural site on earth (-415 meters), the Dead Sea is unique for its high pressure and oxygen tension in addition to the unparalleled combination of natural resources. Furthermore, its balneotherapeutic resorts have been reported to be beneficial for patients with various chronic diseases.

Objectives: To evaluate the safety, quality of life (QoL), exercise capacity, heart failure, and arrhythmia parameters in patients with systolic congestive heart failure (SCHF) and implantable cardioverter defibrillator (ICD) following descent and stay at the Dead Sea.

Methods: The study group comprised patients with SCHF, New York Heart Association functional class II-III after ICD implantation. The following parameters were tested at sea level one week prior to the descent, during a 4 day stay at the Dead Sea, and one week after return: blood pressure, O₂ saturation, ejection fraction (echocardiography), weight, B-type natriuretic peptide (BNP), arrhythmias, heart rate, heart rate variability (HRV), and QoL assessed by the Minnesota Living with Heart Failure questionnaire.

Results: We evaluated 19 patients, age 65.3 ± 9.6 years, of whom 16 (84%) were males and 18 (95%) had ICD-cardiac resynchronization therapy. The trip to and from and the stay at the Dead Sea were uneventful and well tolerated. The QoL score improved by 11 points, and the 6 minute walk increased by 63 meters ($P < 0.001$). BNP levels increased slightly with no statistical significance. The HRV decreased ($P = 0.018$). There were no significant changes in blood pressure, weight, O₂ saturation or ejection fraction.

Conclusions: Descent to, ascent from, and stay at a Dead Sea resort are safe and might be beneficial in some aspects for patients with SCHF and an ICD.

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KEY WORDS: Dead Sea, systolic congestive heart failure, implantable cardioverter defibrillator

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The Dead Sea (415 meters below sea level) is the lowest natural site on earth. It is unique for its combination of natural resources that are unparalleled elsewhere and include, among others, attenuation of the ultraviolet sun rays (UVB>UVA), high atmospheric pressure with higher partial oxygen tension, highly dense seawater rich in various minerals, and a dry hot climate with unpolluted air [1-4]. The balneotherapeutic resorts at the Dead Sea are a major tourist attraction and have been reported to be beneficial for patients with hypertension and for those with dermatologic, rheumatic, pulmonary and cardiac diseases [1,5-7]. In the latter group, a clinical improvement was reported in patients with congestive heart failure and patients with coronary artery disease following acute descent to the Dead Sea [8,9]. However, the impact of the descent and stay at a Dead Sea resort in patients with systolic congestive heart failure after insertion of an implantable cardioverter defibrillator with or without cardiac resynchronization therapy for electromechanical dyssynchrony has not been investigated. Physicians are often confronted with such patients who are wary of traveling to the Dead Sea. It is therefore important to obtain reliable data in order to give these patients accurate and complete information and to dispel biased preconceived notions.

The purpose of this study was to evaluate the safety, the impact on quality of life, exercise capacity, heart failure, and arrhythmia parameters in patients with SCHF and an ICD following the descent and during their stay at a Dead Sea resort.

PATIENTS AND METHODS

In this prospective observational cohort study, we evaluated 19 patients with SCHF from the Barzilai Medical Center out-

SCHF = systolic congestive heart failure
ICD = implantable cardioverter defibrillator

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patient cardiology service: 18 with ICD-CRT and one with ICD alone. Inclusion criteria were: a) stable ischemic heart disease, stage I-II, according to the Canadian Cardiovascular Society grading scale [10]; b) ≥ 14 days after implantation of the ICD-CRT for either primary or secondary prevention; c) moderate to severe left ventricular dysfunction due to ischemic heart disease (ejection fraction $< 35\%$); d) New York Heart Association functional class II-III; and e) age 40–80 years. Exclusion criteria were: a) unstable angina, b) chronic obstructive pulmonary disease, c) uncontrollable arrhythmia, d) NYHA FC I or IV, and e) patient unable to comply with the study requirements. The ICDs were programmed to allow minimal or no atrial pacing (lower rate of 40). In nearly all the patients with a cardiac resynchronization therapy defibrillator both ventricles were paced, while in the patient with an ICD the ventricle was not paced at all.

This study was approved by the Barzilai Medical Center Institutional Review Board. Patients gave informed written consent after the purpose and nature of the study were explained to them.

