Dose-response association of implantable device-measured physical activity with long-term cardiac death and all-cause mortality in patients at high risk of sudden cardiac death: a cohort study

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Abstract

Background: Cardiovascular implantable electronic devices (CIEDs) with physical activity (PA) recording function can continuously and automatically collect patients’ long-term PA data. The dose-response association of implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy defibrillator (CRTD)-measured PA with cardiovascular outcomes in patients at high risk of sudden cardiac death (SCD) was investigated.

Methods: In total, 822 patients fulfilling the inclusion criteria were included and divided into three groups according to baseline PA tertiles: tertile 1 (< 8.04%, n = 274), tertile 2 (8.04–13.24%, n = 274), and tertile 3 (> 13.24%, n = 274). The primary endpoint was cardiac death, the secondary endpoint was all-cause mortality.

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Results: During a mean follow-up of 59.7 ± 22.4 months, cardiac death (18.6% vs 8.8% vs 5.5%, tertiles 1–3, \( P < 0.001 \)) and all-cause mortality (39.4% vs 20.4% vs 9.9%, tertiles 1–3, \( P < 0.001 \)) events decreased according to PA tertiles. Compared with patients younger than 60 years old, older patients had a lower average PA level (9.6% vs 12.8%, \( P < 0.001 \)) but higher rates of cardiac death (13.2% vs 8.1%, \( P = 0.024 \)) and all-cause mortality (28.4% vs 16.7%, \( P < 0.001 \)) events. Adjusted multivariate Cox regression analyses showed that a higher tertile of PA was associated with a lower risk of cardiac death (hazard ratio (HR) 0.41, 95% confidence interval (CI): 0.25–0.68, tertile 2 vs tertile 1; HR 0.28, 95% CI: 0.15–0.51, tertile 3 vs tertile 1, \( P_{\text{trend}} < 0.001 \)). Similar results were observed for all-cause mortality. The dose-response curve showed an inverse non-linear pattern, and a significant reduction in endpoint risk was observed at the low-moderate PA level. The HR for cardiac death was reduced by half with 12.32% PA (177 min), and the HR for all-cause mortality was reduced by half with 11.92% PA (172 min). Subgroup analysis results indicated that older adults could benefit from PA and the range for achieving optimal benefits might be lower.

Conclusions: PA monitoring may aid in long-term management of patients at high risk of SCD. More PA will generate better survival benefits, but even low-moderate PA is already good especially for older adults, which is relatively easy to achieve.

Keywords: Physical activity, Sudden cardiac death, Dose-response association, Implantable cardioverter defibrillator, Cardiac resynchronization therapy defibrillator, Cardiac death, All-cause mortality

Introduction
Sudden cardiac death (SCD) is a serious public health problem worldwide, accounting for approximately 50% of all cardiovascular deaths [1]. An implantable cardioverter defibrillator (ICD) can effectively terminate malignant tachyarrhythmia, prevent SCD and reduce all-cause mortality [2]. A number of studies have indicated that physical inactivity is a risk factor for a variety of chronic diseases [3–5], including cardiovascular morbidity and mortality [6–10].

Previous studies focusing on physical activity (PA) have mostly used self-assessment questionnaires with certain biases and errors, such as recall biases, especially for older participants, due to their education level and cognitive function [11, 12]. As smart wearable devices emerged, researchers began to use objective device-measured PA in clinical studies. However, most studies had smaller sample sizes, and the duration of continuous monitoring could only be performed for a short duration [13]. The number of patients with cardiovascular implantable electronic devices (CIEDs) is increasing noticeably. CIEDs with PA recording function can continuously and automatically collect patients’ long-term PA data. Home monitoring (HM) can detect 24-h PA, and the data are detailed and accurate with high sustainability. More recently, studies have focused on the dose-response relationship of PA and outcomes to determine the best benefit interval. The dose-response association of implantable device measured PA with cardiovascular outcomes in patients with ICDs remains unclear.

Population aging is a common global problem. The population aged 60 years or older reached 962 million in 2017, which was more than double the size of this population compared with that in 1980 [14]. Cardiac diseases are becoming the leading contributors to the disease burden in people aged 60 years and older, accounting for 30.3% of the total [15]. Older people are more likely to have exercise restrictions with decreased PA and a lower rate of compliance with guideline recommendations [16, 17]. Whether older adults with ICDs could benefit from PA and the range for achieving optimal benefits is not well known.

