Dissertation

Indications for and outcome in patients with the wearable cardioverter defibrillator (WCD) in Austria. Results of the Austrian Lifevest Registry

submitted by

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Declaration

I hereby declare that this thesis is my own original work and that I have fully acknowledged by name all of those individuals and organisations that have contributed to the research for this thesis. Due acknowledgement has been made in the text to all other material used. Throughout this thesis and in all related publications I followed the "Standards of Good Scientific Practice and Ombuds Committee at the Medical University of Graz". The data of this thesis have been published in Odeneg T, Ebner C, Mörtl D, Keller H, Dirninger A, Stix G, Föger B, Grimm G, Steinwender C, Gebetsberger F, Stühlinger m, Mastnak B, Haider C, Manninger M, Scherr D. Indications for and outcome in patients with the wearable cardioverter defibrillator (WCD) in a nurse-based training program- Results of the Austrian WCD Registry. Europen Journal of Cardiovascular Nursing 2018: DOI 10.1177/1474515118790365.*ahead of publication* (52).

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Abbreviation

BMI	body mass index
BNP	brain-type natriuretic peptide
bpm	beats per minute
CABG	coronary artery bypass graphting
CAD	coronary artery disease
ECG	electrocardiography
GDMT	guideline-directed medical therapy
ICD	implantable cardioverter defibrillator
ICMP	ischemic cardiomyopathy
LVEF	left ventricular ejection fraction
MI	myocardial infraction
nsVT	non-sustain ventricular tachycardia
PCI	percutaneous coronary intervention
PPCMP	peripartum cardiomyopathy
SCA	Sudden cardiac arrest
SCD	sudden cardiac death
SD	standard deviation
TdP	torsade de pointes
VF	ventricular fibrillation
VT	ventricular tachycardia
WCD	wearable cardioverter defibrillator

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Zusammenfassung

Hintergrund: Der tragbare Kardioverter Defibrillator ist eine sichere und effektive Option zur Überbrückung eines temporär erhöhtem plötzlichen Herztodrisikos oder temporärer Kontraindikation für einen ICD, wobei Tragecompliance eine Schlüsselrolle darstellt.

Ziel: Das Ziel der Studie war eine österreichweite Erhebung von real-world Daten aller Patienten, die einen tragbaren kardioverter Defibrillator in Österreich erhalten haben.

Methode: In der Beobachtungsstudie wurde 448 Patienten mit tragbaren kardioverter Defibrillator in 48 Zentren in Österreich zwischen 2009 und 2016 eingeschlossen.

Ergebnisse: Die Hauptindikationen waren: Schwere nichtischämische Kardiomyopathie (21%), rezenter Myokardinfarkt und perkutane Koronarintervention (20%) oder stabile koronare Herzerkrankung mit perkutaner Koronarintervention/ Bypassoperation (14%). Insgesamt wurden 165 maligne Arrhythmie Events aufgezeichnet, wovon 22 Events (Kammerflimmern oder Kammertachykardie) bei elf Patienten (2.5%) adäquate Schocks zur Folge hatten. Das plötzliche Herztodrisiko variierte zwischen den verschiedenen Ätiologien. Acht von elf (73%) Patienten erhielten den ersten WCD Schock innerhalb der ersten 30 Tage nach WCD Anlage. Des weiteren wurden 15 anhaltende hämodynamisch stabile ventrikuläre Tachykardien bei 15 Patienten aufgezeichnet, sowie konnte bei drei Patienten Vorhofflimmern neu diagnostiziert werden. Zwei Patienten (0.4%) erhielten drei inadäquate Shocks. Die Tragecompliance betrug 23.5 h/d während einer medianen Tragedauer von 54 [1-436] Tagen. Der Grund für die automatischen Alarme waren Artefakte (97%). Ein höherer body mass index war assoziert mit einer höheren Inzidenz von Artefakten und folglich von Fehlalarmen. Der Hauptgründe für die Abnahme des tragbaren Kardioverter Defibrillators waren die ICD Implantation (55.5%) und die Verbesserung der LVEF über 35% (33%).

Konklusion: Der tragbare Kardioverter Defibrillator ist eine sichere und effektive Option für Patienten mit temporär erhöhtem plötzlichen Herztodrisiko oder temporärer ICD Kontraindikation mit einer Gesamtschockrate von 2,5% und einer stark variierenden Schockrate abhängig von den einzelnen Indikationen. Die Tragecompliance zeigte sich als hoch mit einer medianen Tragezeit von 23,5h [1-24], welche durch patientenzentriertes pflegerisches Training und Remotemonitoring potentiell beeinflusst werden können.

Abstract

Background: The wearable cardioverter defibrillator (WCD) is a safe and effective bridging option for patients with temporary elevated risk of sudden cardiac death (SCD) or temporary contraindication for implantable cardiac defibrillator (ICD) implantation. However patient compliance plays the key role.

Objectives: The aim of this study was to provide nationwide real-world data of patients receiving this WCD in Austria.

Methods: Observational study including 448 patients in 48 centres with prescribed WCD in Austria between 2010 and 2016.

Results: Main WCD indications were: severe non-ischemic cardiomyopathy (21%), recent myocardial infarction and percutaneous coronary intervention (PCI) (20%) and stable coronary artery disease with PCI/ coronary artery bypass grafting (14%). Eleven patients (2.5%) received 22 appropriate WCD shocks, and a total of 165 events of malignant ventricular arrhythmias occurred in our patient cohort. However, SCD risk varied between different aetiologies. Eight out of eleven (73%) patients received their first WCD shock within 30 days; Furthermore sustained hemodynamically tolerated VTs were detected in 15 patients and atrial fibrillation was newly detected in 3 patients. Two patients (0.4%) received three inappropriate shocks. Wearing compliance was 23.5 h/d in a wearing period of 54 [1-436] days. The vast majority of automatic alarms occurred due to artefacts (97%). Higher body mass index was associated with higher incidence of artefacts and failed alarms. Main reasons for termination of the WCD therapy were ICD implantation (55.5%) and improvement of LVEF to >35% (33%).

Conclusion: The WCD is an effective and safe treatment option in patients who are either at a temporary elevated risk of SCD or temporary contraindication of ICD implantation, with a 2.5% shock rate overall and a widely varying shock rate depending on WCD indication. WCD compliance remains high with a median wearing duration of 23.5h [1-24], which may be influenced by patient-centred nurse-based training and remote monitoring.

Introduction

Sudden cardiac arrest (SCA) and its consequence sudden cardiac death (SCD) is one of the leading causes of deaths worldwide with 5 million people dying every year (1). More than 300.000 people per year die due to SCD in the USA (2), about 81/100.000 people die per year in Germany (3) and about 15.000 per year die in Austria. Risk prediction of SCD is difficult due to a broad range of estimates on different aetiologies. Increasing age is a strong risk predictor, men are more likely to suffer SCD than women, which corresponds with the emergence of ischemic cardiomyopathy (ICMP) (4). Therefore severe heart failure and/or coronary artery disease are the most common aetiologies for SCD (1, 5). Younger patients are more likely to be affected by genetically predisposed structural disorders, cardiac channelopathies, myocarditis, congenital heart disease and other rare disorders (6,7).

SCD mostly results from ventricular arrhythmia in which treatment consists of delivering immediate direct current electrical defibrillation. Current Guidelines of the European Society of Cardiology recommend insertion of an implantable cardioverter defibrillator (ICD) for patients with structural heart disease and requiring secondary prevention, which means in patients who already suffered from sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) without an identifiable reversible cause or for patients 48 hour post myocardial infarction (MI) and optimised medical therapy. Further ICD implantation may be considered for patients with normal left ventricular ejection fraction (LVEF) and optimal medical therapy if sustained VTs are recurrent. Primary prophylactic ICD implantation is recommended for patients with a LVEF <35% and NYHA class II or III despite optimal medical treatment, but has to take place at least 6 weeks after MI. Patients with non ischemic cardiomyopathy (NICMP), LVEF <35%, NYHA II or III and >3 month on optimal medical therapy should receive an ICD. For all these recommendations a life expectancy of more than one year is mandatory (8). However, immediate ICD implantation is not recommended in patients with a potential reversible SCD risk (i.e. myocarditis), patients undergoing further risk stratification for SCD (i.e. patients with suspected inherited or congenital cardiac disease), or for patients with a temporarily explanted ICD or postponed ICD implantation (i.e. due to ICD associated infection or systemic infection) (9).

Referring to current ESC guidelines patients after risk stratification and diagnosis of NICMP and LVEF <35% should receive a primary preventive ICD after 90 days of being

on maximal tolerated guideline-directed medical therapy (GDMT) (10). In the DANISH trial 1116 patients with symptomatic systolic heart failure and LVEF <35% were randomised to either receiving an ICD or not, this demonstrated no mortality benefit for patients receiving primary preventive ICD who are on maximal GDMT (11). Despite the results of DANISH trial demonstrating no mortality benefit, these patients are of high SCD risk during their medical optimisation period (12). Interestingly a sub analysis of the DANISH trial showed a mortality benefit for patients younger than 59 years who received a primary preventive ICD (13). Further trials have shown that LVEF may recover in over 40% of all patients (14,15). As a result ICD implantation may not become necessary. Patients with myocarditis have the highest mortality in the first 18 month after hospitalisation as Kindermann et al demonstrated in a cohort of 181 patients whereof 13 died due to SCD (16). However the potential for LVEF improvement is significant (17,18). A special and highly vulnerable sub cohort of NICMP is peripartum cardiomyopathy (PPCMP). These patients often present with severely reduced LVEF, but have a high chance of quickly recovering in the first few months (19), it has been shown that these patients have an elevated risk of SCD in the first three to six months (20,21). Mortality rates vary between 2 -56% with about half of the events occurring within the first 12 weeks (12,23-25). LVEF in this subgroup of NICMP patients usually demonstrates a recovery of 30-50% within the first six months of diagnosis (5,26).
A unique reversible cardiomyopathy (CMP) with a favourable prognosis often associated with stress is Takotsubo CMP. Although the vast amount of patients may recover in the first months after diagnosis there is a high risk for ventricular arrhythmia ranging from 1.8% up to 5.6% in the acute phase (27,28). A further population with elevated SCD risk are patients with cardiac sarcoidosis as shown of Kron et al with an appropriate ICD shock rate of 7.1% per year in sarcoidosis patients with decreased LVEF (29). However a consensus statement recommends LVEF re-assessment after optimisation of medication in primary preventive patients and therefore re-evaluation of ICD implantation (30).

In addition, landmark trials such as MADIT, MADIT II and SCD-HeFT showed a temporary contraindication for primary preventive ICD implantation in patients with a LVEF <35% within the first 40 days after myocardial infarction (MI) or patients within 90 days after percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) (10,31-33). The CABG-PATCH trial showed no survival benefit of ICD placement at time of CABG (34). A meta-analysis of MADIT II and SCD-HeFT showed higher NYHA class, lower LVEF and no beta blocker are significant predictors for

appropriate shocks (35). The VALIANT study with a cumulative incidence for SCD of 8.6% showed higher baseline heart rate, impaired creatinine clearance from baseline, LVEF < 40%, cardiovascular re-hospitalisation and atrial fibrillation are associated with an increased risk of SCD. These risk factors change with time after an MI. In the first few weeks after an MI and a LVEF below 30% the SCD risk appears to be 2.3% (36). ICD implantation in the early post myocardial infarction phase is not associated with better outcome and furthermore the possible improvement of the LVEF due to revascularization and/or optimisation of the medical therapy can reduce the risk of SCD and therefore no ICD implantation will be needed (37). The small number of arrhythmic deaths might be overshadowed by a higher number of non-arrhythmic deaths (38). An explanation for this phenomenon might be that patients with prevented SCD may die due to progression of severe heart failure as the DINAMITE and IRIS study showed. The overall mortality was not reduced with ICD implantation early after MI despite significantly reduced SCD events (37, 38). However, LVEF might improve in the first eight weeks after MI and further to this almost half of the patients with acute heart failure and decreased LVEF might improve their LVEF during the first 6 months, hence an ICD implantation will become unnecessary (37,39). Additionally, patients undergoing CABG with LVEF≤35% before surgery have a postoperative 30 day mortality of 4.3-5.1% (40). About 50% of all deaths will be caused by SCD (41). While being on high risk of SCD in the first few months after surgery half of these patients will improve their LVEF in this time (41). For all these patients optimal medical therapy and/or revascularisation and/or other causal therapies should be provided first to improve the LVEF and therefore reduce the risk of SCD. The evaluation of the arrhythmic risk can be evaluated after several weeks or months whether these therapy strategies were successful or not.

Another gap in seamless monitoring and SCD protection are patients with delayed ICD implantation. The delay can be caused by many different reasons, which emerge in clinical practice. Patients, who are waiting for heart transplantation, have a high risk of SCD of up to 40% (42). As waiting lists are long and waiting periods can take up to one year primary preventive ICD implantation can be used to bridge this gap, which is also recommended in clinical practice guidelines (10). However, Implantation of an ICD has risks and is often contraindicated (43). Another group of potentially high risk patients in the first few months are those who had a syncope of unknown cause but high likely of VT/VF origin (44). The persistence and development of arrhythmic substrate or development of a cardiomyopathy with decreased LVEF can be unpredictable in patients with assumed myocarditis or Tako Tsubo CMP(45-47). Immediate ICD implantation is not recommended as SCD death risk

is unknown and may be temporary. Risk stratification in these patients is time consuming and may take a few months while patients being potentially unprotected as SCD can't be immediately excluded (44). Further ICD implantation in patients with inherited cardiac arrhythmic disease, such as i.e. Long QT syndrome, Brugada syndrome or arrhythmogenic right ventricular cardiomyopathy (ARVC) having a high risk of SCD is effective (10). However ICD implantation is accompanied with serious psychological distress or inappropriate ICD shocks. Therefore risk stratification and decision making can take some time (44).

Patients with an already confirmed high risk of SCD and therefore needing an ICD implantation may have the implantation delayed for various reasons such as acute systemic infection or other comorbidities i.e. ventricular thrombus as well as capacity problems in operating theatre.

Increasing numbers of ICD implantations over the last few years lead to an increasing number of complications which subsequently lead to temporary explantation (48). The incidence of ICD associated complications can be up to 6% for infection and up to 18% for lead defects in the first twelve years (49). An antibiotic therapy is mandatory and can last up to several weeks depending on the severity of the infection (50). Re-implantation of a device too early may lead to repeated infection. However these patients remain at high risk of SCD and hospital monitoring is expensive and inconvenient for the patient (51).

For all these patients who have a temporary/transient risk of SCD, contraindications for an immediate ICD implantation or ICD implantation postponement due to other reasons the wearable cardioverter defibrillator (WCD) is a possible temporary treatment option during this phase of being on high risk of SCD, which offers the opportunity to be discharged from the hospital instead of being continuously monitored as an inpatient (52-54).

Currently, the LifeVest© (Zoll Medical, Pittsburg, USA) is the only commercially available WCD. The WCD consists of a monitor and an electro belt, which are connected with a wire (Figure 1A). The monitor is able to release five 150 Joule shocks per arrhythmic event and is worn around the waist or with a shoulder belt as shown in Figure 1 B. It contains two response buttons to avoid inappropriate shocks and a LCD touch screen, which shows the patient's name and is able to give further instruction if needed (Figure 1 D). The second part of the WCD is the electrode belt, which contains 4 dry non adhesive electrodes to provide a two-lead ECG and three defibrillation pads. These defibrillation pads contain small capsules, which automatically releases gel before a shock delivery (Figure 1C) to

avoid burned or irritated skin. Further the electro belt contains a vibrations mechanism to provide additionally to an audible alarm a tactile alarm. The weight of the garment including monitor is about 1.3 kg and can be used for patients with a chest circumference of 66-144cm (55).

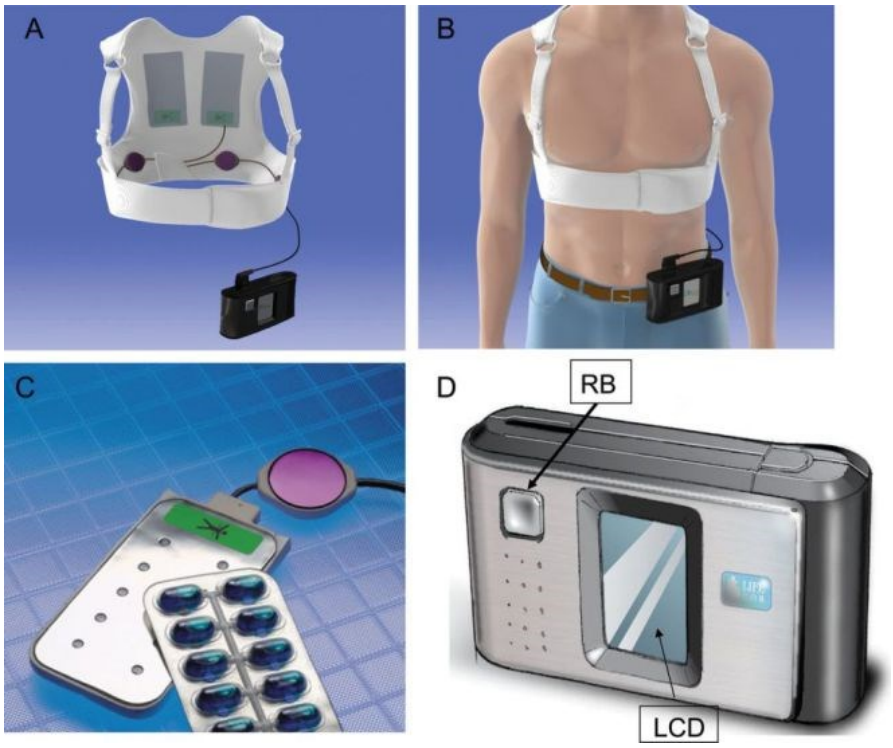

Figure 1. Wearable Cardioverter Defibrillator (WCD) components

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The device continuously monitors the patient's heart rhythm and alerts the patient in case of detection of an arrhythmia. Thus allows a conscious patient to delay the treatment shock by pressing the response buttons. In the case of unconsciousness patient and therefore his/her inability to press the response buttons the device delivers an electrical shock after 60 seconds for ventricular tachycardia (VT) or 25 seconds for ventricular fibrillation (VF) respectively individualised threshold time depending on the physicians programming decision. Shock delivery will be triggered to R wave if possible. The device is able to deliver up to 50 shocks with a fully charged battery, however only 5 shocks per episode will be delivered. If the patient does not convert to normal rhythm after the fifth shock the device stops treatment due to ethical reasons this is in line with ICD programing.

The algorithm to detect arrhythmia is a combination of heart rate analysis and morphology analysis. Heart rate is calculated by QRS detection and analysis of a Fourier transformation frequency plot (60). Morphology analysis uses stability and onset criteria. After measuring heart rate, the algorithm compares it with the pre-programmed threshold for VT of VF. Once the heart rate becomes higher than these thresholds morphology analysis will be completed comparing the current ECG with a baseline ECG in normal rhythm, which is usually done at the first fitting of the WCD (56). The detection algorithm calculates a weighted score based on heart rate, morphology, signal quality and response of the patient by pressing the response buttons. Based on the result of this score the device decides if an arrhythmia is present (57). If the WCD detects a ventricular arrhythmia the device first delivers a vibration alarm directly followed by a siren alarm. From this time point the patient has 60 seconds (25 seconds for VF) to press the response buttons. The siren alarm gets louder and requests the patient to react and press the response buttons to delay the shock. If the patient is unconscious and therefore not able to press these buttons within the programmed threshold time the device alerts the bystanders to not touch the patient, releases gel from the defibrillation pads and delivers a treatment shock. Afterwards the rhythm is analysed again to ensure normal rhythm. If the first shock is not successful the device is able to deliver 4 further shocks per event. The device itself and the treatment sequential are shown in Figure 2.