STUDY PROTOCOL

To assess the effects of the descent to the Dead Sea, the enrolled patients were evaluated at the Barzilai Medical Center, Ashkelon, Israel (sea level) a week prior to the descent to the Dead Sea, during the 4 days of their stay at the Dead Sea, and again at Barzilai Medical Center a week following their ascent. The following parameters were assessed:

- **B-type natriuretic peptide level:** measured a week before descent, on the third day of the stay in the resort, and a week after ascent. The measurement was done using the Triage BNP Test by BIOSITE with a normal range of < 40 pg/ml.
- **Heart rate and rhythm as recorded by the ICD:**
 - ▷ *Arrhythmia:* data regarding ventricular tachycardia, ventricular fibrillation and supraventricular arrhythmias were obtained for the following periods: before the descent to the Dead Sea, during the descent and the stay at the resort, and throughout one week following the ascent back to sea level.
 - ▷ *Heart rate variability:* Continuous HRV was measured as the standard deviation of 5 minute median atrial-atrial intervals (SDAAM) sensed by the device, as previously described [12]. Reduced HRV is considered to be a negative cardiac prognostic factor [13]. Since the ICDs were programmed to allow minimal or no atrial pacing (lower rate of 40), the heart rate and the HRV represent the patients' own sinus rate (atria sensing).

▷ *Heart rate:* daytime at 10:00 and nighttime at 20:00.

- **Patient activity:** an index intended to evaluate physical activity by the patients. The activity sensor in the implanted device accumulated the number of activity counts sensed in each minute. As previously reported, a minute was considered "active" if the counts exceeded a threshold that corresponded to a walk rate of > 95 steps per minute.
- **Echocardiography:** performed a week before the descent, on the third day of stay at the resort, and a week after the return to sea level.
- **Quality of life:** QoL was assessed a week before descent, on the third day of stay, and a week after the return to sea level, using the Minnesota Living with Heart-Failure Questionnaire. The MLHFQ has been widely used and validated to assess QoL in patients with congestive heart failure and to explore the effect of different interventions.
- **Subjects' weight:** assessed with the same digital scale a week before descent, daily during the stay at the resort, and a week following the ascent, at the same hour and with the patients in similar clothing.
- **Blood pressure:** measured a week before descent, a week after the return to sea level, and twice a day (10:00 and 20:00) during the stay at the Dead Sea resort.
- **Blood oxygen saturation:** this was measured with a pulse oxymeter a week before descent, a week after return to sea level, and twice a day during the stay at the Dead Sea area (10:00 and 20:00).
- **Six minute walk test:** this was measured under similar conditions a week before descent, every day during the stay at the resort, and a week after the return to sea level [12].

Additional data (i.e., comorbid factors, characteristics of ischemic heart disease, and current medical treatment) were obtained and analyzed from patient files and computerized hospital databases.

THE DESCENT AND STAY AT THE DEAD SEA RESORT

The patients descended to the Dead Sea and stayed in a hotel in a similar milieu as all other hotel guests. In order to simulate an uncontrolled, vacation-like stay at the resort no special environmental or other conditions for the CHF patients were created. Except for two lectures, during which the subjects were warned about overeating and prolonged stay under extreme weather conditions (i.e., high temperatures), and the daily tests, the patients were free to enjoy the resort's recreational facilities. A low sodium diet was available to the subjects upon request. The patients were accompanied by two physicians (a cardiologist and an internist), an intensive care unit nurse, and a technician with all the necessary ICD monitoring equipment and a full emergency life support kit.

CRT = cardiac resynchronization therapy

NYHA = New York Heart Association

FC = functional class

HRV = heart rate variability

SDAAM = standard deviation of 5 minute median atrial-atrial intervals sensed by the device

QoL = quality of life

MLHFQ = Minnesota Living with Heart-Failure Questionnaire

CHF = congestive heart failure

STATISTICAL ANALYSIS

Data were collected on individual forms, introduced into a database, and analyzed with the SAS software (version 9). Continuous variables are presented as mean \pm SD unless otherwise indicated, and categorical variables are presented as percentages. The Kolmogorov-Smirnov test was used to assess whether a parameter distributed normally and whether a parametric test is appropriate. Comparisons between groups were performed with Student's *t*-test for continuous variables distributing normally. A comparison including more than two time periods was performed using repeated measures test for variables with normal distribution and with the Friedman test for variables with non-Gaussian distribution. For each test, *P* values (two-tailed) $<$ 0.05 were considered statistically significant.

RESULTS

Overall, we evaluated 19 patients after ICD implantation; their median age was 65.3 ± 9.6 years, 16 (84%) were males and 18 (95%) had an ICD-CRT. The baseline characteristics of the study population are presented in Table 1. The trip to and from the Dead Sea as well as the 4 days of stay were uneventful and well tolerated. During the study period no significant events of arrhythmia were recorded by the ICD Holter. As displayed in Figure 1, no statistically significant change in BNP levels was found following the stay at the Dead Sea resort, although a mild non-significant trend of increase was evident in BNP.

