Gender differences and adherence of patients treated with wearable cardioverter-defibrillator: insights from an international multicenter register

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Abstract

Aims The treatment with the wearable cardioverter defibrillator (WCD) may protect against sudden cardiac death (SCD) as a bridging therapy until a cardioverter-defibrillator may be implanted. We analyzed in a multicenter setting a consecutive patient cohort wearing WCD to explore gender differences. **Methods and results** We analyzed 708 consecutive patients, 579 from whom were males and 129 females (age, 60.5±14 vs. 61.6±17 years old; p=0.44). All patients were divided into age quartiles for analysis. While the rate of ischemic cardiomyopathy (ICM) as a cause of prescription of WCD was significantly higher in males as compared to females (42.7% vs. 26.4%; p=0.001), females received it more frequently due to non-ischemic cardiomyopathy (NICM) (55.8% vs. 42.7%); p=0.009). The wear time of WCD was equivalent in both groups (21.1±4.3 hours/days in males vs. 21.5±4.4 hours/days in females; p=0.27; and 62.6±44.3 days in males vs. 56.5±39 days in females; p=0.15). Mortality was comparable in both groups at 2-year-follow-up (6.8% in males vs. 9.7% in females; p=0.55). Appropriate WCD shocks and the incidence of device implantations were similar in both groups (2.4% in males vs. 3.9% in females; p=0.07) (35.1% in males vs. 31.8% in females; p=0.37), respectively. In age quartile analysis, compliance was observed more in older patients as compared to adult patients (87.8% vs. 68.3%; p<0.001). **Conclusion** Compliance for wearing WCD was excellent regardless of gender. Furthermore, mortality and the incidence of device implantations were comparable in both groups. Appropriate WCD shocks tended to be higher in females as compared to males.

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Short title: Gender differences and wearable cardioverter-defibrillator

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Aims

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Methods and results

We analyzed 708 consecutive patients, 579 from whom were males and 129 females (age, 60.5±14 vs. 61.6±17 years old; p=0.44). All patients were divided into age quartiles for analysis. While the rate of ischemic cardiomyopathy (ICM) as a cause of prescription of WCD was significantly higher in males as compared to females (42.7% vs. 26.4%; p=0.001), females received it more frequently due to non-ischemic cardiomyopathy (NICM) (55.8% vs. 42.7%); p=0.009). The wear time of WCD was equivalent in both groups (21.1±4.3 hours/days in males vs. 21.5±4.4 hours/days in females; p=0.27; and 62.6±44.3 days in males vs. 56.5±39 days in females; p=0.15). Mortality was comparable in both groups at 2-year-follow-up (6.8% in males vs. 9.7% in females; p=0.55). Appropriate WCD shocks and the incidence of device implantations were similar in both groups (2.4% in males vs. 3.9% in females; p=0.07) (35.1% in males vs. 31.8% in females; p=0.37), respectively. In age quartile analysis, compliance was observed more in older patients as compared to adult patients (87.8% vs. 68.3%; p<0.001).

Conclusion

Compliance for wearing WCD was excellent regardless of gender. Furthermore, mortality and the incidence of device implantations were comparable in both groups. Appropriate WCD shocks tended to be higher in females as compared to males.

Keywords: Wearable cardioverter-defibrillator; sudden cardiac death; gender differences; female; male.

Introduction

It is well known that an implantable cardioverter-defibrillator (ICD) improves survival and reduces the mortality rate due to ventricular tachyarrhythmias [1-3]. The Danish Cardiac Arrest Registry showed the superiority of early implantation of ICD in patients surviving myocardial infarction (MI) with cardiac arrest [4]. However, some patients do not meet the criteria for ICD implantation or are unable to receive an implantable device such as patients in the acute phase of MI or myocarditis. The wearable cardioverter defibrillator (WCD) may be considered to protect these patients against malignant ventricular tachyarrhythmias and as a bridge to decision for ICD implantation [5]. However, compliance is impaired due to comfort issues [6]. Poor compliance and obesity decreased the efficacy of WCD therapy [7]. In addition, the VEST trial showed no reduction of arrhythmic death as the primary endpoint in recent MI patients with reduced left ventricular ejection fraction (LVEF $< 35\%$) [8].

One cohort study on sudden cardiac death (SCD) reported that WCD treatment is effective in females with a first shock success rate of 95% [9]. WEARIT-II-Registry presented a higher rate of ventricular and atrial arrhythmic events in females as compared to males [10]. However, randomized controlled trials and further data on gender differences are lacking. Therefore, we analyzed in a multicenter setting a consecutive patient

cohort wearing WCD to explore gender differences regarding compliance, rate of appropriate WCD shocks, and mortality.

Methods

Study design

Between April 2012 and March 2019, we included 708 patients with HFrEF who received a WCD (ZOLL Life Vest system, Pittsburgh, USA) at the University Medical Centre in Mannheim, Heidelberg University, Department of Cardiology, University Hospital Frankfurt, Department of Arrhythmias & Invasive Cardiology, St. Georg Hospital Leipzig, and Department of Cardiology, University Hospital of Zurich. This multicenter register is designed as a retrospective cohort registry without any financial support. Patients were treated according to the current European guidelines for heart failure [11].