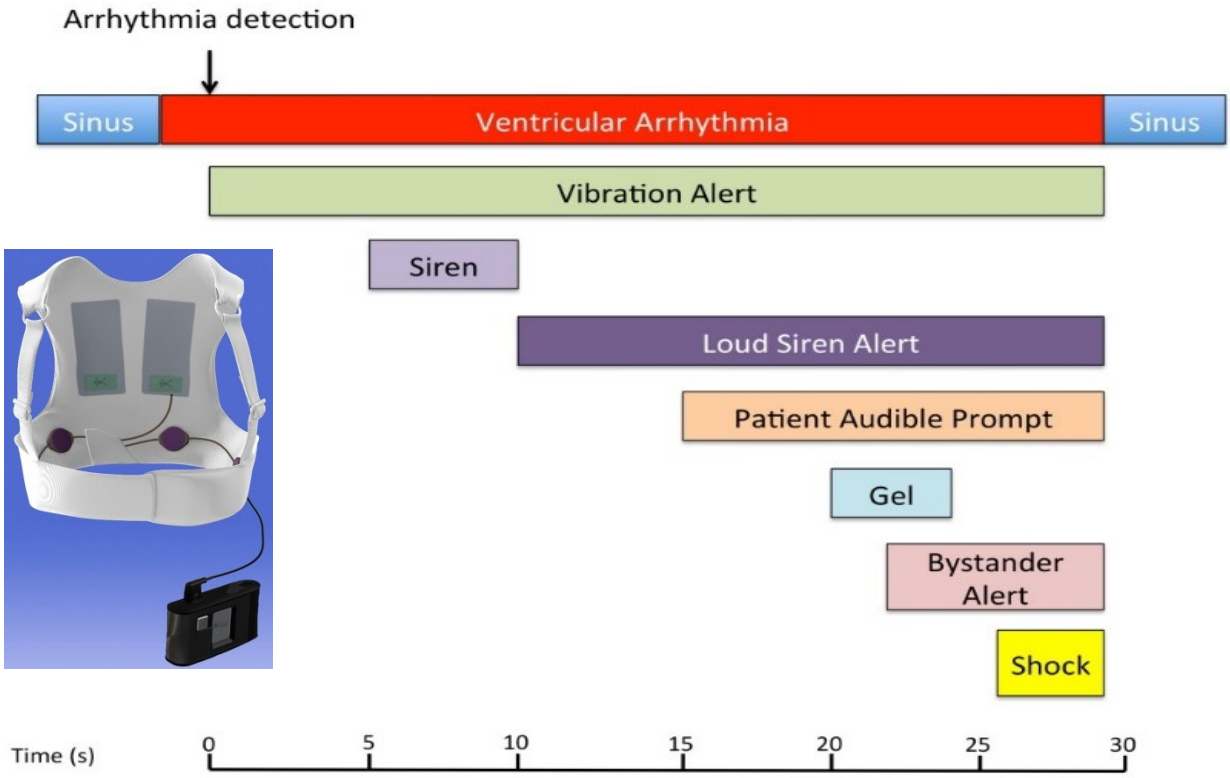

Figure 2: LifeVest© and arrhythmia detection

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Within each alarm sequence the device continuously analysis the rhythm corresponding to the previously described algorithm. If the detections criteria are no longer fulfilled the alarm sequence stops. The combination of this algorithm and the possibility of the patient to press the response buttons should ensure that shocks are only delivered if the tachyarrhythmia lasts longer than 30 seconds and the patient is unconscious.
After a shock delivery the device automatically stores and transmits the ECGs to an online patient management database (Lifevestnetwork). The prescribing and treating healthcare professionals receives a notification of the event for further evaluation. Further ECG data of VT/VF events, asystole or bradycardia will be stored and automatically transmitted to Lifevestnetwork. In the case of tachyarrhythmia storage the ECG starts 30 seconds before the start of arrhythmia and stops 15 seconds after ending of the alarm. If an asystole longer than 16 seconds and signal amplitude of 100µV is detected a five minutes ECGs for asystole events will be stored. Although the device is not able to provide an antibradycardia therapy an alarm sequence is started if the heart rate drops below 20 bpm. In both asystole and bradycardia the device starts the alarm sequence and instructs bystander to call the ambulance and start with resuscitation.

Double counting of a normal rhythm can occur in patients with high T waves and/ or low QRS (55). Therefore a unipolar pacemaker can trigger false alarms of 10% as shown in a cohort of 60 (58). To avoid a vast amount of inappropriate alarms programming the VT detection zone up to 200 bpm might be a solution. However Lapage et al reported a fatal device interaction with the WCD in an 18 year old patient due to underdetection of a VT slower than 200 bpm (59). The authors conclude that a WCD should not be used in patients with unipolar pacemakers (58,59). Furthermore a currently published case report of Manninger et al reported of double counting and a vast amount of inappropriate alarms of the WCD in patient with bipolar pacemaker. The authors programmed the VT detection rate of the WCD to 200bpm and assume that strict heart rate control resolved further misdetection (60). However as whithin patients with unipolar pacemaker programming the VT detection rate up to 200 bpm can lead underdetection with fatal outcome (59).

Additionally to the shock function of the WCD the patient can initiate the storage of an ECG recording by pressing the response buttons for 5 seconds, which allows the use of the device as an event recorder. Whereof slower arrhythmias (under the programmed detection rate) as well as other arrhythmias with therapeutically consequence can be detected i.e. new occurrence of atrial fibrillation (55).

A big advantage of using this device is the possibility to discharge the patient safely with protection and minimising the risk of SCD, this is cost effective if compared to conventional prolonged monitored hospital stay (51). Furthermore, whilst these patients are being protected, it gives the treating physician sufficient time to re-evaluate the SCD risk after an appropriate time, as recommended in current guidelines (4,5). Meanwhile further examinations or up titration of optimal medical therapy can be optimised (56). Over the past years, several observational studies about the WCD showed that the WCD is a safe und useful device to bridge a temporarily increased risk of SCD and is able to terminate malignant arrhythmias appropriately (53,56,61-65). One of the first prospective single centre trial on the WCD to examine the feasibility and efficacy of transthoracic defibrillation for ventricular tachyarrhythmias was published in 1998. The findings demonstrated for the first time the efficacy of the device as 100% of all cahtlab induced VT/VF episodes were successfully terminated with one monophasic 230 joule shock (66). Based on the results of Aurrichio et al two multicentre trials (WEARIT and BIROAD) to test the efficacy and safety of the WCD were induced. The WEARIT trial enrolled patients with symptomatic heart failure (NYHA II-IV) and LVEF below 30%. The BIROAD study enrolled patients with temporary high risk of SCD, whereof most patients had a recent MI

or current bypass surgery. These two independently designed studies were combined due to request of the US Food and Drug Administration (FDA). In a period of three years 289 patients were enrolled (177 in WEARIT/ 112 in BIROAD). Six out of eight VT/VF events were successfully detected and terminated by the WCD. The other two could not be detected due to incorrect wearing of the WCD. A further 12 patients died of which six of them died suddenly, all six did not wear the WCD correctly (53). Since 2001 a new generation of WCDs using synchronised biphasic shocks was tested. The design was improved and made an incorrect electrode placement less likely. The use of biphasic shocks with lower energy showed the same efficacy as a monophasic shock, this was tested within a controlled environment. A further advantage of this technology is a smaller and lighter device design as well as longer battery longevity. Reek at all showed the efficacy and effectiveness of his new device in 12 patients whereof 22 VT/VF episodes were induced during an electrophysiological testing. All of them (100%) were successfully terminated by the WCD. These results lead to commercial approval of the new device (67).

The first single centre registry was published in 2002 from et Reek et al and enrolled 84 WCD patients, of which some were participating in the WEARIT/BIROAD study too. Indications for enrolment in the study were divided in three groups: (1) MI and post SCA, MI and Killip class III/IV or MI and LVEF ≤ 30 plus non sustained ventricular tachycardia (nsVT) or CABG with LVEF≤ 30 and nsVT, (2) patients listed for heart transplantation and (3) patients with an existing ICD indication, but also having a temporary contraindication. The median WCD wearing period was 22.5 h/d for median 118 days. 5 patients (6%) received 7 appropriate shocks and one VF episode was appropriately detected, but could not be treated as the defibrillation electrode was not correctly positioned in the garment. 15% of all automatically triggered alarms were inappropriate due to artefacts. However only one inappropriate shock (1.2%) was reported (68).
Up to date four big multicentre registries enrolling patients with different WCD indications are published (44,61,69,71). Klein et al published the first multicentre experience with the WCD in Germany in 2009. In 43 centres 354 patients with various indication were enrolled: post MI and LVEF<35% (39%), early post CABG and LVEF <35% (25%), risk stratification (myocarditis 10%, inherited channelopathies 3%, SCA survivor 5%), listing for heart transplant (6%), ICD explantation (10%) and delayed ICD implantation (2%). In a median wearing duration of 106 days 27 patients (7.6%) experienced 246 VT/VF events. Out of these 11 patients (3%) received 21 appropriate shocks, whereof 95% were successfully restored to normal rhythm with the first shock. The vast amount of recorded

tachyarrhythmia events (n=228) were sustained VTs, followed by nsVTs (n=8) and other arrhythmias such as sinus tachycardia or SVT (n=8) or asystole (n=2). The VT/VF event rates differed between WCD indications from 5% to 13% with the largest being in highest risk stratification group. In one patient the WCD appropriately detected a VF event, but did not deliver a shock due to misplacement of the defibrillation electrode in the garment. This happened with the WCD of first generation and is no longer possible with the new device. In this cohort 3 inappropriate shocks (0.8%) occurred due to artefacts. Overall 43% of all patients received an ICD after WCD period ranging from 25% (myocarditis) to 79% (prolonged risk stratification) for different indications (44).

One of the first and largest multicentre registries enrolling patients with various WCD indications was published in 2010 by Chung et al. This retrospective registry covered 2002 -2006 and enrolled 3569 patients with various WCD indications: ICD explantation (23.4%), VT/VF events before ICD (16.1%), genetic predisposition to SCD (0.4%), CMP and LVEF≤35% (8.1%), recent MI and LVEF≤35% (12.5%), post CABG and LVEF≤35% (8.9%), recent NICMP and LVEF≤35% (20%), recent MI with normal LVEF (3,8%) and miscellaneous (6.8%). In a median wearing duration of 52.6 days and a mean daily use of 19.9 hours per day 80 sustained VT/VF events in 59 (1.7%) patients occurred, whereof 99% of all events were successfully terminated with the first shock. Shock rates varied between different WCD indications ranging from zero (genetic predisposition, CMP and LVEF≤35%, recent MI and normal LVEF) to 5.1% for ICD explantation. Out of these successfully treated patients 8 died, four of them due to reoccurrence of an arrhythmia. In two patients the electrodes lost contact due to a fall of and therefore were not able to shock the recurrent arrhythmia. In one patient the spouse inhibited the shock delivery by pressing the response buttons and one patient died due to a device interaction of a unipolar pacemaker. Inappropriate shocks occurred in 67 patients (1.9%) mainly due to signal artefacts or SVTs (62).

In 2015 the first and biggest prospective registry (WEARIT II) was published by Kutyifa et al to assess the risk of VT/VF events and identify LVEF improvement after WCD period. 2000 patients with ICMP (40%), NICMP (46%) or congenital/inherited disease (14%) were enrolled. In a median wear time of 90 days and 22.5 h/d 120 sustained VTs in 41 patients occurred, of which 30 events in 22 patients (1.1%) were appropriately shocked. All of these events could be restored to normal rhythm with the first shock. Shock rates varied throughout different WCD indications and were highest for patients with ICMP (3%), as well as for patients with congenital/inherited disease (3%) compared to NICMP (1%). Ten patients (0.5%) received an inappropriate shock due to ECG artefacts. After

WCD period 42% of all patients received an ICD. Main reason for not implanting an ICD after WCD period was LVEF improvement. This first prospective study showed that the WCD can be safely used as a risk prediction tool to identify patients, who would benefit from an ICD (61).
Up to date Wäßnig et al published in 2016 the largest retrospective multicentre registry enrolling 6043 patients in 404 German centres of different WCD indications : DCM (36.7%), ICM (26.9%),NICM (12.2%), ICD explant (11.9%), myocarditis (9.8%), genetic disease (1.4%), heart transplantation (0.7%) and congestive heart failure (CHF) (0.4%). In a median wearing duration of 59 days and 23.1h/d 94 patients (1.6%) received appropriate WCD shocks. Incidence of shock varied throughout different indications ranging from 1% for NICMP up to 4% for congestive heart failure (CHF). Out of all appropriately shocked VT/VF events 11% received more than one shock to restore slower heart rhythm. In 88 patients (94%) the WCD was able to convert the VT/VF event. Four patients died due monomorphic VT and three due to VF as the WCD was not able to convert these events after five shocks. One patient died due to asystole. Most appropriate shocks (70%) occurred in the first 40 days after prescription. Only 0.4% received an inappropriate shock due to signal artefacts. This large nationwide cohort confirms the value of the WCD and underlines further possible WCD indications (69).

Furthermore a small amount of observational subpopulation studies exist to investigate the use, safety and efficacy in different WCD indication groups as follows:

<u>Ischemic cardiomyopathy and myocardial infarction and/ or coronary artery disease</u>

Epstein et al showed a 1.6% WCD shock rate (309 shocks in 133 patients) in 8453 enrolled WCD patients after acute myocardial infarction and an LVEF below 35%, whereof 91% of these patients received successful resuscitation. The time from MI to first shock was a median of 16 days, 75% of all shocks happened in the first months and 96% of all shocks in the first three months. The one year survival rate of 91% implies that patients after MI benefit from WCD defibrillation, particularly during the first 30 days. This SCD survivor may then receive an ICD (64).

Zishiri et al confirmed the high mortality early after revascularization (90days) in a matched cohort of hospital survivor after CABG or PCI with LVEF below 35% with and without WCD. The results showed a significant risk reduction in the WCD group in the early post PCI (10% without WCD vs 2% with WCD) and CABG (7% without WCD vs

3% with WCD). The WCD shock rate was 1.3% in this study. However differences in mortality cannot be solely attributed to therapies of ventricular arrhythmias (VA). Despite the fact of no published randomised prospective trials the authors concluded, that WCD as a bridging tool should be considered (63).

The single centre experience of Kondo et al confirmed this conclusion, enrolling 24 patients early post MI and followed them for 8 months. LVEF improved significantly ($p<0.01$) after WCD period. However two patients (8.3%) received appropriate WCD shocks and 58% of all patients had a need for ICD implantation after WCD period (70).

The recently published study of Kandzari et al examined the frequency of ischemia of WCD treated VT/VF events in patients post acute MI, whereof 96% of these events were successfully shocked. Out of 273 enrolled patients 15.4% had ischemia prior to VT/VF event. Further survival of 24 hours post treatment was high (88% with ischemic VT/VF event vs 84% without ischemic VT/VF event) as well as 30 day cumulative survival (77% with ischemic VT/VF event vs 70% without ischemic VT/VF event). The conclusion from this study is that ischemia is an infrequent cause of VT/VF post MI and defibrillation success or survival was not influenced by aetiology of VT/VF (71).

Summarising the subpopulation of patients after MI/CABG and/or ICMP big registry data showed WCD shock rates range from 1.4% up to 7%. Lowest shock rates were shown in Wäßnig et al for patients with ICMP (1.4%) followed by Kutyifa et al (3%) and Chung et al for patients post MI (2.9%) and Klein et for patients early post MI (5%). Highest shock rates were report for patients post CABG from Klein et al (7%) and Chung et al (8.9%) (44,61,62,69). Further, older patients present with more frequent ventricular arrhythmias as shown in the recently published sub analysis of the WEARIT II registries. Especially older patients with ICMP (≥65 years) have significant higher WCD shock rates ($p=0.034$) than patients younger than 65 years (0.7% vs 3%). Therefore the WCD may play an important role in older population (72).

The prospective WEARIT III registry enrolled 1000 subjects with ischemic cardiomyopathy and heart failure (including NYHA II, III, IV and an ejection fraction ≤ 35%) with WCD. This trial will give insights of clinical course of high-risk cardiac patients with ICMP and WCD, such as left ventricular function recovery, arrhythmia, Implantable Cardioverter Defibrillator (ICD), Cardiac Resynchronization Therapy (CRT), Left Ventricular Assist Device (LVAD) or heart transplantation, and to assess the benefit

of WCD in these patients. The estimated study completion will be in 2019. (ClinicalTrials.gov Identifier: NCT02700880) (73).

Further the VEST trial is the first randomised trial with the WCD at all, randomising patients either to wear the WCD for three months or not. Enrolment is already completed and 2300 patients post acute MI and LVEF ≤35% were included. The results will give insights about the impact of the WCD on mortality by reducing SCD during the first three months after MI. The estimated publication of data will be in 2018 (74).

Non-ischemic cardiomyopathy

Previous studies enrolling patients with newly diagnosed non-ischemic cardiomyopathy and LVEF below 35% conclude that LVEF may recover in the first three months on optimal medical therapy. Nevertheless the SCD risk for NICMP patients range from 0-1.3% in registries enrolling patients of various indications (61,62,69). In WCD study enrolling only heart failure patients shock rates vary form 0% (65,76) and 0.4% (77) to higher shock rates of 5.5% (75). The highest WCD shock rate showed the sub analysis of the PROLONG study with 7% (12).

One of the first studies on newly diagnosed CMP or revascularisation with an LVEF ≤35% was reported in 2012 of Mitrani et al. In this registry 134 uninsured patients were enrolled of whom 57% had NICMP and 43& had ICMP. There were no appropriate shocked VT/VF events, however there was a high number of enrolees lost to follow up (35%). A further eight patients did not wear the WCD and only 27% wore the WCD more than 22.6 hours/day. Three deaths of unknown cause were reported when WCD was returned, which may have been sudden deaths. However, LVEF improved in both groups significantly and no difference between these groups was found and therefore unnecessary ICD implantation was prevented. The authors concluded that LVEF improvement and avoidance of unnecessary ICD implant justifies the utility of the WCD (76).

In contrast Salehi et al reviewed the national US database for WCD patients with NICMP and long term alcohol abuse and enrolled 127 patients. Out of these patients 5.5% had sustained VTs and all (100%) were successfully treated by the WCD. Furthermore 33% of all patients improved their LVEF and only 23.6% received an ICD after WCD period. These results showed a significant risk of VT/VF events in this particular patient cohort (75).

A sub analysis of the US database of 220 patients with CMP (NICMP 61.8%, ICMP 35%, 2.3% mixed aetiology) and LVEF≤35%, who wore the WCD more than one year, confirmed the high risk of VT/VF events as 13 events in 9 patients (4.1%) occurred. Whereof eight appropriate shocks in eight ICMP patients and five appropriate shocks in one NICMP patient occurred. The median prescription duration was 581 days; the median wearing duration was 451 days with a daily wearing duration of 20.4 hours. The main reason for a prolonged WCD prescription was a consistent low LVEF with further ICD evaluation (34%), ICD contraindication (i.e. physical condition, cancer, cardiac thrombus) (23%), patient decision to postpone ICD implantation (17%), not compliant to follow up for ICD evaluation (10%) or continued scope for optimisation of medical therapy (7.7%). More than 16% of all patients improved their LVEF during the prolonged period up to one year due to medical optimisation or natural recovery. Although the inappropriate shock rate was 3.6% none of these patients died of inappropriate shocks and therefore the WCD was concluded to appear safe for a long term use (77).

Patients with acutely decompensated heart failure had 8 arrhythmic events in 5 patients (7%) in a prospective cohort of 75 patients (NICMP 67%, ICMP 33%) enrolled in the SWIFT study. Only one patient in the NICMP group received one appropriate shock. Main arrhythmic events in the NICMP group were non sustained VTs, supraventricular tachycardia or premature ventricular complex. However this study was underpowered to detect VT or determine factors associated with SCD in NICMP patients (78).

Duncker et al showed in the PROLONG study, in which 156 patients with newly diagnosed CMP and LVEF ≤35% (NICMP 55% , ICMP 29%, PPCMP 12% and 4% myocarditis) were enrolled. The mean follow up time was 12 months. After three month 88 patients had a primary preventive indication for ICD implantation. However only 58 of these patients had a primary preventive indication for ICD implantation at the end of follow up. Furthermore 11 patients received 12 appropriate shocks of which two patients were treated beyond the three month period. The decision to prolong the WCD wearing period at the three month follow up visit for another three months was dependent on (1) LVEF 30-35%, (2) increase of ≥5% in LVEF or (3) not optimised heart failure therapy. Prolonged WCD use should be considered to avoid unnecessary ICD implantation, while allowing left ventricular remodelling during intensive drug therapy. The Prolong study showed a significant LVEF improvement (33%) beyond the three month WCD period with relevant risk for ventricular arrhythmia (17). A sub analysis of all NICMP patients (n=117) enrolled in the PROLONG study showed a very high WCD shock rate as 12 sustained

VT/VF in 10 patients (9%) occurred whereof eight patients (7%) received nine appropriate shocks. In contrast to previously published studies with lower shock rates (61,65,69,75,76) for NICMP patients this result confirmed the elevated risk in the first month after heart failure diagnosis as demonstrated in other studies (17,77,79). The authors state that there is a six fold higher risk in newly diagnosed CMP with not optimised medical therapy compared to the chronic phase (11,12). The difference in shock rates between the previous published studies might be explained by a shorter wearing time (12).

In the recently published study of Röger et al confirms the fact of long term LVEF improvement due to optimisation of heart failure therapy although there is a high risk of SCD in a real world registry. Out of the 105 (NICMP and ICMP) enrolled patients five patients (4.8%) (1 NICMP, 1 myocarditis) received five appropriate shocks. The shocks occurred between three and 154 days after discharge. More than half of the patients with ICMP (54.8%) and NICMP (48.8%) improved their LVEF. However 51.4% of all patients received an ICD after WCD period. Within a median follow up time of 18.6 months 5.6% of all patients with implanted ICD after WCD period received an appropriate ICD shock. Furthermore none of the patients without ICD died or had ventricular arrhythmia. Further bradycardia and asymptomatic asystole of 10 seconds during night was detected of the WCD. The authors concluded that WCD might help to optimise the selection of the appropriate device (ICD, pacemaker or combination) after WCD period (79).