The present study aimed to investigate the dose-response association of ICD/CARD resynchronization therapy defibrillators (CRTD)-measured PA with cardiovascular outcomes by long-term continuous HM and further perform subgroup analysis in younger and older adults.

Methods
Study population
Patients from the SUMMIT registry study (Study of Home Monitoring System Safety and Efficacy in Cardiac Implantable Electronic Device-implanted Patients) in China were retrospectively analyzed.

Patients who underwent ICD or CRTD implantation and met the inclusion criteria between May 2010 and April 2014 were included in this study. This study included patients who [1] were older than or equal to 18 years of age [2]; were eligible for an ICD/CRTD in accordance with indications specified by guidelines. These included primary prevention patients who received ICDs or CRTDs on a prophylactic basis without a prior history of SCD, cardiac arrest, or sustained ventricular tachycardia (VT) and secondary prevention patients who experienced resuscitated SCD, cardiac arrest, or sustained VT before ICD implantation; and [3] were implanted with an ICD/ CRTD (Biotronik, Germany) device with HM; and who had [4] survived more than three months after CIED implantation. The exclusion criteria were patients:
the data were collected during the first 30–early after discharge was expected to be less than usual, the Biotronik service center every day. As the PA level matically transmit data stored in implantable devices to 

PA. The Biotronik remote monitoring system can auto-

per 24 h. For example, 10% PA indicated 2.4 h of daily 

resolution was 2 s, and the data were converted into %

60 years or older were defined as the older group [22].

sification in China and a previous study, patients aged 

13.24%, n = 274). According to the guideline for age clas-

sion 1,00 to 109, 111, 120 to 151), and the secondary endpoint was all-cause mortality.

PA recording

PA was measured with an integrated circuit accelerom-

eter embedded in the pulse generator of the ICD/CRTD [18]. The time during which the motion sensors of the Biotronik devices delivered rates higher than the devices’ basic rates was recorded. The accuracy of PA measure-

ment has been validated with treadmill test [19]. The PA 

resolution was 2 s, and the data were converted into % per 24 h. For example, 10% PA indicated 2.4 h of daily 

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matically transmit data stored in implantable devices to 

the Biotronik service center every day. As the PA level 

ey early after discharge was expected to be less than usual, 

the data were collected during the first 30–60 days after 

ICDs/CRTDs implantation, in accordance with previous 

studies [20, 21], and the mean value of 30-day PA data 

was calculated as the baseline PA for each patient.

Data collection

Baseline data for all admitted patients in this study were 

derived from medical records during hospitalization, and 

included age, gender, body mass index (BMI), New York 

Heart Association (NYHA) class, ICD or CRTD implant-

ation, primary or secondary prevention indication, co-

morbidities (ischemic cardiomyopathy, hypertension, 

diabetes, stroke, atrial fibrillation (AF), vascular disease, 

prior myocardial infarction, and pre-implant syncope), 

and medication (renin-angiotensin system blockers, β 

receptor blockers, aldosterone antagonists, statins, loop-

diuretics, digoxins, and amiodarone). Echocardiography 

parameters such as left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD) were evaluated by two experienced echocardi-

ography physicians. And LVEF was calculated using the modified Simpson’s biplane rule.

Groups

All enrolled patients were divided into three groups ac-

cording to baseline PA level tertiles: tertile 1 (< 8.04%, 

n = 274), tertile 2 (8.04–13.24%, n = 274), and tertile 3 (> 

13.24%, n = 274). According to the guideline for age clas-

sification in China and a previous study, patients aged 

60 years or older were defined as the older group [22].

Endpoints

Regular follow-up was conducted with all enrolled pa-

tients. If the patient’s daily transmission was interrupted, 

the clinical research coordinator immediately confirmed 

the patient’s status by contacting the family. The cause 

doof death was based on the death certificate. The primary 

endpoint of the present study was cardiac death (ICD-10 

I00 to 109, 111, 120 to 151), and the secondary endpoint was all-cause mortality.