We divided the collective according to gender (male=579; female=129). Furthermore, all patients were divided into age quartiles for analysis: 161 patients in 14-51 years old group, 375 patients in 52-72 years old group, and 172 patients in 73-91 years old group. Baseline characteristics such as indications for WCD use were gathered. Wear time of WCD and WCD shocks during WCD use were documented. Echocardiographic assessments were collected. The death rate due to a cardiovascular cause during a 2-year-follow-up was evaluated. These data were assessed by chart and/or telephone review at mean 2-year-follow-up. LVEF $>$ 35% led to stop WCD wearing and was recorded as an improvement of the LVEF.

LVEF was calculated by using biplane Simpson's method, using echocardiography and/or cardiac MRI. This study was executed in compliance with the fifth revision of the Declaration of Helsinki regarding investigations in human subjects and the study protocol was approved by the Ethics Committee in all involved centers [12].

Description of WCD

The WCD consists of a two-channel electrocardiogram that records the front-back and left-right site as bipolar leading to continuous electrocardiographic analysis. If a life-threatening heart rhythm such as ventricular tachycardia (VT) or ventricular fibrillation (VF) is detected, it delivers a shock to restore sinus rhythm. The detection until shock delivery takes 45-55 s including initial detection of VT/VF 5 s to 10 s, tachycardia confirmation 10 s, and alarm time 25 s. Shock can be avoided by pressing the stop button. The WCD has a memory for ECG analysis from 30 s before starting the arrhythmia alarm until 15 s after the alarm stop [13].

Statistics

We present the data as mean +- standard deviation for continuous variables with a normal distribution. Median (interquartile range) was used for continuous variables with a non-normal distribution, and as frequency (%) for categorical variables. The Kolmogorov–Smirnov test was used to assess normal distributions. Student's t-test and the Mann–Whitney U-test were used to compare continuous variables with normal and non-normal distributions, respectively. Additionally, the Chi-squared test or Fisher's exact test was used to compare categorical variables. The Wilcoxon signed-rank test was used for paired nonparametric quantitative variables. The McNemar test was used for paired qualitative variables. Statistical analysis was performed using IBM SPSS Statistics for Macintosh (Version 25.0 Armonk, NY, USA: IBM Corp.).

Results

Baseline characteristics of 708 patients with WCD

In this multicenter study, the male group had an average age of 60.5+-14 years old, and the female group of 61.6+-17 years old; p=0.44, respectively. The indication for WCD use was several, **table 1** . In patients who received WCD, 42.7% of males and 26.4% of females suffered from ischemic cardiomyopathy (ICM) with LVEF [?]35%; p=0.001. On the other hand, 55.8% of females and 42.7% of males suffered from non-ischemic cardiomyopathy (NICM); p=0.009. Other indications for WCD were myocarditis, device explanation cause

of device infection, hypertrophic cardiomyopathy (HCM), and channelopathies with a similar frequency in both genders.

Follow-Up

At baseline, the mean LVEF was comparable in both groups (29.5%+-10.98% in males vs. 30.2%+-12.2% in females; p=0.55). At follow-up, the mean LVEF increased during 3-6 months to 37.1%+-12.1% in males and 37.95%+-12.1% in females; p=0.49. The improvement of LVEF was numerically observed in both groups, more in females as compared to males (51.9% vs. 44.7%; p=0.16). The incidence of device implantation was comparable in both groups (35.1% in males vs. 31.8% in females; p=0.37). The wear time of WCD was similar in both groups, 21.1+-4.3 hours/days in males as compared to 21.5+-4.4 hours/days in females; p=0.27, and documented in days 62.6+-44.3 days in males in comparison to 56.5+-39 days in females; p=0.15. The rate of appropriate shocks was similar in both groups, 2.4% in the male and 3.9% in the female group; p=0.07, with a higher tendency in females, **table 1.** In addition, the rate of mortality was comparable in both groups (6.8% in males vs. 9.7% in females; p=0.55)

The quartile range of age

A high incidence of male as gender was observed in all age groups (81.9% in 14-51, 84.8% in 52-72, and 75% in 73-91 years old group). However, ICM was more observed in 52-72- and 73-91-years old groups as compared to 14-51 years old group, respectively (48.3% in 73-91 years old group vs. 18.6% in 14-51 years old group; p<0.001) (44.8%in 52-72 years old group vs. 18.6% in 14-51 years old group; p<0.001). On the other hand, NICM was more revealed in adult as compared to older patients (57.8% in 14-51 years old group vs. 43.7% in 52-72 years old group; p=0.003) (57.8% in 14-51 years old group vs. 36% in 73-91 years old group; p<0.001). Devices were more implanted after WCD wearing in older patients as compared to adult patients (40.7% in 73-91 years old group vs. 26.1% in 14-51 years old group; p=0.005). The compliance was observed more in older as compared to adult patients (87.8% in 73-91 years old group vs. 68.3% in 14-51 years old group; p<0.001). At 3-months follow-up, LVEF was 39.34%+-14.24 in adult group and 36.24%+-11.72 in older patients; p=0.03.