Myocarditis

In one of the first published registries Klein et al showed that a prolonged WCD use for a further 2-3 months was necessary for high risk stratification group of patients, this represented 18% of all patients. This included 10% of patients with assumed myocarditis or newly detected cardiomyopathy (44). In a mean wearing duration of 3 month 5.7% of these patients received appropriate WCD shocks, however only 25% of this patients received an ICD after WCD period (18). Further 6 patients (4%) of the PROLONG study were diagnosed with myocarditis. Although no shocks occurred in this sub cohort, LVEF improved significantly ($p<0.001$) in a prolonged WCD wearing period of more than three months. Therefore potential unnecessary ICD implantation could be avoided (17).

Takotsubo Cardiomyopathy

Patients with Takotsubo Cardiomyopathy have an increased risk of SCD in the first weeks after diagnosis, whereof incidence of ventricular arrhythmia varies from 1-8% (56). The study of Deepraserkul et al included 102 patients with Takotsubo cardiomyopathy and decreased LVEF whereof 2 (1.9%) patients received appropriate shocks in 44 days in the follow up period. Additionally, 70% improved their LVEF, of which 66 of these patients improved within the first three months. Two patients died during WCD wearing period due to asystole or noncompliance of WCD wearing and five patients died after the WCD wearing period. The authors concluded that SCD might persist despite LVEF improvement. Therefore the WCD can be used for risk stratification during to acute and/or prolonged phase (80).

Peripartum cardiomyopathy

Another rare indication for WCD use are patients with peripartum cardiomyopathy (PPCMP) and decreased LVEF as demonstrated by Duncker et al who enrolled 49 patients with an 12% WCD shock rate (20). In the first prospective registry of patients diagnosed with PPCMP wearing the WCD 12 patients were identified of which nine wore the WCD due to severe heart failure (mean LVEF 24.5%) for three month or longer. Two refused to wear the WCD. During median follow up time of 12 months none of the patients died and no syncope or ventricular arrhythmia of the patients without WCD were documented. However three patients (25%) received four appropriate WCD shocks due to VF. All of these events were successfully terminated with the first shock. Furthermore one patient had VF despite LVEF improvement to 45%. Therefore risk stratification based only on LVEF is controversial (81). Frett at al suspected bromocriptine to play a potential role in VT/VF rate occurrence. The author recommends the WCD for five to six months after diagnosis for these patients (82). In contrast in a matched cohort of 107 PPCMP patients versus 159 NICMP patients wearing the WCD for a median of 124 days vs 96 days, no shocks occurred in PPCMP cohort versus one shocked patient in NICMP cohort. 62% of PPCMP patients recovered LVEF versus only 30% of NICMP patients within the first six months. The observed mortality rate was 2.8% for PPCMP patients. However none of these patients died during WCD use (PPCMP) vs 11 (NICMP) and three patients died after WCD use (PPCMP) versus 13 (NICMP) (83). The authors concluded that these patients are of low risk, however the limitation of this study has to be taken in account as the retrospective character and no detailed patients information due to analysis of manufacture's

reimbursement database were used. Therefore the conclusion about the risk might not be correct.

Tachymyopathy

In a sub analysis of Erath et al the usefulness of the WCD for patients with tachymyopathy was shown as LVEF improved significantly (p=0.01), BNP levels decreased more than in the control group and ICD implantation rate was lower. Although none of these patients experienced appropriate shocks during WCD period the use of a WCD might be considered as risk of SCD is uncertain (84).

Sarcoidosis

The successful usage of WCD in a sarcoidosis patients was first published in 2016. A sarcoidosis patient with LVEF of 30% received the WCD in anticipation of LVEF improvement. This patient received an appropriate shock just one day after discharge (85). Further Skowasch enrolled 46 sarcoidosis patients with median LVEF 30% in a registry. In a median wearing duration of 24 days [1-79] 11 VT/VF episodes in 10 patients (22%) were appropriately terminated with the first shock. In 50% of all patients ICD implantation was necessary, however 19% improved the LVEF. Due to ongoing immunosuppressive therapy with the potential to improve LVEF not all patients should receive immediately an ICD and WCD should be used as bridging tool (86).

Heart transplantation and left ventricular assist device (LVAD)

As ventricular arrhythmias are common in patients waiting for heart transplantation or patients in need of an LVAD, ICD implantation poses several risks. Opreanu et al conducted a registry enrolling 121 patients on waiting list for heart transplant and bridged them with a WCD. In a mean wearing duration of 127 days 7 patients (6%) received appropriate WCD shocks. 42% ended the WCD period due to ICD implantation and 11% due to heart transplantation (87). Further Klein et al reported a shock rate of 9% in median wearing duration of 5.4 months in a German multicentre registry enrolling 22 patients on waiting list for heart transplantation. In three patients heart transplantation was withheld due to LVEF improvement (44). Kao et al reported zero VAs in 12 patients in a registry enrolling 89 patients with heart failure. Out of all heart transplantation listed patients 35% improved their LVEF. This should not be seen as a “cure” but patients should rather be continuously evaluated as a relapse might occur. However the WCD may be beneficial in these patients if the waiting time for transplantation is expected not to be long (88).

Furthermore the WCD might be beneficial in patients in need of an LAVD as it's known that these patients are on high risk of VA as well. However up to date no study data are available using the WCD instead of ICD (56,89).

ICD explantation

The use of an WCD in patients with an explanted ICD due to infection gives sufficient time for antibiotics treatment, as well as the supply of a WCD during this phase is more cost efficient than a prolonged hospitalization period (51). Furthermore the WCD shock rate is higher in this subpopulation of up to 5.1% (62,69,90). Tanawuttiwat et al reported a 2% WCD shock rat in a median wearing duration of 21 days and 20h/d after median 14.7 days antibiotics treatment. A further three patients died suddenly not wearing the WCD, which highlights the importance of patient education to increase compliance (91). Up to date the biggest registry of patients wearing the WCD after ICD removal enrolled 8058 patients with a median waiting time for re-implantation of 50 days. In 4% (334 patients) 406 VT/VF events were reported of which 348 were successfully treated by the WCD. In the remaining 54 events a shock was inhibited by conscious patients. Most events occurred in the first weeks after ICD removal (90). For patients with explanted ICD/CRT-D devices the only safe and reasonable bridging option is hospitalisation with continuous rhythm monitoring (92).

Congenital structural heart disease and inherited arrhythmias

The WCD can be safely used in patients with congenital structural heart disease, such as tetralogy fallot, ventricular malformation (non compaction and single ventricle) or multiple abnormalities, and inherited arrhythmias, such as arrhythmogenic right ventricular dysplasia, long QT syndrome or Brugarda as shown the largest WCD registry enrolling patients with congenital heart disease or inherited arrhythmias. Main reason for prescription of WCD was pending genetic testing in the inherited arrhythmias patients and transplant listing for the congenital heart disease patients. Patients with inherited arrhythmias have a higher rate of ventricular arrhythmias as these patients received 3 appropriated WCD shocks versus no shocks, respectively (93).

Other potential indications

Among haemodialysis patients, SCD occurs at a rate of greater than 30 times that of the general population (94). However ICD implantation is patients with multiple comorbidities is controversial and ICD implantation should be assessed only to high risk patients (95). In

a retrospective study LVEF was not predictive of the occurrence of SCD in 80 haemodialysis patients. In fact, 75% of the patients who suffered sudden death had preserved LVEF >35% and arrhythmias accounted for 35% of the total sudden deaths (96). Wan et al enrolled 75 haemodialysis patients with WCD in a registry, whereof 84 sudden cardiac arrest events occurred. Only 18% of the enrolled patients had an LVEF <35%. The 24hours survival was 70.7% and 1-year survival was 50.7%. Therefore the use of a WCD might be associated with better survival in these patients (97). However the WCD might be useful to identify patients clearly in need of an ICD (18). Further studies are needed to demonstrate a survival benefit in patients with chronic renal failure due to WCD use.

Another potential future WCD indication could be patients with chemotherapy induced cardiomyopathy. Onset and outcome are often unpredictable therefore the WCD may help to assess the benefit of an ICD over several months (18). As shown a study of Everitt et al who demonstrated a WCD shock rate of 7% in 59 enrolled patients with diagnosed cancer (98). Furthermore the use of WCD in patients with radiotherapy for lung cancer can be helpful especially if a pre-existing ICD has to be removed due to this therapy (99).

Some drugs bare the risk of causing arrhythmic events by QT prolongation. Antiarrhythmic drugs, antibiotic compounds, antidepressant drugs and some antihistaminic and doping compounds are known to prolong QT (18). Further inotropes and diuretics can contribute to ventricular tachycardia (88). Therefore the WCD might be helpful in some situations.

Due to lack of randomized controlled trial and large nation-wide observational trial data on WCD indications and treatment, we created a nation-wide registry including all WCD patients in Austria since initiation of this therapy in 2009 until March 2016 in order to provide comprehensive real-world data on WCD compliance, appropriate and inappropriate shock rates, complications accompanied with this therapy, as well as ICD implantation rates after termination of WCD therapy. Furthermore, our aim was to investigate whether these parameters vary between different WCD indications.

Methods

448 consecutive Austrian patients were enrolled in this observational registry study , all of whom received a WCD. This study complies fully with the Declaration of Helsinki, has been approved by the institutional review board at the Medical University of Graz, Austria and registered at clinicaltrials.gov (NCT02816047). Anonymized data was contributed by 48 centres from across Austria starting with the first WCD patient in 2009 until March 2016, data contributed by these centres included; baseline demographics, clinical indications, arrhythmic events, clinical outcomes, changes in LVEF and whether an ICD therapy was still indicated at the end of the WCD wearing period as well as analysis of all automatically and manually recorded ECGs. Furthermore, data describing compliance, wearing duration and VT/VF programming was also collected.
Categorization of patients was dependent on underlying disease and reason for prescription resulting in nine WCD indication groups as described in the Table 1 (52).

NICMP	Newly diagnosed non-ischemic cardiomyopathy with left ventricular ejection fraction (LVEF) <35% within 90 days of the start/optimization of heart failure therapy and/or documented VT/VF.
Post MI + PCI	Patients with a recent myocardial infarction (MI) <40 days undergoing PCI and LVEF <35% and/or documented VT/VF.
Stable CAD + recent PCI/CABG	Patients with severe ischemic cardiomyopathy (LVEF <35%) due to stable coronary artery disease within 90 days after revascularization and/or start/optimization of medical therapy and/or documented VT/VF.
Delayed ICD implantation	Patients in whom an ICD is indicated, but immediate implantation is currently not possible due to comorbidities or other reasons.
Myocarditis	Patients with acute myocarditis and a decreased LVEF and/or documented VT/VF.
ICD explantation	Patients with previously implanted ICD, which had to be temporarily removed due to an ICD associated infection.
Acute infection	Patients, who meet indications for an ICD, but implantation has to be

	delayed due to a systemic acute infection.
Bridge to ablation	Patients with documented VT events prior and/or post VT ablation.
Other	This category summarizes all other rare WCD indications, i.e. Brugada syndrome, long QT syndrome, post-partum cardiomyopathy or patients waiting for heart transplantation.

Table 1. Definition of all WCD indications.
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Lifevest© network

The Lifevest network is an online data management system, which allows healthcare professionals to monitor the patients wearing compliance and ECGs. All information are first stored on the monitor and transmitted via Bluetooth to the online data management system whereof the responsible healthcare professions are alerted in case of malign arrhythmia or low wearing compliance.

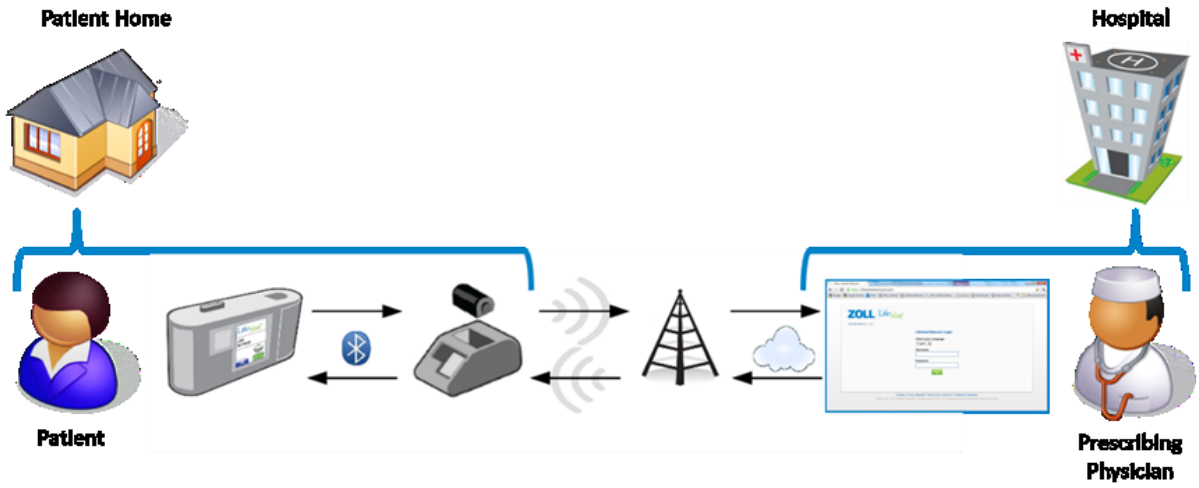

Figure 3: Lifevestnetwork

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Compliance

Wearing compliance is determined in this study by the median daily wearing duration. Daily wearing duration is defined here as the number of hours per day the WCD has been worn. This data was collected from the telemedical Lifevest© network database. Additionally, data regarding the total wearing duration was also collected via the Lifevest©

network database which was subsequently compared and corroborated with hospital records and patients' charts (52).

ECG records

Two members of the research team independently reviewed and analysed the ECGs obtained from the Lifevest© network. All ECGs obtained were categorized into either automatically or manually triggered. Automatically triggered ECGs are defined as all ECGs with suspected arrhythmia identified by the WCD and therefore alarming the patient. These automatically generated ECGs have been further categorized in the study as appropriate alarms or inappropriate alarms. Appropriate alarmed automatically generated ECGs is described here as all recorded ECGs showing sustained VTs (>30 s), VF, Torsades de pointes, asystole, bradycardia <30 bpm, or non-sustained ventricular tachycardia (nsVT) (<30 s). All other alarms (i.e. due to artefacts or supraventricular arrhythmias) were classified as inappropriate. Manually triggered ECGs represent all stored ECGs in which the patient initiated an ECG recording due to symptoms i.e. palpitations. Again these ECGs were also classified as appropriate or inappropriate. Appropriate manually triggered ECGs is defined here as all ECGs showing a slow sustained VT, non-sustained VT, bradycardia or atrial fibrillation. All other alarms (i.e. showing a normal ECG) were classified as inappropriate.

Additionally, further data regarding the detection rate threshold for VT and VF zones were also collected from Lifevest© network database. VT and VF programming zones are usually between 120 and 250. Shock time delay was generally set at 60 seconds for VT and 25 seconds for VF, but could be individualized from 60 - 180 seconds for VT and 25 - 55 seconds for VF at the discretion of the treating physician (52).

Shock

ECGs relating to all shock events recorded by the WCD have been reviewed independently by three members of the Division of Cardiology, Medical University of Graz, Austria. An appropriate shock event is defined here as a biphasic shock which has been delivered due to a VT or VF event. Inappropriate shock events are defined as all WCD shocks delivered for all other reasons other than VF or VT such as signal artefacts or supraventricular tachycardia. Additionally, the time from arrhythmia detection to shock was also analysed together with the reaction time of the patient to press the threshold button of the WCD (52).

Structured educational interactive nurse- based training program for patients with wearable cardioverter defibrillator (WCD) followed by remote monitoring

"All patients received individualised structured educational interactive nurse-based initial training lesson of two hours including a structured lesson of the transitory risk of the patient, depending on the underlying disease, the importance of wearing compliance and the fitting and use of the WCD as well as suggestions for use of the WCD in daily life. Furthermore all patients were registered at the Lifevest© network database, which enables a continued monitoring of the wearing adherence as well as an overview of all recorded ECGs.
The WCD training program for patients consists of a structured educational interactive lesson of about 2 hours, held on day of prescription of the WCD. All teaching personal had undergone dedicated training regarding WCD application. This consists of 3 hours training before being allowed to teach and provide advice regarding WCDs to the patients. Additionally, all had to teach 5 patients under supervision of a WCD expert.

Before direct contact with a patient is made, information about the individual situation, medical history and therapy plan is collected via medical charts and/or the treating healthcare professionals. The patient's history, WCD indication, and patient-specific issues are discussed with the responsible cardiologist.

The treating cardiologist informs the patient prior to the training lesson about the indication for and the basic principles of the WCD. The lesson takes part after prescription of the WCD. An appointment is made with the patient at a time point close to the discharge date, as patients are usually still admitted to the hospital. Furthermore one close relative (usually the partner) of the patient is invited to this appointment if possible. An appropriate 2environment is considered for the appointment to ensure privacy and enable full concentration on the topic of SCD and use of WCD.

The following topics are addressed at the session, which is held together with the treating cardiologist as needed:

1) General information about SCD, individual risk of SCD depending on the underlying disease of the patient and risk stratification, the WCD in general as a bridging option, as well as the WCD in the individualised situation of the patient
2) Information about the components of the WCD

a. Monitoring function:
    - Introduction to the sequence of alarms released by the WCD in case of automatically detected ventricular arrhythmias.
    - Function of the response button which is pressed by the conscious patient in case of siren alarms to abort the shock sequence.
    - The patient has to prove that he is able to press the response buttons, which is checked several times during the training lesson.
    - Information is given about what happens in case of unconsciousness and a release of a shock by the WCD
    - Information and training of the change and recharge of the WCD battery, which is needed every 24 hours, is given
    - Opportunity of inducing a manually stored ECG by pressing and holding the response buttons for 3 seconds in the event of symptoms is trained
    - Information is given about automatic and manual transmission of all ECGs
b. Electrode belt and garment
    - Assembling of the electrode belt and garment: first the assembling is shown by the teaching person, afterwards this should be done by patient alone to ensure he will be able to do so at home
    - Instruction for change and washing of the garment are given
    - Chest circumference is measured and the an appropriate size of the garment is fitted
c. Charging station
    - Information about battery charging is given
    - Information about data transmission and positioning of the charging station is given

3) Use of the WCD in daily life
    a. Information is given about how to handle the WCD when showering or bathing
    b. Information about time point of changing the battery is given. Therefore a plan is made with the patient considering his daily routines at home, which time he/she is mostly at home and therefore the best time point to change the battery

c. Information about how often and how to change and wash the garment is given
d. The patient is informed that he should only take off the WCD (for showering or changing the garment) in attendance of a second person
e. In case of attendance of relatives at the initial teaching lesson information is given about different possible situations, such as shock of the WCD, unconsciousness of the patient when not wearing the WCD (i.e. during shower) and how to support the patient in general. If none of the relatives are able to join this session an additional appointment is made for the relatives. Information is given about journeys abroad with the WCD, especially for flights.
f. Information is given about movement and sports with WCD
g. Possible questions of the patient are answered
h. A 24 hour available hotline number is given in case of further question or technical problems with WCD

Follow up of the patients and remote monitoring is individualised and done as needed. The WCD has the ability to capture information about patient arrhythmic events. This information is uploaded to Lifevest network database automatically. The responsible health care professionals have access to this database and are able to see all automatically and manually recorded ECGs of their patients as well as the patients' wearing adherence. Alerts and notifications can be tailored so that the healthcare professionals can choose which events to be notified for, such as WCD treatments, patient-recorded ECGs, and detected arrhythmia events in which no treatment is given, such as a short run of VT as well as wearing adherence (i.e. less than 20 hour per day). The notification and alerts are automatically sent by email to all treating health care professionals (nurses and physicians). Individualised phone or personal contact is made with the patient as needed to optimise treatment pathways and to improve compliance.

In order to improve compliance, the same health care professional / nurse serves as the primary contact person for the patient. In addition, all ECGs were analysed independently of two members of the research team (one nurse and one physician). ECGs of all shock events recorded by the WCD were reviewed by three members of the research team (one nurse, one physician and one consultant specialised in electrophysiology. "(52)

Statistics

Mean±SD presents continuous variables or median and range (min – max), depending on normality of distribution. Categorical variables are presented as percentages (%) and counts. Continuous variables were compared with Student t test or the Wilcoxon Rank-Sum test (non-normally distributed data), and frequencies with Chi-square analysis or Fishers‘ exact test, as appropriate. Two-tailed P-values <0.05 were considered to indicate statistical significance. Statistical analyses were performed using SPSS 23 (IBM, Armonk, New York, USA) (52).