Statistical methods

Continuous variables are presented as means±SDs, and 
categorical variables are presented as numbers and per-

centages. Baseline characteristics were compared among 

the groups using one-way analysis of variance for con-

tinuous variables and the Chi-square test for categorical 

variables. Cardiac death and all-cause mortality were cal-

culated, and the difference was compared between 

groups with a Chi-square test. Cox proportional hazard 

regression analysis was used to evaluate the association 

between different PA groups for endpoint events. Haz-

ard ratios (HRs) and 95% confidence intervals (CIs) were 

calculated to show the impact. Associations were investi-

gated with stratification according to baseline age. Model 

1 was adjusted for age and gender. Model 2 was further 

adjusted for primary prevention, NYHA class, CRTD im-

plantation, LVEF, LVEDD, β-blockers, and aldosterone 

antagonists. Model 3 was adjusted for factors in Model 2 

and potential mediators on the causal pathway including 

BMI, ischemic cardiomyopathy, hypertension, AF, dia-

betes, and prior myocardial infarction. In addition, a 

restricted cubic spline was used to assess the dose-response 

association between PA and the risk of endpoints. Four 

knots were placed at the 5th, 35th, 65th, and 95th percentiles 

of PA. To specify the PA range for achieving optimal benefits 

as a target value that can be practicable in clinical practice, 

we determined the amount of PA required when the risk 

was halved, and 8.04% PA (lower tertile point) was used as 

the reference (HR = 1.0). A value of P < 0.05 was considered 

significant in all conditions. Statistical analyses were per-

formed using SAS v.9.4 (SAS Institute, Cary, NC, USA) and 

STATA v12.0 (STATA Corp., College Station, TX, USA).

Results

Baseline characteristics

Among a total of 1008 patients, 845 patients with PA 
data were obtained. Nineteen patients with incomplete 
data, 1 patient lost to follow-up, and 3 patients who died 
within 3 months after implantation were excluded. A 
total of 822 patients fulfilling the admission criteria were 
finally analyzed.

Men were dominant in the study cohort (73.8%). The 
average age was 60.8 ± 13.8 years, and the mean baseline 
PA level was 11.0 ± 5.8% (range 0.02–37.66%). The
cohort was divided into three groups according to baseline PA tertiles. Table 1 illustrates the baseline characteristics of the participants.

Significant differences among the three groups were detected for male gender ($P = 0.026$), age at implantation ($P < 0.001$), NYHA class ($P < 0.001$), LVEF ($P < 0.001$), ischemic cardiomyopathy ($P < 0.001$), hypertension ($P = 0.047$), diabetes ($P = 0.005$), stroke ($P = 0.044$), prior myocardial infarction ($P < 0.001$), and use of aldosterone antagonists ($P < 0.001$) and loop-diuretics ($P < 0.001$). No significant differences were found regarding other baseline characteristics (Table 1).

**Clinical outcomes**

The mean follow-up time was 59.7 ± 22.4 months. A total of 90 cardiac deaths (10.9%) and 191 all-cause mortality events (23.2%) occurred. The percentage of cardiac death (18.6% vs 8.8% vs 5.5%, tertiles 1–3, $P < 0.001$) and all-cause mortality (39.4% vs 20.4% vs 9.9%, tertiles 1–3, $P < 0.001$) events decreased according to baseline PA tertiles.

A total of 462 patients were aged 60 years or older (56.2%). Compared to patients younger than 60 years, older patients had a lower average PA level (9.6% vs 12.8%, $P < 0.001$) but higher rates of cardiac death (13.2% vs 8.1%, $P = 0.024$) and all-cause mortality (28.4% vs 16.7%, $P < 0.001$) events (Fig. 1).

**PA and cardiac death**

Multivariate Cox regression analyses showed that a higher level of PA was inversely associated with cardiac death (HR 0.40, 95% CI: 0.25–0.66, tertile 2 vs tertile 1; $P < 0.001$).