Discussion

We present the clinical outcome including mortality rate in WCD patients divided into male and female groups up to 2 years. The main findings of the study are (1) The improvement of LVEF was revealed in both groups; (2) Mortality rate was similar in both groups; (3) The wearing time is comparable in male and female participants, but the appropriate shock rate tended to be higher in females as compared to males.

The WCD may be considered in selected patients with a high risk of SCD, if the implantation of conventional ICD is temporarily contraindicated (e.g. poor LVEF after acute myocardial infarction until LV function improves, before heart transplantation) [14]. Therefore, the American Heart Association (AHA), American College of Cardiology (ACC), Heart Rhythm Society (HRS), and European Society of Cardiology (ESC) provide class II, level of evidence C for the use of WCD in these selected patients [15, 16].

Epidemiological data

Both groups had a similar average age of 60.5+-14 in males and 61.6+-17 years old in females. While 42.7% of males suffered from ICM with LVEF [?]35%, only 26.4% of females suffered from ICM who received WCD. Following our data, the Israeli-ICD registry showed comparable epidemiological frequency regarding gender differences. The average age in both genders was similar, 64+-14 in females and 64+-13 in male participants. In addition, ICM was significantly more observed in males as compared to the female group (79% vs. 46%). On the other hand, more women suffered from dilated cardiomyopathy (DCM) in comparison to men's participants (38% vs. 18%) [17]. In the VEST trial, the device group consisted of 72.8% male participants with the percutaneous coronary intervention (PCI) during the index hospitalization [8]. Males have a higher propensity for developing coronary heart disease as well as ICM [18]. To summarize, our multicenter data corresponds with previously published ICD data.

Adherence

The wear time of WCD was comparable in males with 21.1+-4.3 and female group with 21.5+-4.4 hours/days, the rate of compliance was revealed in 77% of male and 84.5% of female participants, there were no significant differences in this regard. One observational study has presented a similar adherence rate with daily use of 23 h per day in 6043 patients [19]. The wear time in the VEST trial was 18 h, also less than the wear time in our patients [8]. Most cases of death occurred in patients who were not using the WCD [8]. In this regard, one important and possible cause for death was non-compliance in wearing the WCD. However, suffering from cardiac arrest during the index MI, and an increase of creatinine were independent predictors for a high WCD wearing time [20]. In addition, the indication for WCD in one large cohort was equivalent in accordance with our study concerning the different number of cases including ICM or DCM, genetic or congenital disease, ICD explanations, or myocarditis [19]. In our quartile age analysis, adherence was more observed in older as compared to adult patients. In this regard, the WEARIT-France study showed that younger age was associated with lower compliance [21].

Clinical Efficacy

In male and female patients, the incidence of appropriate shocks was comparable, but with a higher tendency in females. In 1998, Auricchio et al. presented successfully arrhythmia detection and defibrillation in 9 patients out of 10[22]. Other randomized trials showed the safety and efficacy of WCD in the termination of VT/VF. In this regard, first shock success was in 79 of 80 (99%) among all patients from whom were 74% male participants, respectively [23].

Impact on mortality

The mortality rate was similar between both genders in our multicenter register. For this purpose, one large trial investigating gender differences after ICD showed no differences in the mortality rate between males and females during follow-up [17]. In the United States (US) registry, WCD use reduced the rate of mortality up to 67% reduction analyzed with the propensity-score-matching method [24]. In this trial, 19% of all participants were female and 3-month-mortality was 2.2% in all patients. In the VEST trial, the mortality rate was 3.1% at 3 months [8]. These rates are less than in our trial, but our follow-up time is longer as compared to US-registry and VEST trial. In addition, the VEST trial had high selected exclusion criteria as compared to our real-world experience.

To summarize, in a real-world setting, we do not observe any differences in adherence, efficacy, and impact on mortality in male and female patients after WCD use. The improvement of LVEF was observed in both groups. However, LVEF improved more in adult than in older patients.

Limitations

Our trial has several limitations. The majority of patients were male to make qualitative assessments. We did not evaluate other diagnostic methods as MRI to identify patients with a high risk for arrhythmias and SCD. The order of WCD was based on individual patient risk. In the follow-up time, the cause of death was not reported and could not be analyzed.

Conclusion

The same level of patient compliance for wearing WCD was revealed in both groups regardless of gender differences. At follow-up, LVEF improved in both groups. The mortality rate was comparable in both groups.

Conflict of interest

The authors declare that they have no conflict of interest.

Clinical perspectives

WCD is a good treatment approach in patients suffering from reduced left ventricular ejection fraction for example after myocardial infarction or myocarditis to avoid unnecessary implantation of implantable cardioverter-defibrillator regardless of gender.

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Table legend

Table 1: Baseline characteristics in males vs. females with Wearable Cardioverter Defibrillator (WCD)

Table 2 : The impact on outcome according to quartile of age

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