Results

Baseline characteristics

Overall 448 patients in 48 centres from all regions of Austria were enrolled, with a median of 4 [1-77] patients per centre. The number of WCD prescriptions increased significantly over the years ($p<0.05$), starting with 2 WCD prescriptions in 2009 and 2 prescriptions 2010, followed by 9 WCD prescriptions in 2011, 33 prescriptions in 2012, 59 prescriptions in 2013, 124 prescriptions in 2014 and 180 prescriptions in 2015. (Figure 3)

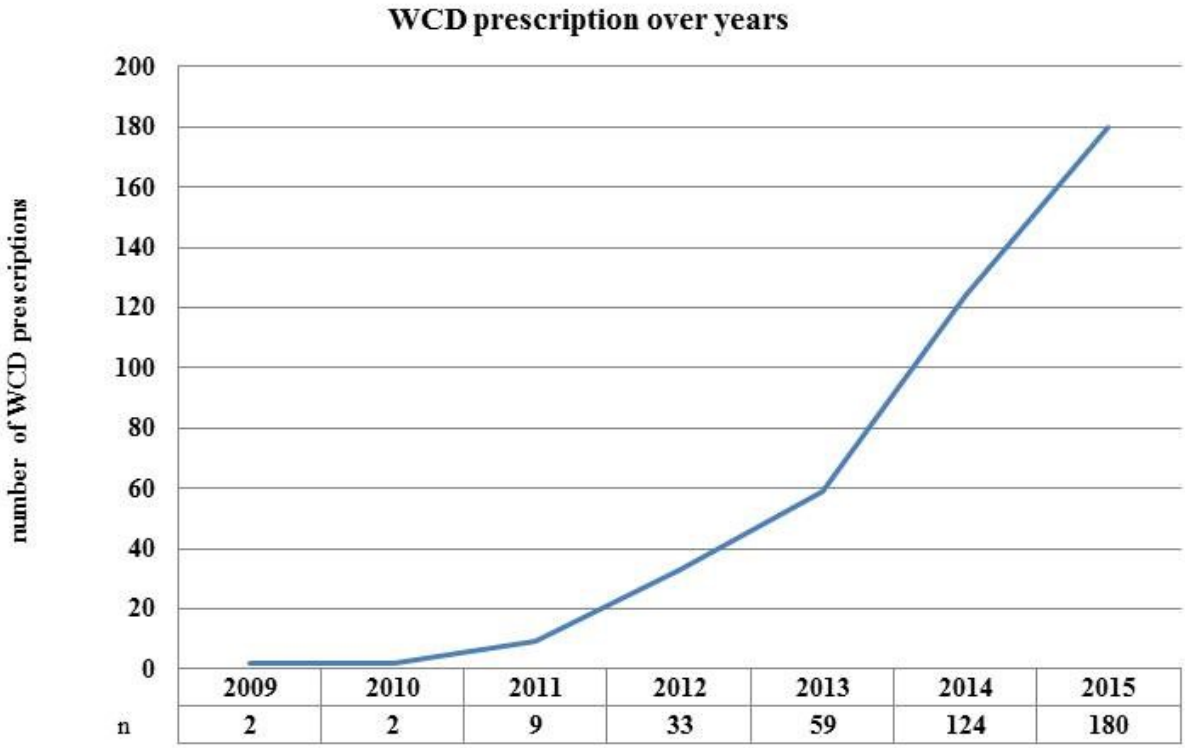

Figure 4. WCD prescriptions over years

The mean age of WCD patients was 59±14 years, 24% were female, the mean LVEF at baseline was 33±15% and mean BMI was 27±5. 216 (48%) patients received the WCD for secondary prevention of SCD, respectively already had sustained ventricular arrhythmias (VT or VF). Most patients (n=117, 53%) had VT events before WCD prescription, whereas 96 patients (44%) suffered from VF and 8 patients (3%) had Torsade de pointes at baseline. The remaining 52% received the WCD for primary prevention of SCD. Patients receiving the WCD for secondary prevention were 60±15 years, 55 (25%) were female and the mean LVEF at baseline was 38±15. Whereas patients receiving WCD for primary prevention were 59±14 years, 5 (23%) were female and the mean LVEF at baseline was 32±15 When group to age quartiles most patients (n=67, 35%) with VT/VF event were between 58 and 68 years, followed by patients older than 68 years (n=63, 29%) and patients younger than 49 years (n=49, 23%). Patients between 49 and 57 years had less VT/VF events before WCD prescription (n=42, 19%).

The baseline characteristics at time point of WCD prescription (baseline) of all 9 Austrian regions are shown in Table 2a.

	all	Styria	Vienna	Upper Austria	Vorarlberg	Lower Austria	Carinthia	Tyrol	Salzburg	Burgenland
N	**448**	180	91	55	35	34	27	10	10	6
Age (years)	**59 ± 14**	63 ±13	54 ±15	55 ±12	57 ±17	60 ±12	56 ±17	47 ±10	65 ±13	61 ±15
Female gender (%)	**24**	22	27	29	17	29	15	50	30	0
VT/VF event before WCD	**48**	51	37	45	40	76	30	60	50	67
LVEF baseline (%)	**33 ± 15**	33 ± 15	33 ± 15	31 ± 14	38 ± 19	29 ± 14	30 ± 19	38 ± 18	27 ± 6	38 ± 11

Table 2a . Patient characteristics at baseline/ WCD prescription in different region

Variables	ALL	NICMP	Stable CAD + recent PCI/CABG	Post MI + PCI	Myocarditis	ICD explantation	Acute infection	Bridge to ablation	Delayed ICD implantat	Other
N	**448**	94	62	88	45	46	18	11	54	30
Age (years)	**59 ± 14**	58 ± 13	64 ± 12	59 ± 12	48 ± 12	60 ± 13	64 ± 15	58 ± 15	62 ± 17	59 ± 15
Female gender (%)	**24**	25	14	18	29	30	11	46	27	34
VT/VF event before WCD	**48**	17	53	40	62	39	6	73	63	83
Arterial hypertension (%)	**74**	68	91	92	29	67	72	55	75	56
CAD (%)	**52**	22	100	100	2	44	50	27	94	42
Atrial fibrillation (%)	**24**	29	33	18	9	20	28	36	31	17
LVEF baseline (%)	**33 ± 15**	24 ± 12	30 ± 14	33 ± 10	30 ± 15	33 ± 12	40 ± 16	47 ± 15	37± 18	49 ± 17

Table 2b. Patient characteristics at baseline/ WCD prescription in different indications.

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Indications

The indications for all 448 patients who received a WCD in Austria 2009-3/2016 were as follows; 94 (21%) severe non-ischemic cardiomyopathy, 88 (20%) recent myocardial infarction and PCI, 62 (14%) stable coronary artery disease (CAD) with recent PCI and/ or CABG, in 54 patients (12%) ICD implantation had to be postponed due to reasons other than systemic infection (i.e. ventricular thrombus or institutional capacity reasons), 45 (10%) acute myocarditis with impaired left ventricular function and/ or documented VT/VF, 46 (10%) temporary ICD explantation due to infection or device malfunction, 18 (4%) ICD indication, but acute systemic infection, 11 (2%) were bridged to ablation and 30 (7%) had other rare indications (i.e. Long QT syndrome (n=6), Brugada syndrome (n=1), post-partum cardiomyopathy (n=1), bridge to heart transplantation (n=1), Takotsubo (n=1), other (n=11), unknown (n=9) as shown in Figure 5 (52).

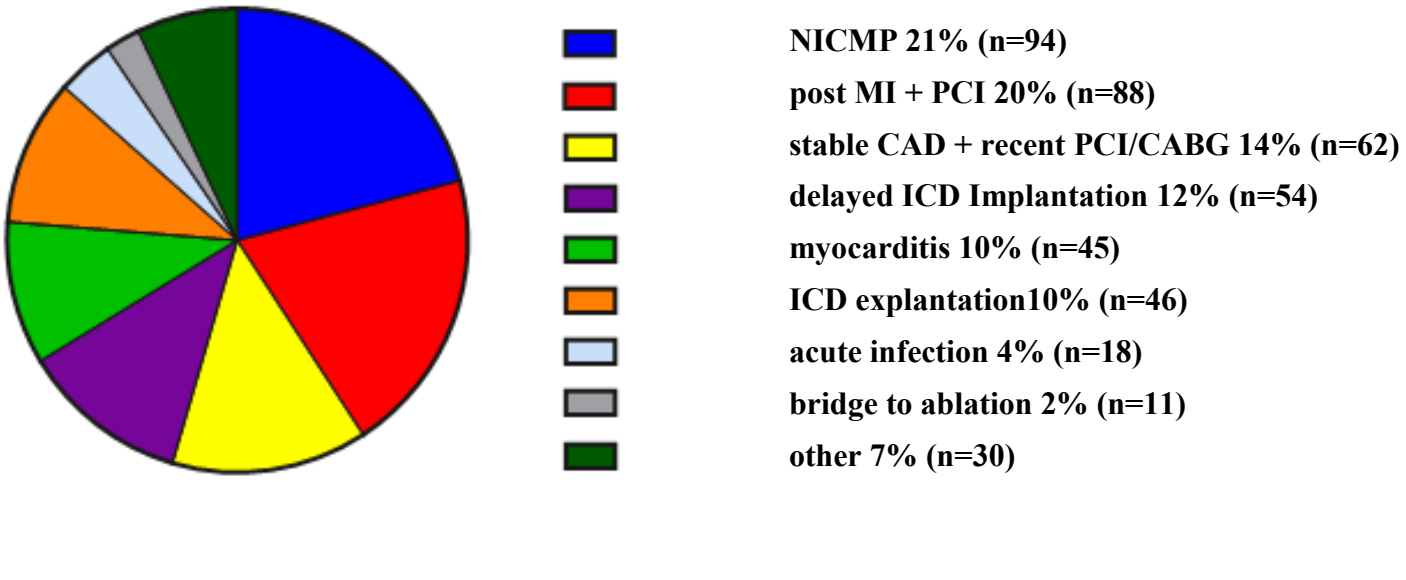
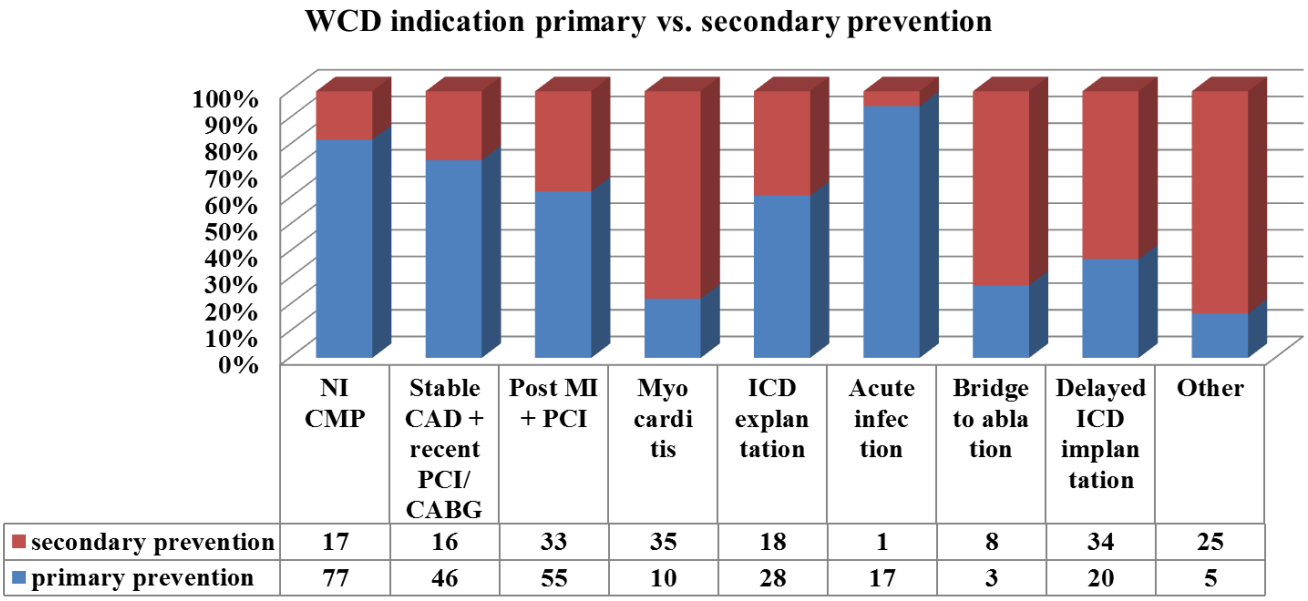


Figure 5. Indications for WCD prescription

The vast majority of patients in indication groups of myocarditis, bridge to ablation, delayed ICD or other had VT/VF events before prescription of the WCD. In contrast most patients in the indication group of NICMP, Stable CAD + recent PCI/CABG, post MI+PCI, ICD explantation or acute infection received the WCD for primary prevention as shown in Figure 6.



	NI CMP	Stable CAD + recent PCI/ CABG	Post MI + PCI	Myo cardi tis	ICD explan tation	Acute infec tion	Bridge to abla tion	Delayed ICD implan tation	Other
secondary prevention	17	16	33	35	18	1	8	34	25
primary prevention	77	46	55	10	28	17	3	20	5

Figure 6: WCD indication primary vs secondary prevention

Wearing duration and compliance

The median duration of WCD use was 54 [1-436] days. The cumulative wearing duration was 80.8 years in the total patient cohort. Wearing duration varied regarding the WCD indication, age quartiles and gender. Patients with myocarditis had the longest wearing duration (median 84 [4-312] days), followed by patients with NICMP (median 77 [3-298] days), patients after recent MI (median 63 [1-248] days), compared to patients, who had a delayed ICD implantation had the shortest wearing duration (28 [3-283] days). When patients were grouped by age quartiles (<49 years, 49-58years, 59-67years , >67years), patients in second age quartile (49-58 years, n=87) had the longest wearing duration (in median 68 [1-436]) days), whereas patients in fourth quartile (>67 years, n=122) had the shortest wearing duration (median 43 [1-179] days. Median wearing duration per day was 23.5 [1-24] hours. There were no differences in compliance for patients wearing the WCD more or less than 60 days (23 (3-24) h/d vs. 22 (1-24) h/d; p = ns). Patients did not differ in daily wearing compliance regardless of age quartile, gender or WCD indication (Table 3) (52).

	Daily use (hours)	p values	Days of wear (days)	p values
WCD use				
overall, median (range)	23.5 (1-24)		54(1-436)	
WCD use by gender				
Male, median (range)	23.4(1-23.9)	p=ns	54(1-436)	p=ns
Female, median (range)	23.7(9.7-23.9)		58(4-298)	
WCD use by age quartile				
<49 years, median (range)	22.9(0.3-23.9)	p=ns	63(1-248)	p<0.005
40 to 57 years, median (range)	23.3(0.1-24)		68(1-436)	
58 to 68 years, median (range)	23.5(0.1-23.9)		53(1-280)	
>68 years, median (range)	23.8(1-23.9)		43(1-179)	
WCD use by indication				
Post MI + PCI	23.5(0.1-23.9)	p<0.005	63(1-248)	p<0.005
Stable CAD + recent PCI/CABG	23.7(9.6-23.9)		57(6-161)	
NICMP	23.4(0.1-24)		77(3-298)	
ICD explantation	23.8(0.1-24)		36(1-436)	
Myocarditis	22.7(0.3-23.9)		84(4-312)	
Acute infection	23.6(17.1-23.9)		41(6-182)	
Bridge to ablation	21.4(16.5-23.9)		47(32-244)	
other	22.8(6.9-23.9)		55(1-312)	
Delayed ICD implantation	23.6(9.8-23.9)		28(3-283)	

Table 3. WCD use by gender, age and WCD indication.

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79 patients (18%) had a mean daily wearing duration of less than 20 hours per day, the mean age was 53±14 years, 19% were female, baseline LVEF was 34±15, mean BMI was 28±5 and 29 patients (37%) received the WCD for secondary prevention of SCD. The distribution of WCD indication of these patients is shown in Figure 7a.

A smaller amount, 15 patients (3%) had a mean daily wearing duration of less than 10 hours per day, the mean age was 59±14 years, 7% were female, baseline LVEF was 33±15, mean BMI was 27±5 and 9 patients (60%) received the WCD for secondary prevention of SCD. The distribution of WCD indication of these patients are shown in Figure 7b.

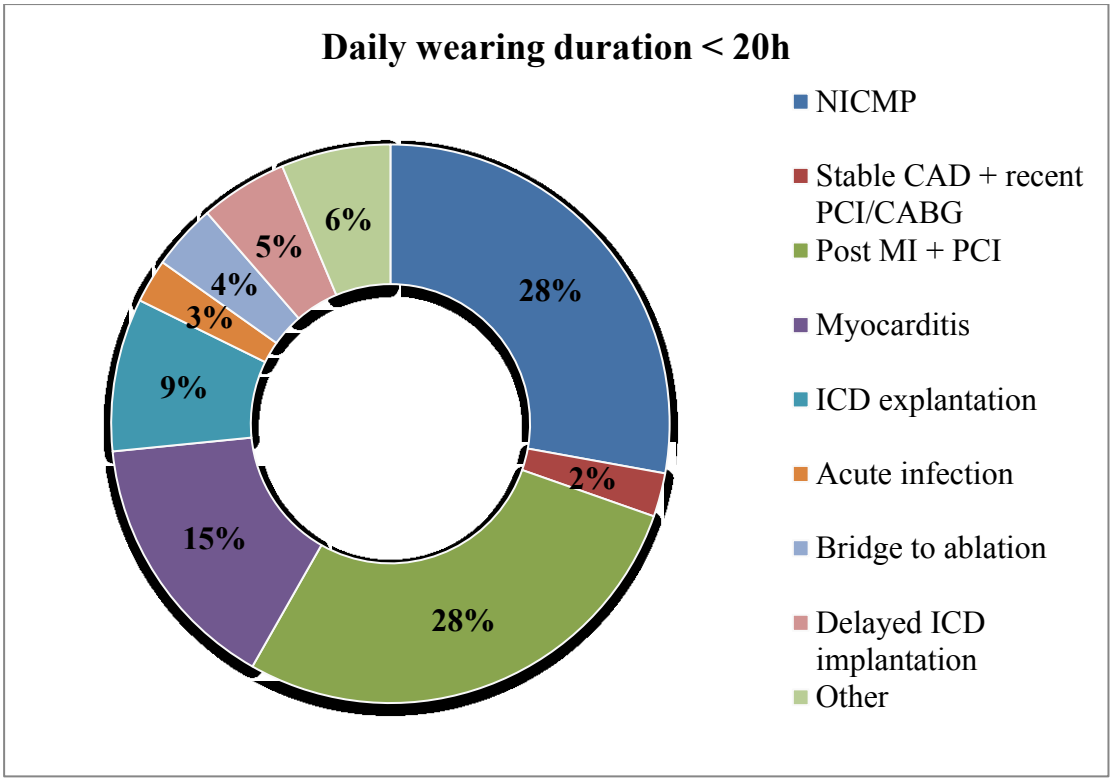


Figure 7a. Distribution of WCD indication with daily wearing compliance < 20h

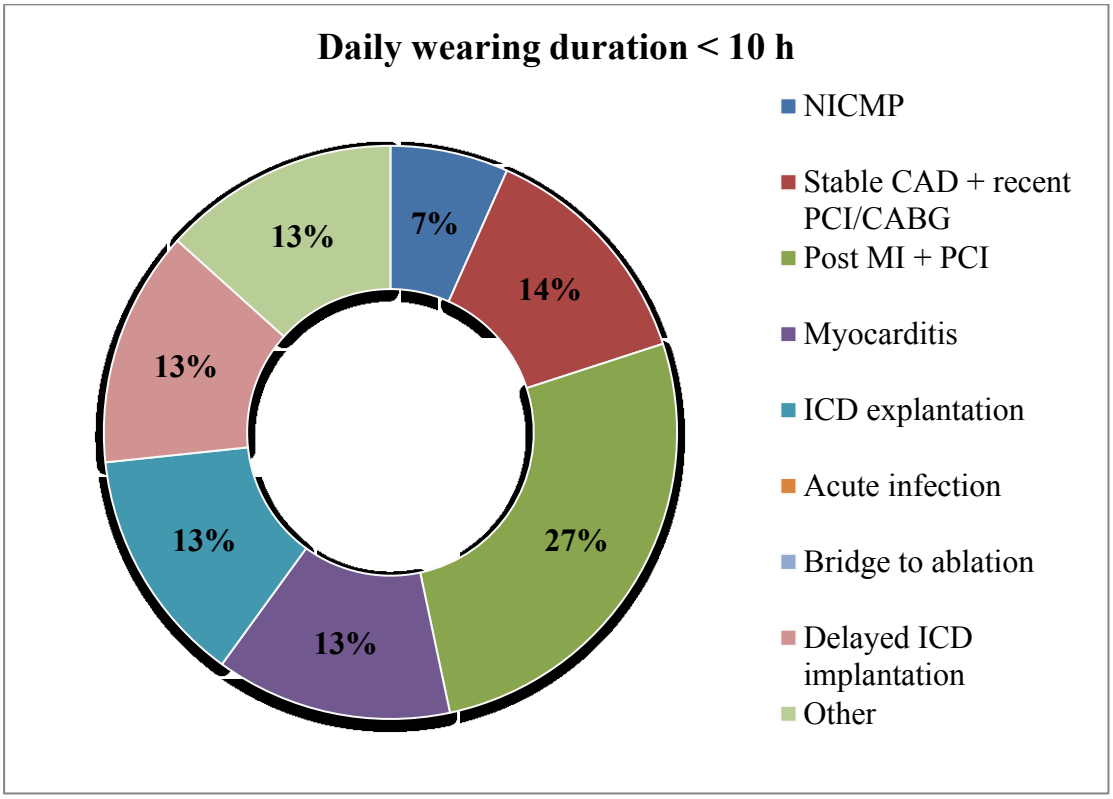


Figure 7b. Distribution of WCD indication with daily wearing compliance < 10h

Wearing compliance did not differ between patients received the WCD for primary prevention (23.3 [7.6-23.9] h/d) and patients who already experienced a VT/VF event (23.5 [9.9-23.8] h/d) and therefore receiving the WCD for secondary prevention of SCD. Wearing compliance did not change after receiving a WCD shock.