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**Table 1 Baseline Clinical Characteristics**

| Demographics | Total ($n = 822$) | Tertile 1 ($n = 274$) | Tertile 2 ($n = 274$) | Tertile 3 ($n = 274$) | $P$ value |
|--------------|------------------|----------------------|----------------------|----------------------|-----------|
| Male         | 607 (73.8)       | 187 (68.3)           | 206 (75.2)           | 214 (78.1)           | 0.026     |
| Physical activity, % | 11.0 ± 5.8 | 4.9 ± 2.0            | 10.6 ± 1.5           | 17.5 ± 3.9           | < 0.001   |
| Age at implantation, years | 60.8 ± 13.8 | 65.5 ± 13.2          | 61.1 ± 13.4          | 55.7 ± 13.1          | < 0.001   |
| BMI, kg/m2   | 23.6 ± 3.4       | 106 (38.7)           | 143 (52.2)           | 171 (62.4)           | < 0.001   |
| CRTD         | 217 (26.4)       | 82 (29.9)            | 76 (27.7)            | 59 (21.5)            | 0.069     |
| Comorbidities |                  |                      |                      |                      |           |
| Ischemic cardiomyopathy | 281 (34.2) | 115 (42.0)           | 103 (37.6)           | 63 (23.0)            | < 0.001   |
| Hypertension | 259 (31.5)       | 92 (33.6)            | 66 (23.9)            | 71 (25.9)            | 0.047     |
| Diabetes     | 78 (9.5)         | 39 (14.2)            | 20 (7.3)             | 19 (6.9)             | 0.005     |
| Stroke       | 16 (1.9)         | 10 (3.7)             | 3 (1.1)              | 3 (1.1)              | 0.044     |
| Atrial fibrillation | 90 (10.9) | 31 (11.3)            | 26 (9.5)             | 26 (9.5)             | 0.615     |
| Valvular disease | 39 (9.5) | 8 (2.9)              | 8 (2.6)              | 8 (2.6)              | 0.204     |
| Prior myocardial infarction | 128 (15.6) | 45 (16.4)            | 23 (8.4)             | 23 (8.4)             | < 0.001   |
| Pre-implant syncpe | 175 (21.3) | 57 (20.8)            | 52 (19.0)            | 66 (24.1)            | 0.334     |
| Echocardiography |              |                      |                      |                      |           |
| LVEF, %      | 42.7 ± 14.9      | 40.2 ± 14.6          | 42.9 ± 14.5          | 44.9 ± 15.3          | < 0.001   |
| LVEDD, mm    | 58.6 ± 13.1      | 58.9 ± 12.0          | 58.7 ± 13.6          | 58.1 ± 13.6          | 0.586     |
| Medication   |                  |                      |                      |                      |           |
| Beta-blockers | 507 (61.7)       | 169 (61.7)           | 167 (61.0)           | 171 (62.4)           | 0.940     |
| ACEIs/ARBs   | 321 (39.1)       | 116 (42.3)           | 106 (38.7)           | 99 (36.1)            | 0.327     |
| Aldosterone antagonists | 295 (35.9) | 14 (45.3)            | 96 (35.0)            | 75 (27.4)            | < 0.001   |
| Statins      | 192 (23.4)       | 71 (25.0)            | 65 (23.7)            | 56 (2.4)             | 0.313     |
| Loop diuretics | 340 (41.4) | 134 (48.9)           | 119 (43.4)           | 87 (31.8)            | < 0.001   |
| Digoxins     | 170 (20.7)       | 68 (24.8)            | 54 (19.7)            | 48 (17.5)            | 0.096     |
| Amiodarone   | 250 (30.4)       | 87 (31.8)            | 84 (30.7)            | 79 (28.8)            | 0.755     |

**Abbreviations:** ACEIs angiotensin-converting enzyme inhibitors, ARBs angiotensin receptor blockers, BMI Body Mass Index, CRTD cardiac resynchronization therapy and implantable cardioverter-defibrillator, LVEDD left ventricular end-diastolic dimension, LVEF left ventricular ejection fraction, NYHA class New York Heart Association class
HR 0.25, 95% CI: 0.14–0.45, tertile 3 vs tertile 1; \( P_{\text{trend}} < 0.001 \). The results remained statistically significant after adjustment for confounders including age, gender, primary prevention, NYHA class, CRTD implantation, LVEF, LVEDD, \( \beta \)-blocker use, and aldosterone antagonist use (Model 2). After additional adjustment of potential mediators, including BMI, ischemic cardiomyopathy, hypertension, AF, diabetes, and prior myocardial infarction, the results were similar (Model 3). The results from Model 2 and Model 3 were consistent, and as obesity and comorbidities are very common and related to clinical diagnosis and treatment decisions for ICD patients, in the present study, findings from Model 3 were used as the main results (Table 2).