The changes in various parameters before, after, and throughout the stay at the Dead Sea are presented in Table 2. No significant changes in blood pressure (systolic and diastolic), heart rate (day or night time), O₂ saturation, weight, and LV function were found when comparing the measurements at the Dead Sea with those before and after the stay. However, during the stay the heart rate variability and ICD activity index decreased, while a significant improvement was observed in the 6 minute walk test that increased by a mean of 63 meters, and in the QoL score that decreased (improved) by a mean of 11 points [Figure 2].

DISCUSSION

In this study we found that descent and stay at the Dead Sea, the lowest natural site on earth, are safe and could even be beneficial in some aspects for patients with systolic congestive heart failure and an implantable cardioverter defibrillator. To our knowledge this is the first evaluation in such a specific group of cardiac patients. More specifically, no significant arrhythmia, ventricular tachycardia, ventricular fibrillation, or any supraventricular arrhythmia events (e.g., atrial fibrillation/flutter) were observed in these highly prone patients

BNP = B-type natriuretic peptide
LV = left ventricular

Table 1. Baseline characteristics of the study population (n=19)

| Parameter | N=19 | Comorbid factors | N=19 |
|-------------------------------|-----------------|--------------------|------------|
| Age (yrs) | 65.3 \pm 9.6 | CVA | 2 (10.5%) |
| Male | 16 (84.2%) | PVD | 0 (0.0%) |
| Time from implantation (days) | 342 \pm 332 | CRF | 3 (15.8%) |
| Indication: primary | 14 (74%) | Dyslipidemia | 16 (84.2%) |
| CRT-D | 18 (94.7%) | COPD | 2 (10.5%) |
| History of MI | 9 (47.4%) | Anemia (Hb<12) | 8 (42.1%) |
| Inferior | 1 (5.3%) | | |
| Anterior | 7 (36.8%) | Smoker | 1 (5.3%) |
| Lateral | 1 (5.3%) | Medications | |
| | | Aspirin | 16 (84.2%) |
| s/p CABG | 6 (31.6%) | Beta-blockers | 18 (94.7%) |
| DCM | 5 (26.3%) | Nitrates | 3 (15.8%) |
| NYHA FC | | ACE Inhibitors | 17 (89.5%) |
| I | 0 (0%) | | |
| II | 11 (57.9%) | Diuretics | 12 (63.2%) |
| III | 8 (42.1%) | Insulin | 1 (5.3%) |
| IV | 0 (0.0%) | Steroids | 1 (5.3%) |
| | | Ca blockers | 1 (5.3%) |
| Severe LV dysfunction | 18 (94.7%) | Oral hypoglycemic | 3 (15.8%) |
| Normal-mild | 0 (0.0%) | | |
| Moderate | 1 (5.3%) | Statins | 15 (78.9%) |
| Severe | 18 (94.7%) | | |
| Ejection fraction (%) | 23.4 \pm 10.7 | | |

MI = myocardial infarction, CABG = coronary artery bypass graft, COPD = chronic obstructive pulmonary disease, CRF = chronic renal disease, CVA = cerebrovascular accident, DCM = dilated cardiomyopathy, PVD = peripheral vascular disease, ACE = angiotensin-converting enzyme

Figure 1. BNP levels before descending, after ascending, and during the stay at the Dead Sea resort