Wearing compliance increased over the years as shown in Figure 8.

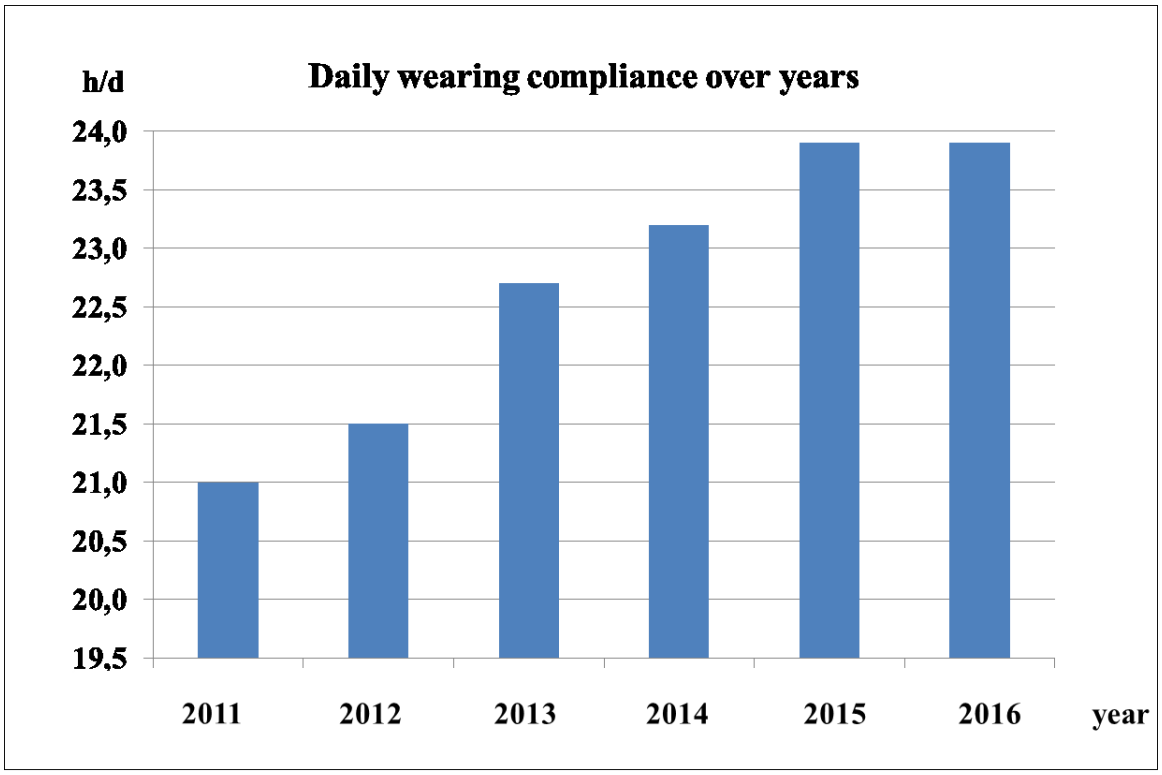
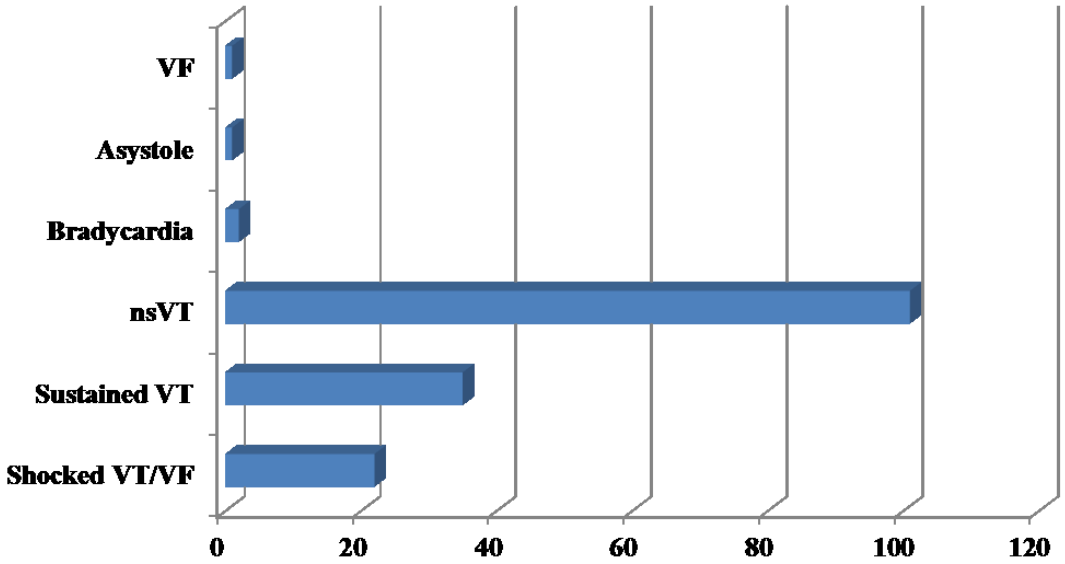


Figure 8. Daily wearing compliance over years

The main programming of the VT/VF detection zones were 180/220 beats per minute (bpm) (41%), 150/200 (20%) and 170/200 (12%). The mean programmed patient response time was 69±14 seconds (VT) and 25±1 seconds (VF).

10201 ECGs in 300 patients (67%) were automatically recorded whereof 165 (median 2 [1-37]) of these ECGs in 44 patients (9,8%) showed sustained VT, VF, Torsade de pointes (TdP), nsVT, bradycardia or asystole and therefore were classified as appropriate automatically recorded ECG and further appropriate warning of the patient (52).



n=165	Shocked VT/VF	Sustained VT	nsVT	Bradycardia	Asystole	VF
n	22	35	101	2	1	1
%	12	21	61	1	0.5	0.5
patients	11	15	33	2	1	1

Figure 9. Reason for appropriate automatic ECGs

"The remaining10036 automatically recorded ECGs showed artefacts (97%) or other arrhythmias (3%)"(52).

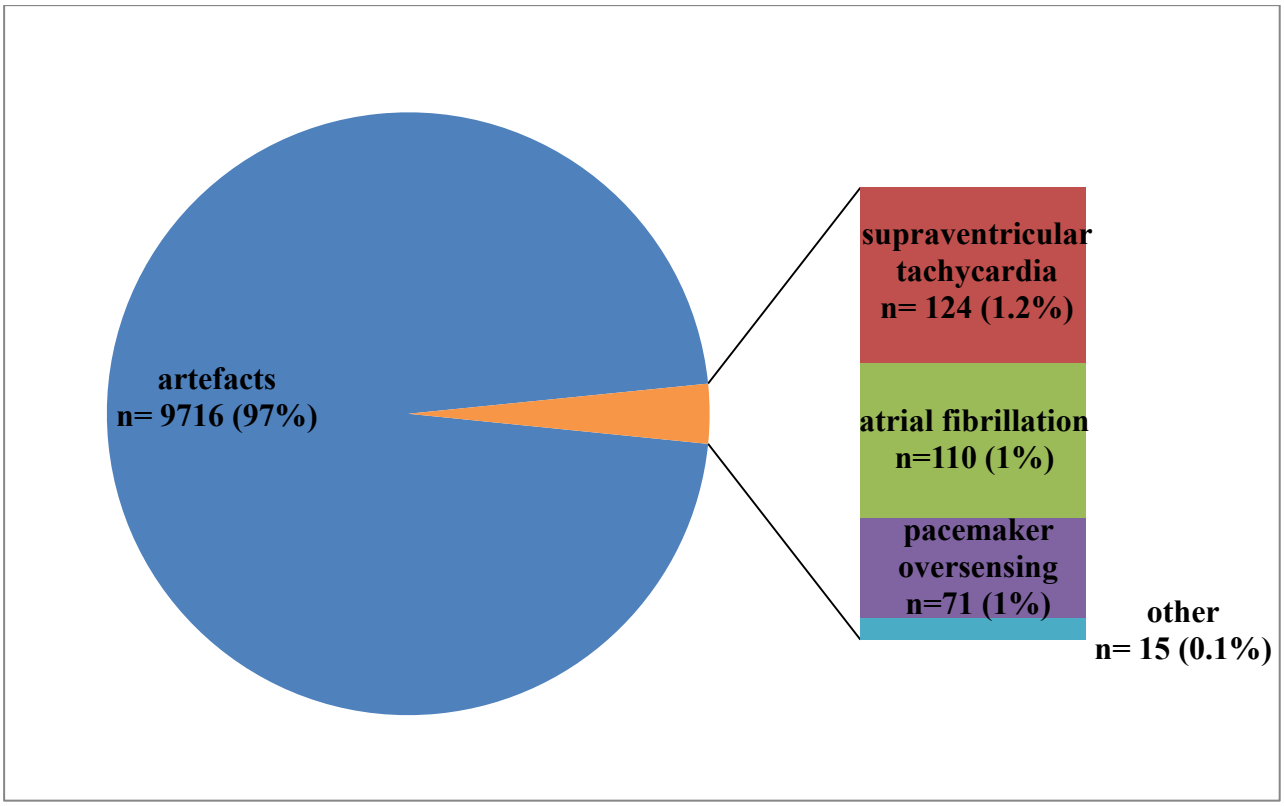


Figure 10. Reason for inappropriate automatic ECGs

Number of inappropriate alarms and VT programming zone was analysed. Patients with programmed VT zone of 150 bpm had a significant higher amount ($p<0.001$) of inappropriate alarm (273 per patient) versus patients programmed to 160 bpm (34 per patient), 170 (28 per patient) or180 bpm threshold (17 per patient).

Appropriate automatic alarms and inappropriate automatic alarms were correlated with body mass index (BMI). The groups where categorised to normal weight (BMI 18 - <25), overweight (BMI 25 - <30), adipositas (BMI 30 - <35) and adipositas per magna (BMI ≥ 35). In total BMI was available for 236 patients. There was no significant difference in the number of appropriate or inappropriate automatic alarms comparing the normal weight group to the overweigh group (p=ns) or the adipositas group (p=ns). Comparing the adipositas per magna group there was a significant difference in amount of appropriate automatic alarms ($p<0.05$) as well as the amount of inappropriate automatic alarms ($p<0.05$). As shown in Figure 11 the amount of inappropriate automatic alarms were higher in patients with a BMI ≥ 35 as well as the amount of appropriate automatic alarms were lower.

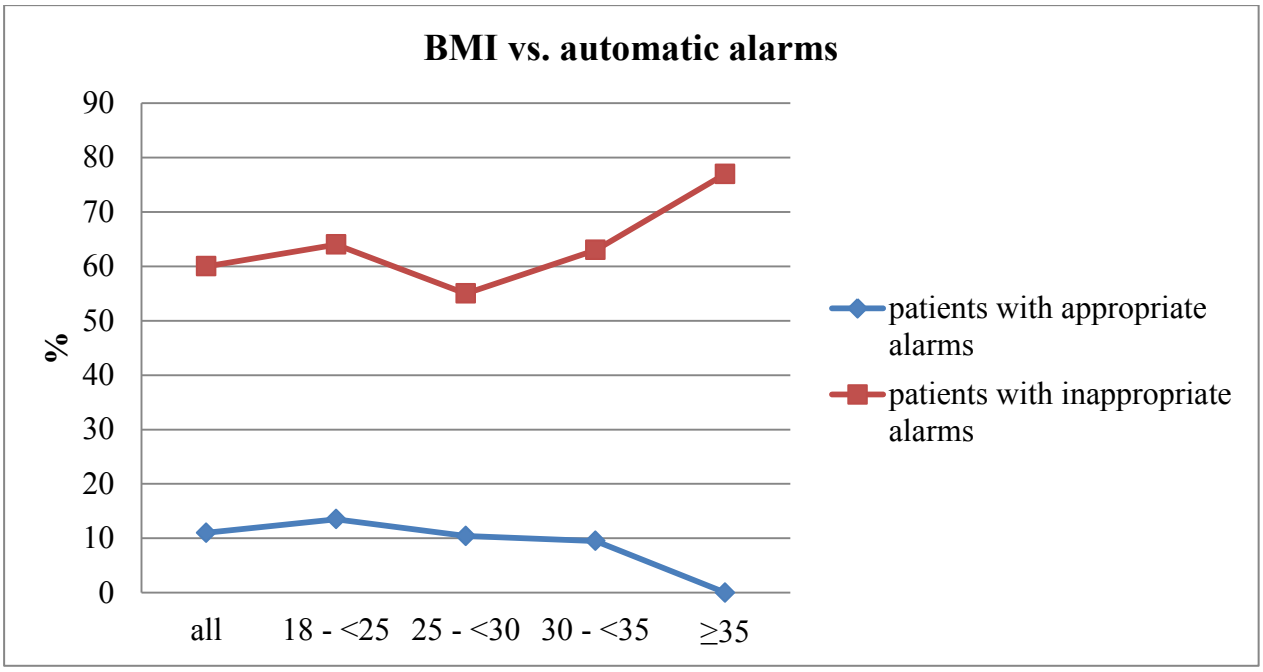


Figure 11: BMI vs. inappropriate and appropriate automatic alarm

Inappropriate automatically generated alarms were lower in age group 58 – 68 years (p=ns) and significantly lower (p<0.05) in patients older than 68 years. The amount of appropriate alarms was higher in patients younger than 49 years (p< 0.05). (Figure 12)

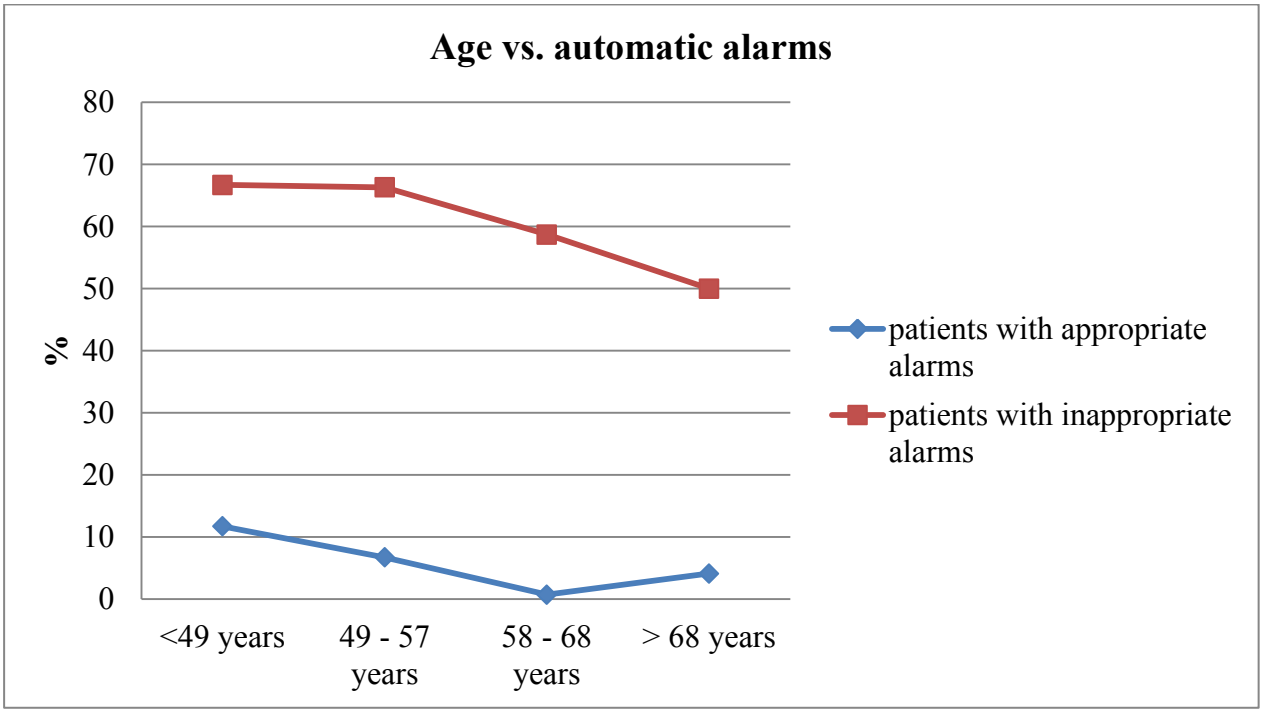
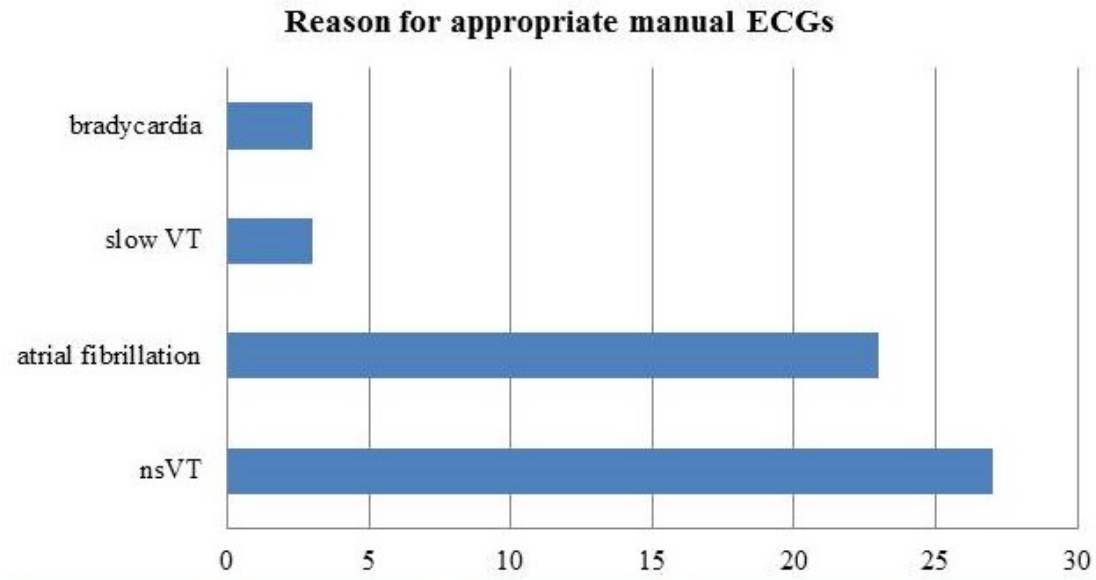


Figure 12: Age vs. automatic alarms

The WCD as an event recorder during periods of symptoms was used by 248 patients, who induced 2787 manually recorded ECGs among 56 (2%) were classified as appropriate containing atrial fibrillation, nsVTs, slow sustained VTs or bradycardia as shown in Figure 13. Additionally atrial fibrillation was newly detected in 3 patients.



n=56	Bradicardia	Slow VT	Atrial fibrillation	nsVT
n	3	3	23	27
%	5.5	5.5	41	48

Figure 13. Reason for appropriate manual ECG

The remaining 2731 ECGs were classified as inappropriate. The reason for inappropriate manual ECGs was ventricular extrasystole in 16 ECGs, sinus tachycardia in 2 ECGs or 2713 ECGs showing a normal rhythm .

Out of the 448 patients 11 (2.5%) received 22 appropriate WCD shocks for 19 VT/VF events (9 VT and 10 VF events). In 16 events (8VT / 8VF) only one WDC shock was required for restoration of sinus rhythm (84%). One VT event was appropriately terminated with the second shock and one VF was appropriately terminated after the third shock. In one individual case VF was appropriately detected and treated by the WCD however, the patient converted to asystole and died following unsuccessful resuscitation attempts. In total, 18/19 (95%) VT/VF events

could be successfully treated with WCD shocks, and 18/22 (82%) of WCD shocks successfully converted VT/VF to sinus rhythm. The overall shock rate in our cohort was 0.02 shocks (2.3%) per patient-month. The mean heart rate of all 9 shocked VT events was 214±38 beats per minute (52).

Patients with appropriate shocks had a mean age of 68±13 years, 18% were female and mean LVEF at baseline was 29±16. WCD indications in patients with an appropriate shock were delayed ICD implantation due to acute infection (n=2/18; 11.1%), ICD explantation (n=4/46; 8.7%), post MI + PCI (n=3/88; 3.4%), myocarditis (n=1/45; 2.2%) and stable CAD + recent PCI/ CABG (n=1/62; 1.6%). 10 out of these 11 patients already had a VT/VF event before WCD prescription. Only the shocked patient with myocarditis received the WCD for primary prophylactic reason. No patient with NICMP (n=94) received a shock due to VT/VF during the WCD period.The median time from WCD prescription to a shock event was 7 days [2-151]. Eight out of eleven patients (73%) received their first WCD shock within 30 days. Figure 14 demonstrates the shock rate over WCD wearing time (52).