**PA and all-cause mortality**

The dose-response association of PA with all-cause mortality was similar, as shown in Table 3. A higher PA level was significantly related to a lower risk of all-cause mortality (HR 0.46, 95% CI: 0.33–0.64, tertile 2 vs tertile 1; HR 0.23, 95% CI: 0.15–0.35, tertile 3 vs tertile 1) in a dose-response pattern (Model 1, \( P_{\text{trend}} < 0.001 \)). In Model 2 and Model 3, the associations between PA and all-cause mortality were similar, and results from Model 3 were used as the main results (Table 3).

**PA range for achieving optimal benefits regarding cardiac death and subgroup analysis of younger and older adults**

To further investigate the association of PA with the endpoints, dose-response curves were constructed, and a subgroup analysis of older and younger adults was performed. As shown in Fig. 2a, a significant reduction in cardiac death risk was observed at low-moderate PA levels. The risk was halved when the PA level was 12.32% (approximately 177 min), after which additional benefit of more PA was quite limited (Fig. 2a). Subgroup analysis showed that older patients could also benefit from PA, and low-moderate PA reduced the risk of cardiac death in older adults more rapidly than in younger adults. For example, using the same amount of PA as a reference, younger patients needed 16.82% PA (approximately 242 min) to achieve half of the risk, while older patients only need 10.88% PA (approximately 157 min) (Fig. 2b and c).

**PA range for achieving optimal benefits for all-cause mortality and subgroup analysis of younger and older adults**

The association of PA and all-cause mortality was similar, as shown in Fig. 3. A significant reduction in all-cause mortality risk was observed at the low-moderate level of PA (the HR was halved with 11.92% PA, approximately 172 min). Similarly, subgroup analysis showed that this dose-response association remained in older patients. To obtain half of the risk of all-cause mortality, younger patients needed 13.02% PA (approximately 187 min), while older patients only need 11.12% PA (approximately 160 min) (Fig. 3b and c).

**Discussion**

The main findings of the present study were as follows. First, there was an inverse dose-response association of ICD/CRTD-measured PA with long-term cardiac death and all-cause mortality in patients at high risk of SCD. Second, the association exhibited a non-linear pattern, and a significant reduction in cardiac death and all-cause mortality risk was observed with a low-moderate level of PA. Third, subgroup analysis results indicated that older adults could benefit from PA, and the range for achieving optimal benefits might be lower.
We demonstrated the dose-response association of PA with cardiovascular outcomes. This finding was consistent with previous studies. Schnohr et al. found an inverse dose-response relationship between PA and both coronary heart disease and all-cause mortality in healthy individuals [23]. Joseph et al. observed PA had an inverse dose-response effect on all-cause mortality in hypertension patients [24]. In addition, Ekelund published a meta-analysis confirming the dose-response association between wearable accelerometry measured PA and all-cause mortality [13]. However, in those studies, PA was based on questionnaires with low accuracy or a wearable device with a short detection period. In contrast, our study was conducted in patients at high risk of SCD risk with ICDs/CRTDs that had continuous PA recording function [19, 25]. HM technology allowed the instantaneous transmission of stored device data and enabled the continuous and longer acquisition of PA data. In addition, the present study conducted a long-term follow-up of the target population, and the real-time status of each patient could be obtained through remote HM.