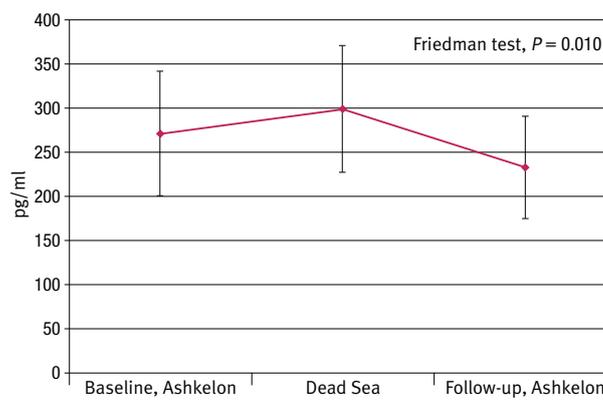
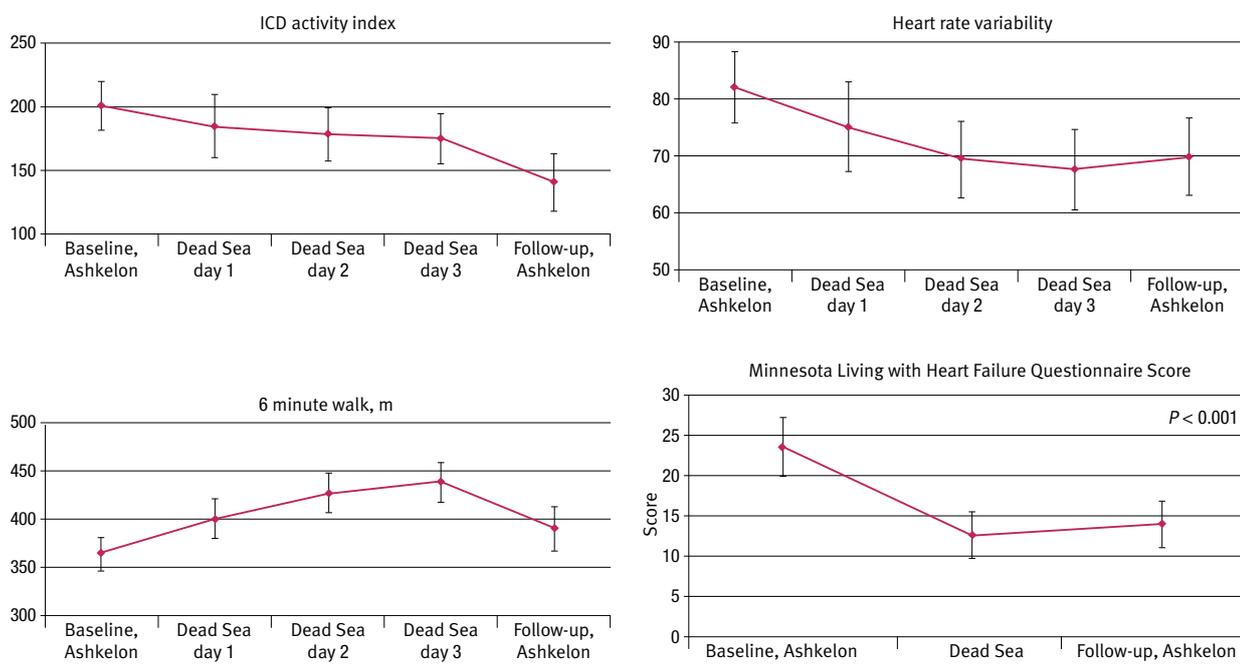


Table 2. Changes in measured parameters according to study period

| | The visit before descent | Dead Sea day 1 | Dead Sea day 2 | Dead Sea day 3 | The visit after ascent | P |
|---------------------------------|--------------------------|----------------|----------------|----------------|------------------------|----|
| Day time heart rate (bpm) | 73.2 ± 8.3 | 72.6 ± 8.5 | 73.3 ± 9.1 | 74.8 ± 12.2 | 74.3 ± 9.5 | NS |
| Night time heart rate (bpm) | 67.2 ± 8.0 | 67.7 ± 8.9 | 67.2 ± 8.1 | 67.7 ± 9.3 | 68.4 ± 8.1 | NS |
| Blood pressure, systolic (mmHg) | 126.1 ± 22.4 | 124.37 ± 13.78 | 128.66 ± 14.98 | 120.6 ± 15.0 | 126.4 ± 19.9 | NS |
| Blood pressure, diastolic mmHg | 75.7 ± 12.6 | 71.82 ± 10.24 | 77.29 ± 9.48 | 73.5 ± 10.7 | 75.6 ± 12.4 | NS |
| Weight (kg) | 78.0 ± 14.1 | 80.0 ± 14.7 | 78.3 ± 14.3 | 78.5 ± 14.6 | 77.9 ± 14.1 | NS |
| O ₂ saturation (%) | 96.2 ± 1.3 | 96.26 ± 1.48 | 96.29 ± 1.42 | 95.8 ± 1.3 | | NS |
| Ejection fraction (%) | 23.4 ± 10.7 | | | 22.1 ± 6.6 | 22.1 ± 6.6 | NS |