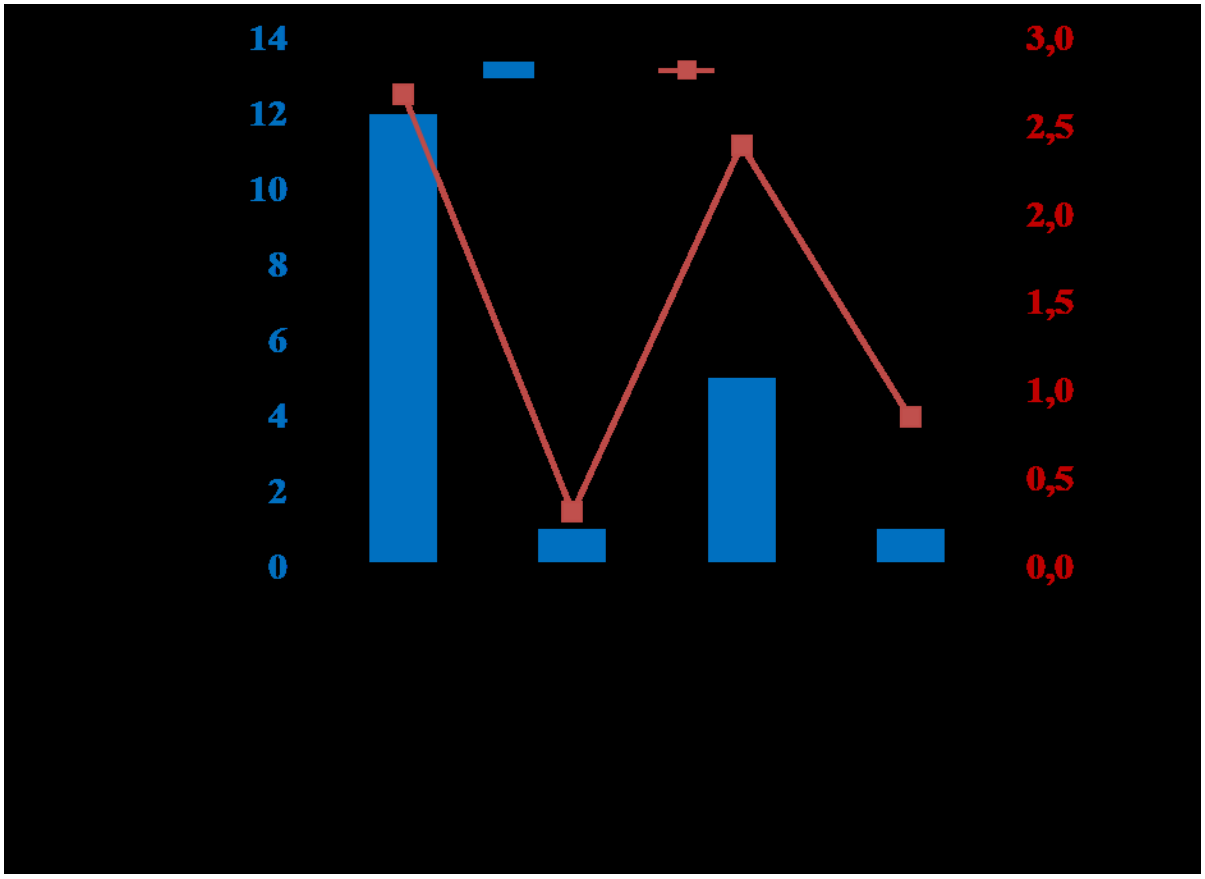


Figure 14. Temporal distribution of VT/VF events during WCD period

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Eight out of the eleven appropriately shocked patients received an ICD after the WCD period, one patient underwent CABG and two patients subsequently died due to terminal heart disease after termination of WCD therapy. In most appropriately shocked patients (8 out of 11, 72%) the WCD was prescribed in a centre, which is able to implant ICDs.
Two patients (0.4%) received a total of three inappropriate shocks: In one patient, the WCD misdetected a motion artefact and the conscious patient did not respond to the WCD alarm. One patient had two sustained VT events (225 bpm, 199 bpm), which terminated 18 seconds and 4 seconds, respectively, before WCD shock treatment was delivered. Five patients had WCD-caused side effects. Four patients suffered from contact dermatitis, which was treated with local administration of corticosteroids. One patient had a pressure mark, which resulted in termination of WCD treatment (52).

Termination of WCD treatment

Of all 448 patients, 52 (12%) still had an ongoing WCD prescription by the end of the analysis. The main reason for termination in the remaining 396 patients was the implantation of an ICD which was in 220 patients (55.5%). 130 (59%) out of these 220 patients already had a documented VT/VF event before WCD prescription and therefore already had an indication for for ICD implantation. However in 8 (9%) out of the remaining 90 patients the WCD documentation revealed that no shock was delivered to haemodynamic stable self-terminating sustained VT events during a median wearing duration of 56 [24-171] days, which caused ICD implantation.

These patients were significantly older than the overall population ($p<0.05$) with a mean age of 76±13 years. All of them were male (100%). Furthermore the LVEF was significantly lower than in the overall study population ($p<0.05$) with a mean LVEF of 24±11%. WCD indications in patients with primary preventive WCD prescription and not shocked haemodynamic stable self-terminating sustained VT events were NICMP (n=3/8; 37.5%), myocarditis (n=1/8; 12.5%), stable CAD + recent PCI (n=1/8; 12.5%), delayed ICD implantation due to capacity problems (n=1/8; 12.5%) and ICD explantation of primary preventive ICD due to an ICD associated infection (n=2/8; 25%).

The other 82 patients did not improve their LVEF after optimisation of heart failure medication and received an ICD for primary prevention of SCD. (Figure 15)

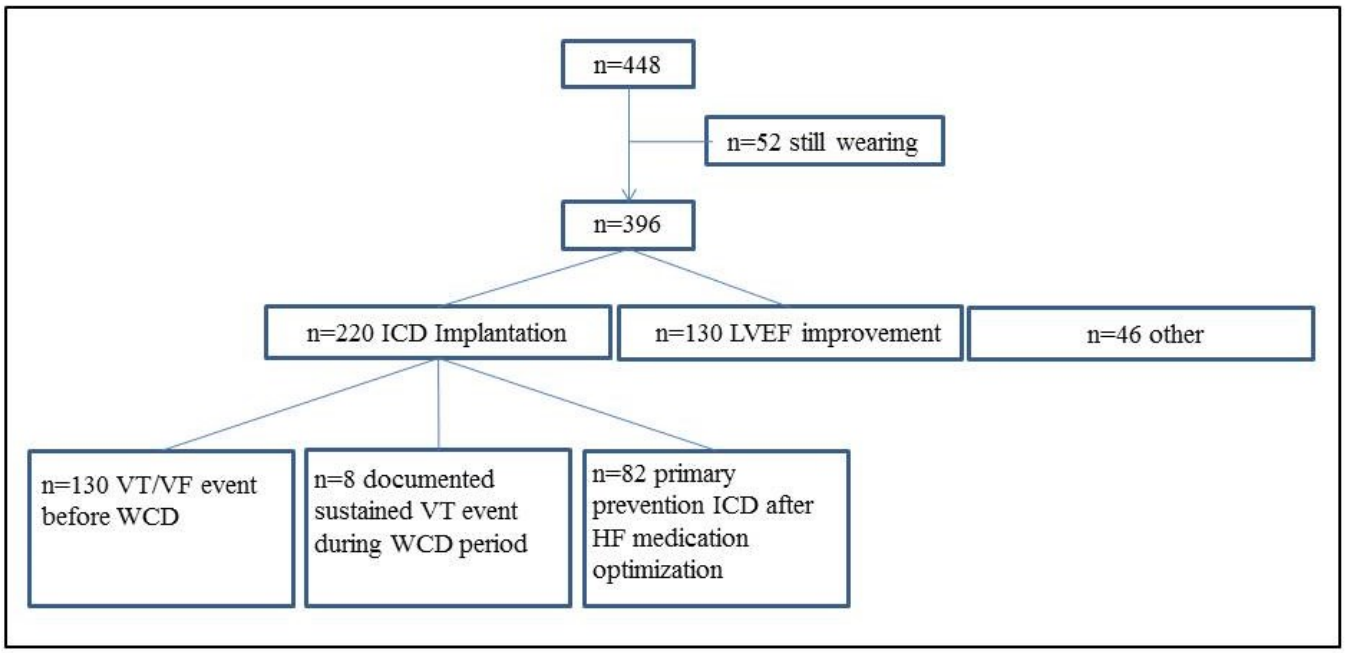

Figure 15. Reason for WCD termination/ Reason for ICD implantation after WCD period

Overall 130 patients (33%) improved their LVEF above 35% and therefore no longer had an ICD indication. WCD treatment was discontinued due to patients' preference in 17 patients (4%). Patients who withdraw further use of WCD were 51±16 years, 24% were female, mean BMI was 28±3 and 6 (35%) patients received the WCD for secondary prevention of SCD. The median wearing duration was 33 [1-224] days. Among these 17 patients 197 ECGs in 10 patients (59%) were automatically recorded. Whereof two of these ECGs in one patient (6%) showed episodes of nsVTs and appropriately alarmed the patient. The remaining195 ECGs were inappropriate showing 189 (97%) artefacts and 6 (3%) SVTs. Furthermore 121 ECGs were manually induced by the patients. Two ECGs in two patients (12%) showed nsVTs, however all other ECGs showed a normal ECG.

Further reasons for WCD termination were ablation (n=8; 2%), PCI/CABG (n=7; 2%), terminal disease (n=6; 1.5%), monitoring at the intensive care unit (n=2; 0.5%), side effects (n=1; 0.25%) or heart transplantation (n=1; 0.25%). Four patients (1%) died during the WCD prescription period, three of them due to asystole and terminal heart failure, two did not wear the WCD at time of death. The third patient was documented as having received an appropriate

shock due to VF, which subsequently degenerated to asystole. The fourth patient did not wear the WCD at the time of death and died of unknown reason (Figure 16) (52).

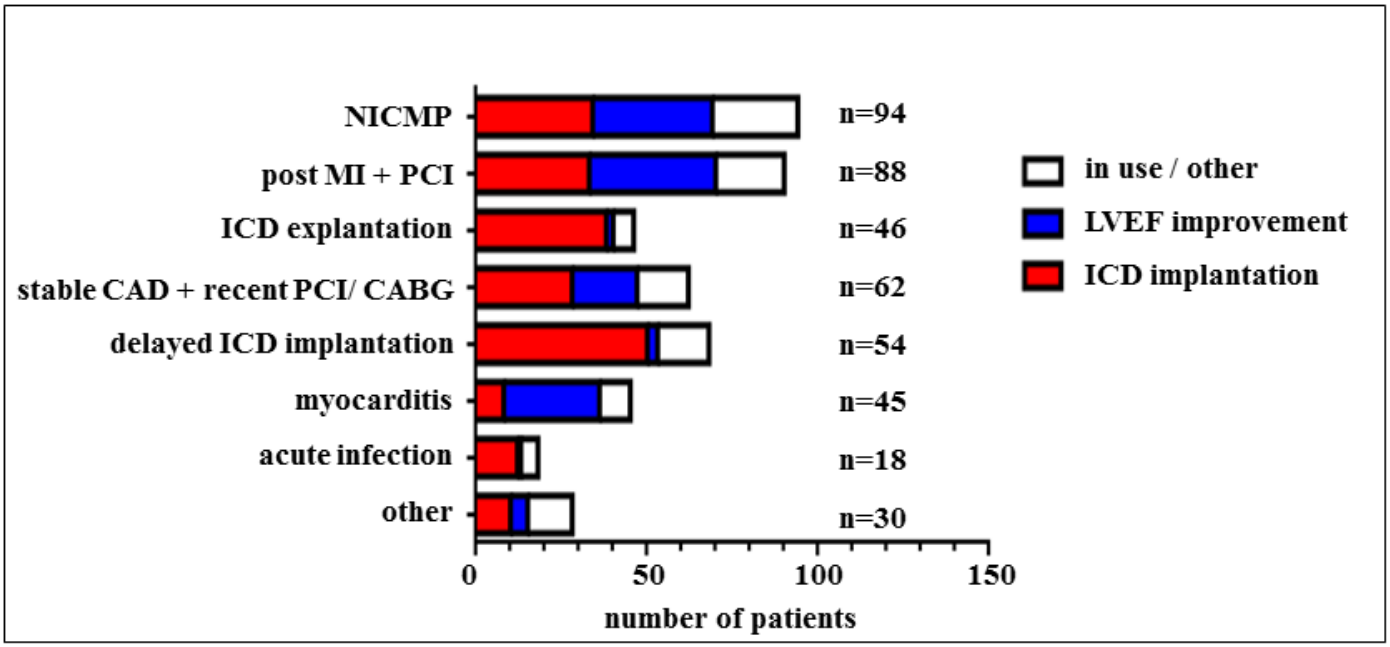

Figure16. Reason for WCD termination

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Four groups with possible reversible causes of SCD were identified, specifically patients with stable CAD and recent PCI/ CABG (LVEF at baseline 30±14% vs. LVEF at WCD end 39±13%, $p<0.001$), patients post MI and PCI (LVEF baseline 33±10% vs. LVEF end 39±12%, $p<0.001$), patients with myocarditis (LVEF baseline 31±14% vs. LVEF end 42±13%, $p<0.001$) and patients with NICMP (LVEF baseline 24±11% vs. LVEF end 35±14%, $p<0.001$), all four groups demonstrated a significant improvement in their LVEF during the WCD wearing period (Figure17).

By the end of WCD treatment 34/69 (49%) of all patients with NICMP, 33/70 (47%) of all patients post MI and PCI, and 28/47 (60%) of all patients with stable CAD and recent PCI/CABG still required an ICD after the WCD period. Almost all patients (38/40, 95%) with an ICD explantation due to ICD associated infection received an ICD after WCD period.

However, due to significant improvement in LVEF, only 9/41 (22%) of all myocarditis patients received an ICD after the WCD wearing period vs. 211/355 patients (59.4%) in all other WCD indication groups combined. One myocarditis patient (n=1/45; 2.2%) was appropriately

shocked during the WCD period due to a VT event and received an ICD after the WCD period (52).

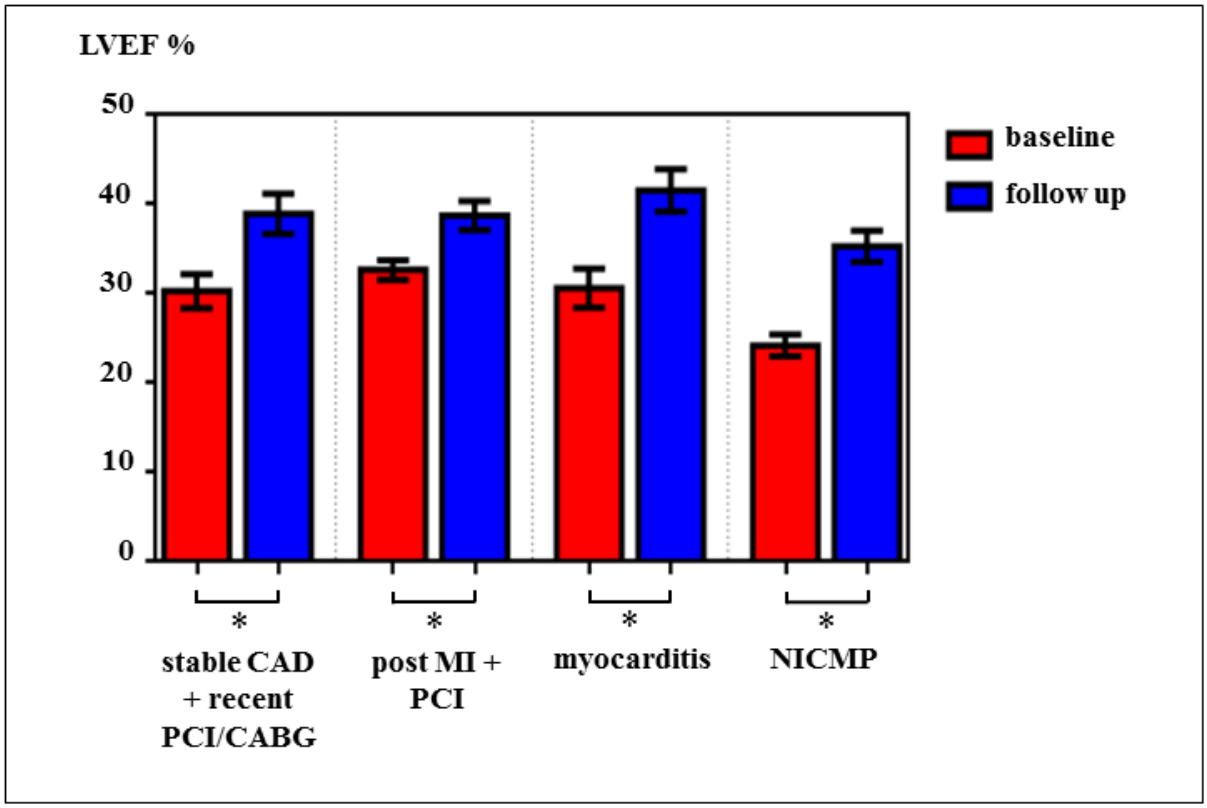

Figure 17. LVEF improvement during WCD period

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Discussion

This observational study of the Austrian WCD Registry enabled us to evaluate a large cohort of patients who had received a WCD over 7 years. Aspects of this evaluation included clinical indications, wearing compliance, arrhythmic events, clinical outcomes, changes in LVEF and whether there was a continued need for an ICD after WCD treatment period had ended (52).

Baseline characteristics and WCD indication

Our data showed the number of prescribed WCDs increased significantly over the last years ($p<0.05$). Up to date no published data about the amount of WCD prescription over the last years exist. We assume the reason for raising numbers of prescription are caused on one hand by the fact, that the use of the WCD is recommended in the ESC guidelines for management of patients with ventricular arrhythmias and the prevention of SCD (6), which was published in 2015 and on the other hand by becoming more familiar in Austria due to augmented marketing of the manufacturer.

Comparing the overall distribution of WCD indications in our study to the 4 largest registries (44,61,62,69) there is a variance in classification of patients at high risk of SCD. Whereas Wäßnig et al (69) with 6043 enrolled patients had the most prescribed WCD for DCMP (36,7%) followed by ICMP (26,9%), in the registry of Klein et al (44) with 354 enrolled patients, most received the WCD early after post MI (39%) or post CABG (25%). Further in the WEARIT II study where 46% of all patients had ICMP followed by NICMP with 40% (61). Most patients in the registry of Chung et al with 2274 enrolled patients received the WCD after ICD explantation (23,4%) followed by NICMP (20%)(62). The variance of these registries may be explained by the different classification strategy of WCD indication as well as not always being easy to define precisely the criteria to which WCD indication group the patient belongs to, as sometimes patients have more than one underlying disease and/or some results of examinations are still missing (e.g. myocardial biopsy). Furthermore the experience and specification of prescribing physicians may play a role for prescription of the WCD, for example as seen in the distribution of WCD indication in the region of Burgenland, where only patients after myocardial infarction (83%) and patients with acute infection (17%) received a WCD. These results indicate that this is not a representation of all patients with a possible WCD indication in this region. However, the sample size was small especially in

some regions whereof some hospitals just started to prescribe the WCD in 2016. We assume the more patients are enrolled nationwide the more the distribution of WCD indication will approximate to results of other nation-wide data.

Comparing the baseline characteristics age and gender to previously published multicentre studies (mean age 57-62 years, 21-30% female) (44,61,62,69) the results were comparable to our study (mean age 59 years, 24% female). Patients with Myocarditis or NICMP seemed to be younger than patients with post MI or stable CAD, 48±12 or 58±13 versus 59±12 or 64±12 respectively. The WEARIT II study showed a similar tendency (61). The amount of female patients with an underlying non-ischemic CMP (including myocarditis) were slightly higher than ischemic CMP (including stable CAD and post MI), 25% (29%) versus 14% and 18% respectively. This tendency was shown in other big registries where the number of female patients were higher in NICMP compared to ICMP (61,62,69). In WEARIT II the proportion of females was highest in NICMP (36%) and lowest in ICMP (23%) (61), similar results were confirmed by Wäßnig et al (69). The reason of age differences might be caused by the underlying disease as patients with NICMP are older and more likely to be male.

VT/VF events before WCD prescription were present in 48% of all patients in our study cohort, which was much higher than in the WEARIT II registry with an overall 8.5% events prior to WCD prescription; 7.2% in NICMP patients and 11% in ICMP patients respectively (61). Further Chung et al reported 16% having a VT/VF event prior to WCD (62). The amount of VT/VF events prior to WCD prescription was highest in patients with myocarditis (77%) and patients bridged to ablation (72%) followed by ICD explantation (39%) and post MI (38%) in our study cohort. The difference might be caused by different strategies of risk evaluation from different prescribing physicians.