Previous studies focusing on implantable device-measured PA in ICDs/CRTDs patients did not describe its dose-response association with cardiovascular outcomes. Kramer et al. found an increase in baseline PA was associated with reduced all-cause mortality in

| Table 2 | Cardiac death outcomes and multivariate cox regression analyses |
|----------------|---------------------------|----------------|---------------------------|----------------|----------------|
| Tertile 1 | No. of events | 51 | No. of participants | 274 | Model 1 | Ref. | Ref. | Ref. | P trend | < 0.001 |
| Tertile 2 | 24 | 274 | 0.40 (0.25–0.66) | 0.42 (0.26–0.69) | 0.41 (0.25–0.68) |
| Tertile 3 | 15 | 274 | 0.25 (0.14–0.45) | 0.26 (0.14–0.48) | 0.28 (0.15–0.51) |

| Age, years | < 60 | Tertile 1 | 10 | 76 | Ref. | Ref. | Ref. | 0.127 |
| Tertile 2 | 11 | 121 | 0.57 (0.24–1.35) | 0.76 (0.31–1.85) | 0.82 (0.33–2.04) |
| Tertile 3 | 8 | 163 | 0.29 (0.11–0.74) | 0.39 (0.15–1.06) | 0.47 (0.17–1.26) |

| ≥ 60 | Tertile 1 | 41 | 198 | Ref. | Ref. | Ref. | < 0.001 |
| Tertile 2 | 13 | 153 | 0.35 (0.19–0.65) | 0.34 (0.18–0.65) | 0.34 (0.18–0.64) |
| Tertile 3 | 7 | 111 | 0.25 (0.11–0.57) | 0.24 (0.11–0.55) | 0.25 (0.11–0.57) |

| Table 3 | All-cause mortality outcomes and multivariate cox regression analyses |
|----------------|---------------------------|----------------|---------------------------|----------------|----------------|
| Tertile 1 | No. of events | 108 | No. of participants | 274 | Model 1 | Ref. | Ref. | Ref. | P trend | < 0.001 |
| Tertile 2 | 56 | 274 | 0.46 (0.33–0.64) | 0.47 (0.34–0.66) | 0.46 (0.33–0.64) |
| Tertile 3 | 27 | 274 | 0.23 (0.15–0.35) | 0.24 (0.15–0.37) | 0.24 (0.16–0.38) |

| Age, years | < 60 | Tertile 1 | 26 | 76 | Ref. | Ref. | Ref. | < 0.001 |
| Tertile 2 | 20 | 121 | 0.40 (0.22–0.72) | 0.55 (0.30–1.01) | 0.55 (0.30–1.01) |
| Tertile 3 | 14 | 163 | 0.21 (0.11–0.40) | 0.28 (0.14–0.56) | 0.29 (0.15–0.59) |

| ≥ 60 | Tertile 1 | 82 | 198 | Ref. | Ref. | Ref. | < 0.001 |
| Tertile 2 | 36 | 153 | 0.49 (0.33–0.73) | 0.47 (0.31–0.70) | 0.46 (0.31–0.70) |
| Tertile 3 | 13 | 111 | 0.24 (0.13–0.44) | 0.23 (0.12–0.41) | 0.23 (0.13–0.43) |

Model 1 adjusted for age and gender; Model 2 further adjusted for Model 1 plus primary prevention, NYHA, CRT-D, LVEF, LVEDD, β-blockers, and aldosterone antagonists; Model 3 adjusted factors in Model 2 and potential mediators on the causal pathway including BMI, ischemic cardiomyopathy, hypertension, AF, diabetes, prior myocardial infarction.
Fig. 2 Dose-response curve of PA and cardiac death in total and different age groups; PA, physical activity. The bold and the dashed lines represent the estimated risk ratio (hazard ratio, HR) and the 95% confidence interval, respectively. The horizontal dashed line indicates that the HR value is 0.5, and the intersection of the vertical dashed line and the curve indicates the corresponding PA value.
Fig. 3 Dose-response curve of PA and all-cause mortality in total and different age groups; PA, physical activity. The bold and the dashed lines represent the estimated risk ratio (hazard ratio, HR) and the 95% confidence interval, respectively. The horizontal dashed line indicates that the HR value is 0.5, and the intersection of the vertical dashed line and the curve indicates the corresponding PA value.
patients with ICDs [21]. Zhao et al. verified the relationship of PA with cardiac death and provided a cut-off value [20]. Based on those previous studies, we further found an inverse non-linear dose-response association in patients ICDs/CRTDs and a significant reduction in cardiac death/ all-cause mortality risk was observed with low-moderate PA levels. This finding was consistent with most previous studies regarding the dose-response pattern of PA [6, 7, 13]. However, Cheng et al. found a linear dose-response association and high PA had more obvious cardiovascular benefits than moderate PA [26]. Hupin et al. concluded the greatest reduction in risk occurred in those who changed from performing no moderate-to-vigorous physical activity (MVPA) to performing some MVPA [27]. The level of PA and the benefit pattern might depend on the person’s health status and ability to perform PA. The population examined in the present study had severe heart disease, and the amount of total PA might be lower than those participants in the studies mentioned above. According to current guidelines, the recommended PA amount for older adults duplicate those for younger adults [28]. However, for many older adults, the recommended amount of PA may be excessive, explaining why the compliance rate of older individuals, is extremely low [16, 17, 29]. Researches on the benefit of PA in the older population were inconsistent. Cheng et al. concluded the benefit of PA was decreased for those aged over 65 years [26]. Another study showed older adults needed higher moderate and high-intensity exercise to gain benefit [30]. Hupin suggested even low doses of MVPA should be encouraged for older adults in their daily lives. The present study found older patients with ICDs/CRTDs could obviously benefit from PA and a significant reduction in cardiac death and all-cause mortality risk was observed with low-moderate level of PA. Older patients might need less dose of PA to reduce the risk of all-cause mortality and cardiac death by half. Therefore, for older adults, especially those who are at risk of sudden death and implanted with ICD, PA is worth recommending, and attention should be paid to the PA range resulting in optimal benefits which was easy to achieve. This result might be due to the decrease in the overall metabolic intensity of older adults.