Figure 2. Parameters changing significantly following the descent and stay at the Dead Sea resort. Bars represent standard error



throughout the study period. A minor increase in BNP levels was demonstrated; however, it did not reach statistical significance. Although such a change could potentially derive from the uncontrolled diet and the acute environmental and climate changes, based on the improvement in the distances covered during the 6 minute walk, the stable ejection fractions and the patients' weight at the Dead Sea, we believe that no deterioration in the CHF status occurred. This is further supported by Abinader et al. [8], who found an improvement in exercise performance – increased time on treadmill, maximum oxygen consumption (VO₂max), patients' rate of perceived exertion as measured by the Borg scale, and O₂ saturation throughout exercise – in patients with CHF after healing of myocardial infarction following descent to the Dead Sea. Furthermore, the latter study described an increase in

cardiac output at rest, resulting mostly from a reduction in systolic blood pressure (reduced afterload). The authors ascribed these improvements mainly to increased oxygen saturation at rest, a potential reduction of left ventricular end-diastolic pressure by magnesium, and increased venous return resulting from the higher barometric pressure at the Dead Sea. Similarly, in a different report, Abinader et al. [9] found an increase in exercise duration and improvement in wall motion after exercise in patients with known coronary artery disease following descent and stay at the Dead Sea, ascribed as well to the increased venous return and oxygenation. On the other hand, in the current study we did not find a change in oxygen saturation, ejection fraction, or blood pressure at rest. These discrepancies could result from the differences between the cohorts; our cohort consisted of less

than 50% of subjects after a myocardial infarction and 26% with dilated cardiomyopathy in addition to an ICD-CRT implantation in nearly all subjects. Thus, it is possible that patients with significant coronary artery disease are more likely to benefit from the natural enrichment of oxygen and increased barometric pressure at the Dead Sea. A previous study by Paran et al. [14] found a decrease in both systolic and diastolic blood pressure in hypertensives who underwent balneotherapy in the Dead Sea area. This decrease diminished towards the end of their stay. The latter study, in addition to the finding of stable blood pressure in our cohort throughout their stay, further supports the safety of the Dead Sea resort in CHF patients with ICD-CRT and hypertension as well.

Heart rate variability, a known prognostic marker in patients with CHF [15], was found to decrease following descent to the Dead Sea. However, this decrease was relatively mild and was not accompanied by a change in heart rate, another significant and potentially even more important prognostic marker in cardiac patients [16,17]. Ascent to a high altitude was previously reported to reduce HRV [18,19], with a significant correlation between the decrease in arterial oxygen saturation and the decrease in HRV [20]. Thus, opposite to our findings, an increase in HRV would have been expected following descent to a low altitude such as the Dead Sea. Although it is possible that the reduction in HRV in our study stemmed from a different time frame of measurements [21], further study is required to more extensively evaluate HRV changes in patients at the Dead Sea and explore the physiological mechanisms behind the changes.

In this study we also found a reduction in the ICD activity index, which we believe is the result of a more leisurely lifestyle during the vacation rather than deterioration in exercise ability.

We found a significant improvement in QoL as measured by the MLHFQ following descent and stay at the Dead Sea resort. Importantly, this positive effect remained for a week after ascending back to sea level. This positive effect might have resulted from the improvement in exercise performance or the vacation itself. Either way, higher QoL as measured by the MLHFQ has been shown to be a strong marker of reduced mortality among CHF patients [22].

LIMITATIONS

A few limitations of our study should be addressed. First, the duration of the study was relatively short. We chose the current duration since we believe it represents the average length of stay at a Dead Sea resort. Nevertheless, a more prolonged evaluation in these patients is of interest. Second, some of the changes we found (e.g., improvement in QoL and in the 6 minute walk) could result, at least partially, from the leisurely atmosphere of the vacation itself rather than from

the unique environment and climate at the resort; in that sense the vacation is a confounder. Hence a similar study with a control group (e.g., staying at a recreational resort at sea level) is warranted to better isolate the magnitude of such changes. Third, the sample size was relatively small and might have prevented reaching statistical significance in several parameters; we believe additional study with a larger sample should be conducted. Fourth, no monitoring or control of subjects' diet and physical activity was performed to simulate as closely as possible a regular vacation at the resort. It might therefore be informative to perform such monitoring in order to more extensively characterize the effects of these factors on the various changes occurring as a result of the exposure of such heart patients to the Dead Sea environment.

CONCLUSIONS AND CLINICAL IMPLICATIONS

In the current study we have shown for the first time that the descent and the stay at the Dead Sea resort are safe and even seem to be beneficial in some clinical aspects for patients with systolic heart failure and an ICD. Following this study we believe that when faced with this question by such patients, physicians can confidently and clearly assure the safety of the descent to the Dead Sea. Nevertheless, further studies of longer duration, in larger cohorts, and preferably with a control group are warranted to extensively evaluate the changes and the physiological mechanisms behind them.

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