Further to this only the WEARIT II registry reported LVEF at baseline (25%) which was slightly lower than in our study (33%). We assume that this might be caused by the fact that almost half of our enrolled patients received the WCD for secondary prevention and therefore had a normal LVEF.

Wearing duration, Compliance and nurse base training

As any medical therapy compliance is one of the most important factors for success in therapy and so it is with WCD therapy. Our results showed a very high wearing compliance of 23.5 [1-24] hours per day in a median wearing duration of 54 [1-436] days. Comparing these

results with other multicentre registry data compliance was slightly lower as reported by Klein et al 21.3 hours/day in mean 3.5 months wearing duration, Chung et al. 19.9 hours per day in median wearing duration of 52.6 days and Wäßnig et al with 23.1 hours per day in a median wearing duration of 59 days (44,52,62,69) . Currently no WCD specific data is published about the impact and effects of a nurse based training program including remote monitoring (52), however Schlitt et al and Klein et al highlights the importance of psycho social care for all WCD patients to reduce fear of device malfunction and ensure continuous wearing as well as integration in daily life (44,52,100). To the same conclusion came Wan et al who stated wearing compliance is dependent on dedicated fitting and training personal as well as thorough explanation about the need of uninterrupted wearing of the device (101). Furthermore in a prospective evaluation of 60 patients the vast majority reported a feeling of safety and trust after appropriate training (44). In a recently published health technology assessment the authors argued that patients would be afraid of possibly preventing an appropriate shock due to a lack of knowledge about making such a decision. Firstly the authors state this without any reasonable scientific proof. Secondly in our study of 10201 WCD alarms that occurred due to a suspicion of an arrhythmia by the WCD only 1.6% of all ECG showed ventricular arrhythmias, whereof 2.5% were appropriately shocked due to loss of consciousness. The remaining 100036 alarms were successfully supressed by patients. This clearly stands against the fear of patients of inadequately suppressing a shock. Furthermore as described above within the two hours initial induction training sessions patients learn to suppress the WCD every single time they hear the alarm to avoid a 150 Joule shock while being conscious. If an alarm is constantly reoccurring patients are supposed to call the 24/7 technical hotline and/or to seek a hospital admission/input in case of feeling unwell. However looking at a recently published prospective multicentre randomised controlled trial enrolling patients with type 2 diabetes receiving either tele monitoring or not, higher medication compliance and lower fasting glucose concentration were shown in the tele monitoring group (102). We conclude that individualised nurse based initial training followed by continuous remote monitoring via lifevestnetwork can affect the wearing compliance and outcome of the patients (52). Non-compliance, which led to sudden cardiac death, was reported of Tanawuttiwat et al in three patients, who died suddenly while not wearing the WCD (91). Furthermore the WEARIT/BIROAD study reported six sudden deaths, whereof one did not wear the WCD correctly, however the new design of the newer generation of WCDs does not allow wrong fitting (53). Our study results showed none of the patients died suddenly although 2 patients died of unknown cause while not wearing the WCD in the first years of

commencing the registry (2012). No deaths whilst not wearing the WCD occurred after 2013. Additionally, daily wearing compliance increased over the years (52). This might be explained with an increase in learning curve due to educational training as well as management of remote monitoring as this is covered in every procedure or training that is newly started in a team.

No significant difference in hours of daily usage was found regardless of gender, age or indication for WCD prescription, which is in line with our results and also in line with other registries (52,61,62,69,103). There was no significant difference in compliance for patients wearing the WCD more or less than 60 days, which is in contrast to previous published studies, who reported a longer a wearing duration is associated with higher wearing compliance (42,44). Data of premature discontinuation due to comfort issues, or adverse reaction rates varied from 4-14% with the highest dropout rate of 24% in WEARIT/BIROAD study (44,53,62, 83,93). The higher percentage in this study might be explained by using a first generation WCD, which was heavier and bigger. These results were in line with our rate of 4% of premature discontinuation. We conclude either patients wear the WCD or decide to wear it not at all at a very early stage. A continuous remote monitoring could help to keep these rates low, however 100% compliance and zero% drop out rate is illusionary as it is with any other therapy. Wearing compliance less than 20 hours per day was shown in 18% of all patients and wearing compliance of less than 10 hours per day in 3%. Comparing body mass index (BMI) we found a higher BMI in non-compliant patients, 28 and 27 for patients with compliance of less than 20 h/d and less than 10h/d respectively, which was slightly higher than the overall BMI of 26. This was also reported in the health technology assessment of Ettinger et al (104). In contrast Wan et al reported in an analysis of 547 overweight or obese patients who experienced at least one appropriate WCD shock no difference in daily wear time due overweight or obesity (101). However in the manufacturer database used for this analysis 1135 patients received appropriate WCD shock. Only patients with known BMI were included, hence 561 appropriately shocked patients were excluded, which might have had an influence. So we conclude the body shape might be an influencing factor in wearing compliance.

Ettinger et al state that prescription of a WCD might cause fear and stress due to further arrhythmias which potentially result in death (104). However in our cohort 60% of patients wearing the WCD less than 10 hours received the WCD for secondary prevention of SCD. So we conclude although these patients already experienced a ventricular arrhythmia, which

potentially might have resulted in death if not treated appropriately, decided to not wear the WCD properly each day. Furthermore wearing compliance overall did not differ between patients receiving the WCD for primary or secondary prevention, 23.3h/d versus 23.5h/d respectively. To our knowledge up to this current date no results of primary versus secondary prevention in WCD patients are published. Therefore, experiencing a VT/VF event might not influence wearing compliance.

The total wearing duration varied when patients were grouped by age quartile (<49 years, 49-58 years, 59-68 years and >68years) with longest wearing duration in patients between 49 and 58 years. Patients who were 69 years and older had the shortest wearing duration. Additionally the wearing duration was longest for patients with myocarditis (median 84 days) and NICMP (median 77 days) compared to post MI (median 63 days) or CAD (median 57 days). The wearing duration might be influenced by the fact that younger patients are more likely to have myocarditis or NICMP in contrast to older patients who suffer from MI or CAD, 48±12 or 58±13 versus 59±12 or 64±12 respectively. The same tendency is shown in other registries (69). This difference might be caused by age-specific underlying disease leading to WCD prescription accompanied with different treatment pathways (52). Shortest wearing duration had patients with delayed ICD implantation (median 28 days), patients with explanted ICD (median 36 days) and patients with acute infection (median 41 days). Same tendency was shown in other registries with median wearing duration of 43 days (69). In the biggest registry up to date enrolling more than 8000 patients wearing a WCD due to ICD removal a median wearing duration of 50 days was reported (90). In contrast to that Tanawuttiwat et al reported a median wearing duration of 21 days with a median antibiotics treatment of 14 days (91). We conclude that treatment severity of infection leading to ICD explantation as well as systemic infection delaying an ICD implantation might have been different and therefore explain the prolongation of wearing duration.

Appropriate and inappropriate alarms

A vast amount of alarms (10201) were recorded in 300 patients (67%), whereof only 165 ECGs in 44 patients (9.8%) showed ventricular arrhythmias. Out of these arrhythmias the main aetiologies were 61% nsVTs, followed by 21% sustained haemodynamically tolerated VT episodes and 12% shock VT/VF episodes. Similar results found Klein et al recorded 246 tachyarrhythmia events in 27 patients (7.6%) out of 354. Interestingly 139 VT/VF events were recorded in one patient wearing the WCD for 7 years due to long QT syndrome. Of the

remaining 26 patients, 17 had a single VT event detected and nine patients had 2-37 tachyarrhythmia events. There were 228 sustained VT/VF, 8 nsVTs and 8 sinus tachycardia events. Evaluating noise alarms in 47 patients with a wearing duration of 4021 days and 21.1h/d an occurrence of one false alarm every 13.4 days was calculated (44). Further, in an analysis of 608 patients who wore the WCD for 20355 days 11174 alarms were detected (105). The vast number of these alarms (77.4%) were lasting less than 10 seconds hence no need for patient interaction to press the response buttons. Only 2.7% were lasting longer than 25 seconds, whereof 76.8% were withheld by using the response buttons. However 5 resulted in inappropriate shocks and 19 were appropriately shocked (105). None of the previous published studies give a line-up and breakdown of the number and reasons of inappropriate alarms (104). However, some authors state that the most common reason for inappropriate alarms are artefacts (44,56). This is in line with our results, which firstly showed that 10036 (97%) automatically recorded ECGs showed artefacts. The remaining 3% showed SVT (1.2%), atrial fibrillation (1%), pacemaker oversensing (1%) or a normal ECG (0.1%). Additionally we evaluated inappropriate automatic alarms and BMI. When comparing patients with a BMI of 35 or more inappropriate alarms were significantly higher and appropriate alarms significantly lower. Similar results were shown in Wan et all as obese patients experienced 7 % higher noise rate compared to normal weight. Therefore the body shape may play an important role in inappropriate alarming and might influence wearing compliance. As a first study we evaluated inappropriate alarming in age groups and found a significant lower inappropriate automatic alarms in patients older than 68 years compared to patients younger than 49 years. Younger patients might be more active and as a result motion might have caused a higher artefact rate. Noise alarms can limit daily activity and cause sleep disturbance (18). Inappropriate alarming due to artefacts might be reduced by tightening of the garment (44).

The WCD was used as event recorder and created 2787 ECGs of which 2% were showing bradycardia, slow sustained VT, atrial fibrillation or nsVTs. In three patients atrial fibrillation was newly detected. Some of these recordings led to optimisation of treatment pathways, such as stroke prevention in the newly detected atrial fibrillation group or pacing therapy for patients with bradycardia. More importance should be paid to the function of the WCD as a possible event recorder to optimise patient treatment pathways and subsequently can lead to better outcome.

Arrhythmic events

Appropriate WCD shock rates of most registries (61,62,69) (1.1 – 1.7% within a median wearing duration of 2 months) are slightly lower compared to our study with a 2.5 % shock rate within a median wearing duration of 54 days. Only one registry (64) with 354 enrolled patients showed higher event rates (3.1%). As the registry of Wäßnig et al, Chung et al and Klein et al received their data from a databased maintained by the manufacturer (ZOLL Lifevest) the link between clinical data and this database is missing. Whereas baseline demographics like LVEF at time point of prescription or VT/VF event before WCD period were not evaluated. This makes it harder to hypothesise about the reason of different WCD event rates. Only the WEARIT II registry evaluated these data. We assume that the reason for slightly higher WCD event rate in our study might be caused by the fact 48% of patients enrolled had already experienced a VT/VF event before WCD prescription compared to 9% in the WEARIT II study (61). The shock rates varied according to indication with significant higher shock rates of 8.7% in the ICD explantation cohort. This tendency was also shown by Wäßnig et al (69) with 3.2% , and Ellenbogen et al (90) with a shock rate of 4% and Chung et al 5.1% (62) . However the reason for higher event rates in the ICD explantation group in our study cohort might be due to an already confirmed high risk of SCD with prior ventricular arrhythmias before the WCD period in 39% of all patients (52). The acute inflammatory state and the assumption of components in antibiotics might be a possible additional trigger for malignant arrhythmias (18,52). Patients post MI had an event rate of 3.4% and patients with stable CAD + recent PCI/ CABG had an event rate of 1.6% in our cohort. Summarising the previously published studies with the subpopulation of patients after MI/CABG and/or ICMP data showed WCD shock rates ranging from 1.4% up to 8.3% (61-64,69,103). Especially older patients with ICMP (≥65 years) have significant higher WCD shock rates (p=0.034) (72). The randomised VEST trial will give insights about the impact of the WCD on mortality by reducing SCD during the first three months after MI (74). One patient (2.2%), who received the WCD for primary prevention, was appropriately shocked. Current literature reported event rates of up to 5.7% in patients with myocarditis (84). However a WCD wearing period or even a prolonged period of more than six months will give sufficient time for LVEF recovery, while being temporary protected (18,44,84).

No patient with NICMP received a shock due to VT/VF during the WCD period in our cohort, however three patients had sustained haemodynamic tolerated VT which subsequently lead to ICD implantation. Comparing these results to other multicentre studies enrolling

different WCD indications an event rate of 0-1.3% was reported (61,62,69). In WCD study enrolling only heart failure patients, shock rates vary form 0% (65,76) and 0.4% (77) to higher shock rates of 5.5% (75). The highest WCD shock rate showed the sub analysis of the PROLONG study with 7% (12). Studies with 0% event rate mainly included less patients and might not be powered to give sufficient data about patients with NICMP. This might be the reason for our results too.

Most WCD shocks (73%) occurred within the first 30 days after prescription with a median time to first shock of five days (52). The VAILANT study reported a higher risk in the first weeks after MI (36). Further, there is a six fold higher SCD risk in patients with newly diagnosed NICMP who are not on optimised medical therapy compared to the chronic phase (11). However the SCD risk may be even longer as reported in the PROLONG study where two patients received appropriate WCD shocks beyond the three months (17). Additionally, 13% in the registry of Klein et al received appropriate WCD shocks in a prolonged phase of risk assessment (44). This is in line with our results as one patient received one appropriate WCD shock beyond three months. Therefore the WCD might be considered for a prolonged use in some situations especially when further LVEF improvement is potentially achievable. Successful termination of first shock was reported between 89% -100% of all VT/VF events (44,61,62,69), which is slightly higher than in our cohort (85%) but still in range. The reason might be a higher secondary prevention rate (48%) and slightly more ill patients with more comorbidities in our cohort.

Inappropriate shock rates were low (0.4%) and comparable to other registry like WEARIT-II (0.5%), Chung et al (1.9%), Klein et al (0.8%) or Wäßnig et al (0.4%)(44,52,61,62,69). Comparing inappropriate WCD shock rates to inappropriate ICD shock rates are higher (1.5% for patients with dual/triple-chamber ICDs and 2.5% for patients with single-chamber devices) (52,103). The reason may be due to suppression of a WCD shock by pressing the response button of a conscious patient (52). Despite an increasing number of WCD prescriptions there has been no reported deaths due to an inappropriate shocks (56). Reasons for inappropriate shocks were artefact or a sustained VT which terminated 4 and 18 seconds before shock. In current literature main reason for inappropriate shocks were artefacts. Further reasons were SVT, pacemaker oversensing or nsVT (105). This study firstly reported an inappropriately shocked WCD event due to sustained VT terminating before shock. The reason for not pressing the response buttons is unclear. However the importance of psycho-social care for all WCD patients to reduce inappropriate shocks and ensure continuous

wearing as well as integration in daily life and good initial training with continuous support or remote monitoring is important (44,52,100).

Reason for termination of WCD/ LVEF improvement

Main reason for WCD termination was ICD implantation (55.5%), whereof 59% had already VT/VF events before. In contrast the WEARIT-II registry's main reason for WCD termination was ICD implantation in only 42% (61). The reason for the difference may be caused by different baseline characteristics such as secondary prevention in 48% in our study versus 9% in the WEARIT II. Although more than half of the patients received an ICD 33% improved their LVEF (52). Patients with stable CAD and recent PCI/ CABG ($p<0.001$), patients post MI and PCI ($p<0.001$), patients with myocarditis ($p<0.001$) and patients with NICMP ($p<0.001$) improved their mean LVEF significantly during the WCD wearing period. Same results were shown from Binkley et al after a median 40 month wearing period LVEF in paiients with dilated CMP improved signficantly (15) This is further associated with decreased mortality, which was also confirmed in other studies (62,106,107). Even patients with ICD may improve theire LVEF (108). Furthermore, patients after MI improve theire LVEF after the initial 40 days period and have a confirmed relevant risk for ventricular arrhythmias (109). Patients with NICMP recover their LVEF in the first six months after diagnosis (110). The PROLONG study showed 33% improved LVEF in a prolonged wearing period of WCD beyond three months, therefore implantation of an ICD would have been too early (78). The vast amount (76%) patients with myocarditis improved LVEF signficantly during a median wearing period of 84 days with subsequently no further need for ICD implantation. However one myocarditis paitent received an appropriate shock and one patient had a sustained heamodynamically tolerated VT, which subsequently led to ICD implantation (52). There is a confirmed risk of SCD in patients with myocardits (111) which was also shown in several studies using the WCD as a promising bridging therapy during the critical period until full recovery (52,57,111). LVEF improvement might be due to the medical therapy strategies adopted (52). Duncker et al reported an appropriately shocked WCD patient despite LVEF improvement to 45%. Therefore risk stratification based only on LVEF is controversial (81). A prolonged WCD wearing period should be considered to allow efficient medical therapy and give the possibility of LVEF recovery and further avoid unnecessary ICD implantation. In our study 49% of all patients with NICMP received an ICD after WCD period. Although the DANISH trial showed no survival benefit in NICMP patients implanted with an ICD for primary prevention 4.3% in ICD group died suddenly compared to 8.2% in

the control group. Nonetheless the patient population is not comparable to our study cohort or other published studies enrolling WCD patients as patients in DANISH were on optimal medical therapy before enrolment in contrast to WCD study population (11,52).
Same results was demonstrated by the DEFINITE study as no significant survival difference between ICD group and control group was found, but a high mortality risk within the first 3 months after diagnosis of NICMP was illustrated (52,112). On the other hand, shock rates varied form 0-8.3% in observational WCD studies (44,61,62,69,75). Conflicting study results and guidelines with space for interpretations may have influenced physicians' preferences in WCD prescription, however our results confirmed the SCD risk of NICMP as 3 patients had sustained VT events before optimisation of medication in a median wearing duration of 84 days. We agree with the results of the PROLONG study where medical therapy optimisation beyond three months to allow for possible LVEF improvement at a later date (52,81)
This registry demonstrated the significant importance of the WCD as a bridging tool for all patients with high risk of SCD due to decreased LVEF, also giving sufficient time to facilitate possible LVEF improvement even beyond the recommended waiting periods while patients being protected from SCD.

Future direction

As the WCD has been shown effective and safe in terminating VT/VF events further studies indicate the importance as a possible health and event recorder as well as. The new generation of WCDs are able to instruct a 6-minute walk test (6MWT). Walking is fundamental to independence and cardiovascular well-being, with this test being one of the common tools to track patients objectively. The TRENDS study evaluated the accuracy and reliability of the WCD guided 6MWT performed at home in comparison to a conventional test. Furthermore patients are able to answer questions regarding their health on the touchscreen of the WCD. This study has already completed patient enrolment and results will be published in 2018 (74)

Furthermore, the HEARIT study measures non- invasive heart sounds and evaluates changes in a period of three months and compares them with clinical evidence of heart failure decompensation. Enrolment will be completed in 2019 (113)

The heart failure optimisation study tests prospectively the hypothesis that additional LVEF recovery occurs between 90 and 180 days in heart failure patients on optimal medical therapy, which will be completed in January 2019 (114).

All these ongoing studies are paving the way for paying more attention to the WCD as a health monitoring device during a period of high risk of SCD.

Implications for practice

The results of the Austrian WCD registry have several implications: (1) WCD shock rate varies between different aetiologies ranging from 0-8.7%. The WCD protects patients from dying suddenly during the time of risk assessment or contraindication of an ICD (2) LVEF improved significantly in all groups with a possible reversible cause of SCD in a wearing duration of three months and beyond. Optimisation of a maximally tolerated medical therapy strategy might last longer than three months and LVEF might improve later on. A prolonged WCD use gives time to facilitate possible LVEF improvement and may avoid unnecessary ICD implantation. (3) Especially young patients with myocarditis might benefit the most of WCD use even beyond three months as shown in 88% of all patients ICD implantation was not necessary (4) High quality initial patient-centred nurse-based training followed by continuous remote monitoring lead to high wearing compliance, low inappropriate shocks and timely interaction in the case of manually or automatically stored ECGs, if needed.

Limitations

During the study period (2009-3/2016) no detailed guidelines for WCD use were published. The conflicting literature about the WCD and the fact no randomised trial has been published up to date may have influenced the individual physician's assessment in terms of determining which patient is a candidate for a WCD. This fact might have led to a patient selection bias (1).

Conclusion

The WCD is an effective and safe treatment option in patients at either a temporary/transitory elevated risk of SCD or a temporary contraindication of ICD implantation. With varying WCD shock rates between different aetiologies and conflicting study results as well as the absence of concrete standardized guidelines leading to differences in risk assessment and indication categorisation there is scope to improve and best evaluate the need for a WCD. It might be arguable that WCD prescription should only be done by physicians who will decide on ICD implantation as well. Additionally, a prolonged WCD wearing period should be considered in patients with further possible potential for LVEF improvement or when maximum tolerated medical therapy is not reached after three months. WCD compliance remains high, despite prolonged WCD wearing duration which might be caused by patient-centred nurse-based training and remote monitoring.