Modern medicine has made great progress in many aspects, and patients are currently receiving improved treatment with novel drugs and devices. However, PA is a safe, inexpensive, easily accessible, and environmentally friendly therapy that patients often fail to implement. Our results demonstrated the importance of maintaining a certain level of daily PA in people already suffering from severe heart diseases. The range required for optimal benefits is not very high, especially for older adults, and is relatively easy to achieve. In clinical practice, it is important to understand the range of PA which could achieve optimal benefits. In addition, PA monitoring is very effective and can be introduced for all patients with CIEDs. PA monitoring can be further used in long-term management of patients with cardiovascular and even other chronic diseases.

Limitations
The present study analyzed the dose-response association of objective PA and the long-term prognosis of patients at high risk of SCD. Nevertheless, several limitations should be stated. First, we only included patients with implanted devices, which might cause selection bias. Second, despite of adjustment for multiple covariates, we did not take socioeconomic status (SES) into consideration, and several adjusted variables could be potential mediators. The possibility of overadjustment bias in Model 3 should be noted. Lastly, the conclusions were based on reverse causation, and residual confounding may still exist, thus more prospective studies with larger samples are needed to further validate our findings.

Conclusions
PA monitoring may aid in long-term management of patients at high risk of SCD. More PA will generate better survival benefits, but even low-moderate PA is already good especially for older adults, which is relatively easy to achieve.

Abbreviations
ACEIs: Angiotensin-converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; BMI: Body Mass Index; CI: Confidence interval; CIED: Cardiovascular implantable electronic devices; CRTD: Cardiac resynchronization therapy defibrillator; HM: Home monitoring; HR: Hazard ratio; ICD: Implantable cardioverter-defibrillator; LVEDD: Left ventricular end-diastolic dimension; LVEF: Left ventricular ejection fraction; MVPA: Moderate-to-vigorous physical activity; NYHA: New York Heart Association; PA: Physical activity; SCD: Sudden cardiac death; SES: Socioeconomic status; VT: Ventricular tachycardia.

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None.

Authors’ contributions
XYL, SZ1 and SZZ contributed to the conception or design of the work. XYL and SZ1 contributed to the acquisition, analysis, and interpretation of data for the work. XYL and SZ1 drafted the manuscript. KPC, WH, YGS, JFY, ZGL, WX, SZZ critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Availability of data and materials
The datasets generated and analyzed during the current study are not publicly available due to the Fuwai Hospital regulations, but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
The present study complied with the Declaration of Helsinki and was approved by the ethics committee of Fuwai Hospital (the chief institute) and
all other participating organizations, and all patients provided written informed consent before entering this study.

Consent for publication
Not applicable.

Competing interests
No authors have any conflicts of interest to disclose.

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