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Appendix

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Indications for and outcome in patients with the wearable cardioverter defibrillator (WCD) in a nurse-based training program- Results of the Austrian WCD Registry

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Abstract

Background: The wearable cardioverter-defibrillator (WCD) is a treatment option for patients at temporarily high risk for sudden cardiac death (SCD) or in whom implantation of a cardioverter defibrillator (ICD) is temporarily not possible.

Objectives: The aim of this study was to provide real-world data of patients receiving this therapy in a nurse-based WCD training program.

Methods: Registry including all patients prescribed with a WCD in Austria between 2010 and 2016. Overall 448 patients received a WCD in 48 centres. Patients received a structured nurse-based WCD educational initial training followed by remote monitoring.

Results: Main indications were: severe non-ischemic cardiomyopathy (21%), recent myocardial infarction and percutaneous coronary intervention (PCI) (20%) and stable coronary artery disease with PCI/ coronary artery bypass grafting (14%). Eleven patients (2.5%) received 22 appropriate WCD shocks. Two patients (0.4%) received three inappropriate shocks. SCD risk varied between different aetiologies. Eight out of eleven (73%) patients received their first WCD shock within 30 days. Main reasons for termination of the WCD therapy were ICD implantation (55.5%) and improvement of LVEF to >35% (33%).

Conclusion: The WCD is an effective and safe treatment option in patients at either transiently elevated risk of VT/VF or mandated postponed ICD implantation, with a 2.5% shock rate over a median 54 days WCD treatment period. However, both WCD shock rate and ICD implantation rate vary widely depending on the WCD indication. A nurse-based WCD training is associated with high patient adherence with a median wearing duration per day of 23.5 [1-24] hours.

Keywords: wearable defibrillator, sudden cardiac death, arrhythmia, lifevest, ICD

Introduction

Every year 5 million people worldwide die from sudden cardiac death (SCD). Severe heart failure and/or coronary artery disease are the most common aetiologies for SCD.[1] Current guidelines recommend the implantable cardioverter defibrillator (ICD) for patients with structural heart disease for secondary prevention, i.e. in patients who already suffered from sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). Furthermore ICD implantation is recommended as primary prevention in patients with a left ventricular ejection fraction (LVEF) <35%[2] despite optimal medical treatment. However, early ICD implantation can be problematic in some situations, especially in patients with a potential reversible SCD risk (i.e. myocarditis), patients undergoing further risk stratification for SCD, or for patients with a temporarily explanted ICD or postponed ICD implantation (i.e. due to infection).[3] In addition, some patients with a LVEF <35% have a temporary contraindication for an ICD (patients within the first 40 days after myocardial infarction (MI) or patients within 90 days after percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)).[4] For all these patients the wearable cardioverter defibrillator (WCD) is a possible treatment option.

Currently, the Lifevest© (Zoll Medical, Pittsburg, USA) is the only commercially available WCD. It continuously monitors patients' heart rhythm, alerts and subsequently shocks the patient externally in case of detection of a malignant arrhythmia. Patients' understanding of the temporary SCD risk and continuous wearing adherence are the most important factors of a successful WCD protection of the patient. Therefore, a structured nurse-based WCD training of the patient and a continuous nurse-based tele monitoring might have a positive effect on wearing adherence.

Within the past years, several small observational studies about the WCD showed that the WCD is a safe und useful device to bridge a temporarily increased risk for SCD and appropriately terminates malignant arrhythmias.[5-12] Due to lack of randomized controlled trial and large observational trial data focusing on structured nurse-based WCD educational initial training followed by remote monitoring , we created a nation-wide registry including all WCD patients in Austria since initiation of this therapy in 2010 until 2016 in order to provide comprehensive real-world data on appropriate and inappropriate WCD shock rates, complications accompanied with this therapy, as well as ICD implantation rates after termination of WCD therapy. In Austria, all initial WCD trainings and fittings were

conducted by specifically trained registered nurses working either in the field of cardiology or intensive care. Therefore, WCD adherence was also investigated.

Methods

The Austrian WCD Registry enrolled all consecutive 448 Austrian patients, who received a WCD between 2010 and 2016. Our study complies with the Declaration of Helsinki, was approved by the institutional review board at the Medical University of Graz, Austria and registered at clinicaltrials.gov (NCT02816047). In addition all patients signed informed consent. 48 centres in Austria contributed anonymized data, starting with the very first WCD patient in 2010 until March 2016, including baseline demographics, clinical indications, arrhythmic events, clinical outcomes, changes in LVEF and the need for ICD therapy. Patients were categorized into nine WCD indication groups depending on underlying disease and reason for prescription as described in the Table 1.
Furthermore data describing adherence, wearing duration and VT/VF programming were collected.

Structured nurse-based WCD educational initial training followed by remote monitoring

All patients received an individualised structured educational interactive nurse-based initial training lesson of two hours including a structured lesson of the temporary risk of the patient, depending of the underlying disease, the importance of a wearing adherence and the fitting and use of the WCD as well as suggestions for use of the WCD in daily life. Furthermore all patients were registered at the Lifevest© network database, which allows a continuous monitoring of the wearing adherence as well as an overview of all recorded ECGs. More detailed information about the initial training and remote monitoring can be found in appendix 1.

Adherence

Adherence was defined by the median daily wearing duration. Daily wearing duration was defined as hours per day the WCD was worn. This information was collected from the tele medical Lifevest© network database. The total wearing duration was also collected via the Lifevest© network database as well as from hospital records and patients' charts.

ECG records

ECGs obtained from the Lifevest© network were reviewed and categorized as appropriate alarms or inappropriate alarms. All ECGs were analysed independently of two members of the research team (one nurse and one physician). ECGs of all shock events recorded by the WCD were reviewed by three members of the research team (one nurse, one physician and one consultant specialised in electrophysiology. Appropriate alarms were defined as all automatically recorded ECGs showing sustained VTs (>30 s), VF, Torsade de pointes, asystole, bradycardia <30 bpm, or non-sustained ventricular tachycardia (nsVT) (<30 s). All other alarms (i.e. due to artefacts or supraventricular arrhythmias) were classified as inappropriate.

Additionally, data about the detection rate threshold for VT and VF zones were collected from Lifevest© network database. Shock time delay was generally set at 60 seconds for VT and 25 seconds for VF, but could be individualised 60 - 180 seconds for VT and 25 - 55 seconds for VF at discretion of the treating physician.

Shock

ECGs of all shock events recorded by the WCD were reviewed by three members of the research team (one nurse, one physician and one consultant specialised in electrophysiology). An appropriate shock event was defined as a biphasic shock, which was delivered due to a VT or VF event. Inappropriate shock events were defined as all WCD shocks delivered for other reasons such as signal artefacts or supraventricular tachycardia.

Statistics

Continuous variables are presented as mean±SD, or median and range (min – max), depending on normality of distribution. Categorical variables are presented as percentages (%) and counts. Continuous variables were compared with Student t test or the Wilcoxon Rank-Sum test (non-normally distributed data), and frequencies with Chi-square analysis or Fishers‘ exact test, as appropriate. For comparing two or more idenpendent samples the Kruskal-Wallis test was used. Two-tailed P-values <0.05 were considered to indicate statistical significance. Groups were compared by WCD indication. Statistical analyses were performed using SPSS 23 (IBM, Armonk, New York, USA).

Results

Baseline characteristics

Overall 448 patients in 48 centres in Austria were enrolled, with a median of 4 [1-77] patients per centre. The mean age was 59 ± 14 years, 24% were female, and the mean LVEF at baseline was 33±15%. 216 (48%) patients had sustained ventricular arrhythmias (VT or VF) prior to WCD therapy, whereas the remaining 52% received the WCD for primary prevention of SCD. Baseline demographics are shown in Table 2.

Indications

Among all 448 patients who received a WCD in Austria 2010-2016, 94 (21%) had severe non-ischemic cardiomyopathy, 88 (20%) had a recent myocardial infarction and PCI, 62 (14%) had stable coronary artery disease (CAD) with recent PCI/ CABG, in 54 patients (12%) ICD implantation had to be postponed for reasons other than systemic infection (i.e. due to ventricular thrombus or institutional capacity reasons), 45 (10%) had acute myocarditis with impaired left ventricular function and/ or documented VT/VF, 46 (10%) had a temporary ICD explantation due to infection or device malfunction, 18 (4%) had an ICD indication, but acute systemic infection, 11 (2%) were bridged to ablation and 30 (7%) had other rare indications (i.e. Long QT syndrome (n=6), Brugada syndrome (n=1), post-partum cardiomyopathy (n=1), bridge to heart transplantation (n=1), Tako Tsubo (n=1), other (n=11), unknown (n=9).

Wearing duration and adherence

The median duration of WCD use was 54 [1-436] days. The cumulative wearing duration was 80.8 years in the total patient cohort. Wearing duration varied regarding the WCD indication, age quartiles and gender. Median wearing duration per day was 23.5 [1-24] hours. There were no differences in adherence for patients wearing the WCD more or less than 60 days (23 (3-24) h/d vs. 22 (1-24) h/d; p = ns). Patients did not differ in daily wearing adherence regardless of age, gender or WCD indication (Table 3).

WCD events

The main programming of the VT/VF detection zones were 180/220 beats per minute (bpm) (41%), 150/200 (20%) and 170/200 (12%). The mean standard WCD response time was 69±14 seconds (VT) and 25±1 seconds (VF) for all shocked VT/VF events in our patient cohort.

Among all 448 enrolled patients 10201 ECGs in 300 patients (67%) were automatically recorded by the WCD. Of those, 165 were classified appropriate showing a ventricular arrhythmia . The remaining autmoatically recordings (n=10036) in 290 patients showed artefacts, suparventricular tachycardia, atrial fibrillation or pacemaker oversensing.

The WCD as possible event recorder in case of symptoms was used by 248 patients, who induced 2787 manually recorded ECGs. Of those 2% were classified as appropriate containing atrial fibrillation, nsVTs, slow sustained VTs or bradycardia. Atrial fibrillation was newly detected in 3 patients. The remaining ECGs (n= 2731) were classified as inappropriate. The reason for inappropriate manual ECGs were ventricular extrasystole, sinus tachycardia or a normal rhythm. (Table 3)

Eleven of the 448 patients (2.5%) received 22 appropriate WCD shocks for 19 VT/VF events (9 VT and 10 VF events).

16 events (8VT/8VF) were terminated with the first shock to sinus rhythm (84%). One VT event was appropriately terminated with the second shock and one VF was appropriately terminated after the third shock. In one patient, VF was appropriately detected and treated by the WCD however; the patient converted to asystole and died following unsuccessful resuscitation attempts. In total, 18/19 (95%) VT/VF events could be successfully treated with WCD shocks, and 18/22 (82%) of WCD shocks successfully converted VT/VF to sinus rhythm. The overall shock rate in our cohort was 0.02 shocks (2.3%) per patient-month. The mean heart rate of all 9 shocked VT events was 214±38 beats per minute.

WCD indications in patients with an appropriate shock were delayed ICD implantation due to acute infection (n=2/18; 11.1%), ICD explantation (n=4/46; 8.7%), post MI + PCI (n=3/88; 3.4%), myocarditis (n=1/45; 2.2%) and stable CAD + recent PCI/ CABG (n=1/62; 1.6%). 10 out of these 11 patients already had a VT/VF event before WCD prescription. Only the shocked patient with myocarditis received the WCD for primary prophylactic reason. No patient with NICMP (n=94) received a shock due to VT/VF during the WCD period.

The median time from WCD prescription to a shock event was 7 days [2-151]. Eight out of eleven patients (73%) received their first WCD shock within 30 days. Figure 1 demonstrates the shock rate over WCD wearing time as well as patients at risk over wearing period. Eight out of the eleven appropriately shocked patients received an ICD after the WCD period, one patient received a CABG and two patients subsequently died due to terminal heart disease after termination of WCD therapy.

Two patients (0.4%) received a total of three inappropriate shocks: In one patient, the WCD misdetected a motion artefact and the conscious patient did not respond to the WCD alarm. One patient had two sustained VT events (225 bpm, 199 bpm), which terminated 18 seconds and 4 seconds, respectively, before WCD shock treatment was delivered.

Five patients had WCD-caused side effects. Four patients suffered from contact dermatitis, which was treated with local administration of corticosteroids. One patient had a pressure mark, which resulted in termination of WCD treatment.

Termination of WCD treatment

Of all 448 patients, 52 (12%) still had an ongoing WCD prescription by the end of the study. The main reason for termination in the remaining 396 patients is shown in Figure 2. Four patients (1%) died during the WCD prescription period, three of them due to asystole and terminal heart failure, two of which did not wear the WCD at time of death. The third patient was described previously having received an appropriate shock due to VF, which subsequently degenerated to asystole. The fourth patient did not wear the WCD at the time of death and died of unknown reason (Figure 2).

We evaluated four groups with possible reversible cause of SCD, specifically patients with stable CAD and recent PCI/ CABG (LVEF at baseline 30±14% vs. LVEF at WCD end 39±13%, $p<0.001$), patients post MI and PCI (LVEF baseline 33±10% vs. LVEF end 39±12%, $p<0.001$), patients with myocarditis (LVEF baseline 31±14% vs. LVEF end 42±13%, $p<0.001$) and patients with NICMP (LVEF baseline 24±11% vs. LVEF end 35±14%, $p<0.001$), all of which improved their mean LVEF significantly during the WCD wearing period.
At the end of WCD treatment 34/69 (49%) of all patients with NICMP, 33/70 (47%) of all patients post MI and PCI, and 28/47 (60%) of all patients with stable CAD and recent

PCI/CABG required an ICD after the WCD period. Almost all patients (38/40, 95%) with an ICD explantation due to ICD associated infection received an ICD after WCD period.

However, due to significant improvement in LVEF, only 9/41 (22%) of all myocarditis patients received an ICD after the WCD wearing period vs. 211/355 patients (59.4%) in all other WCD indication groups. One of these myocarditis patients (n=1/45; 2.2%) was appropriately shocked during WCD period due to a VT event and received an ICD after WCD period.

Discussion

The Austrian WCD Registry evaluated clinical indications, arrhythmia events, wearing adherence, clinical outcomes, changes in LVEF and the need for ICD after WCD treatment period of all patients who received a WCD in our country between 2010 and 2016. Thus, this is one of the largest and most comprehensive WCD registries to date. Our registry is unique because it collected baseline demographic data and especially WCD-related follow up data in detail, and it provides information about a structured educational interactive nurse-based training program with individualised remote monitoring of WCD patients.

The appropriate shock rates of earlier studies[5,13] (2-3% within a median wearing duration of 2 months) are comparable to our study with a 2.5 % shock rate within a median wearing duration of 54 days. Whereas the shock rates varied according to indication, the ICD explantation cohort had significant higher shock rates of 8.7%, which was also shown by Wäßnig et al[13] with 19/100 patients, and Ellenbogen et al [14] with a shock rate of 4%. The reason for the higher event rate in the ICD explantation group might be that all patients had a confirmed high risk of SCD due to LVEF<35% and/or ventricular arrhythmias before the WCD period, with the acute inflammatory state being a possible additional trigger for malignant arrhythmias.
In 28/37 (76%) of all patients in the myocarditis cohort LVEF improved significantly during WCD period (84 [4-312] days). Therefore, these patients no longer had an indication for an ICD. Nevertheless one of these patients (n=1/45; 2.2%) received an appropriate shock from the WCD. The SCD risk in patients with severe myocarditis was confirmed by another cohort study.[15] Current guidelines[4] recommend the WCD as a bridging option for patients with inflammatory heart disease and poor LVEF. In addition, several studies showed the WCD as promising bridging therapy for SCD of patients with myocarditis during the critical period

until full recovery.[16,17] The significant improvement in LVEF within this patient group is likely due to the medical therapy strategies adopted. However, even transient severe impairment in LVEF does lead to a higher risk of SCD and therefore temporary protection with a WCD within this period is needed.

In the NICMP cohort 49% of all patients received an ICD after the WCD period and none of these patients received a WCD shock. The DANISH trial demonstrated no survival benefit for patients with NICMP from current ICD implantation. However, in DANISH 4.3% of these patients in the ICD group died due to SCD compared to 8.2% in the control group.[18] Nevertheless the enrolled patients in DANISH were on optimal medical therapy, however the enrolled patients in the Austrian WCD registry were patients with newly diagnosed cardiomyopathy. Therefore a comparison might be not appropriate. The DEFINITE study showed no significant survival difference between ICD group and control group, but demonstrated a high mortality risk within the first 3 months after diagnosis of NICMP.[19] On the other hand, smaller observational studies demonstrated WCD shock rates of 5.5% within the first 51 days of wearing.[20] The lack of clear guidelines and conflicting study results may have influenced physicians' preferences concerning patient selection for a WCD in this patient population.

Surprisingly, 3 out of 88 post MI patients (3.4%) received a WCD shock, underscoring the potential role for this therapy in the post MI patient cohort. The elevated SCD risk in this patient cohort was originally shown in the VALIANT study with 2.3% event rate in the first month after MI.[21]

Adherence is an important aspect of any medical therapy and particularly so with WCD therapy. The adherence was higher than in any other reported study with a median wearing duration of 54 [1-436] days and a median wearing duration per day of 23.5 [1-24] hours. We conclude that this might be a result of an individualised nurse-based WCD training and fitting, as well as continuous tele monitoring via Lifevest network database. As reported in previously published studies by Klein et al[22] (mean wearing period of 3.5 months with a mean wearing time/day of 21.3 hours), Chung et al. (wearing duration of 52.6 days with a adherence of >90% wear time in more than 50% of all patients[6] and Wäßnig et al (median wearing duration of 59 days with 23.1 hours of daily use)[13] there was no significant difference in hours of daily usage regardless of gender, age or indication for WCD prescription, which is in line with our results. In contrast, total wearing duration varied when patients were grouped by age quartile (<49 years, 49-58 years, 59-68 years and >68years). Patients between 49 and 58 year had the longest wearing duration while patients of 69 years

and older had the shortest. This difference might be caused by age-specific indications leading to WCD prescription and therefore different treatment pathways.
Comparing the VT/VF event rates from other registries like WEARIT-II with 22 out of 2000 appropriately shocked patients (1.1%), the national registry from Chung et al with 59 out of 3569 appropriately shocked patients (1.7%), the German registry from Wäßnig et al with 94 out of 6043 appropriately shocked patients (1.6%) or the German registry from Klein et al with 11 out of 354 appropriately shocked patients (3.1%) our study showed comparably high (2.5%) appropriately shocked patient rates.[5,6,13,22] Although the mean LVEF in WEARIT-II was lower than within our registry (25 vs. 33%), only 9% of all patients in the WEARIT-II had malignant arrhythmias before the WCD period compared to our registry with 48%. This may well be the reason for the slightly higher event rates in the Austrian WCD registry. 8 out of 11 (73%) received their first WCD shock within 30 days with the median time to first shock of 5 days. While WCD may be vital early after WCD prescription, VT/VF rates remain low after >30 days of WCD treatment.

The inappropriate shock rate (0.4%) was low in our registry and comparable with other WCD studies like WEARIT-II (0.5%), Chung et al (1.9%), Klein et al (0.8%) or Wäßnig et al (0.4%).[5,6,13,22] Furthermore this inappropriate shock rate was lower compared to ICD studies with an inappropriate shock rate at 1 year (1.5% for patients with dual/triple-chamber ICDs and 2.5% for patients with single-chamber devices).[23] This may well be due to the ability to suppress the WCD shock by pressing the response button by a conscious patient.

The WEARIT-II registry[5] evaluated patient's follow up and the main reason for WCD termination was ICD implantation (42%) followed by LVEF improvement (40%) as well as other reasons. In contrast, we found a higher ICD implantation rate (55%). This might be due to the fact that the Austrian WCD registry had a higher number of patients who received the WCD for secondary prevention (48%) than in the WEARIT-II registry.
Although 220 patients (55.5%) received an ICD after WCD, 130 patients (33%) improved their LVEF and therefore reduced their risk of SCD. This confirms the importance of the WCD as a bridge to decision tool. This registry also demonstrated the significant importance of this device for all patients with suspected or confirmed myocarditis and reduced LVEF or sustained ventricular arrhythmia. One patient with myocarditis received an appropriate shock for a VT event during the WCD wearing period and only 22% later required implantation of an ICD.

Limitations

During the majority of the study period (2010-2016) no detailed guidelines for WCD treatment were published. There was a high range of various indications for WCD prescription, which may have been influenced by individual physician's assessment as to which patients were thought to be at high risk of SCD. This might have led to a patient selection bias. Further no patient related outcome measures (PROM) were collected, which could have contributed interpretation on adherence data.

Implications for the practice

The results of the Austrian WCD registry have several implications: (1) The WCD appears to be safe, as only two patients received an inappropriate shock and no patient died as a result of under- or misdetection of the WCD. (2) The WCD is an effective tool, as 18/19 VT/VF events could be terminated to regular rhythm by means of a WCD shock. (3) The VT/VF rate in a real-world setting is significant, with a reported 2.5% event rate over a median WCD wearing duration of slightly less than two months. (4) A nurse-based WCD training program is associated with high WCD wearing adherence. Based on the high adherence rate seen in our study, this patient-centred nurse-based approach may serve in daily clinical practice as a tool to maximize the effect of the WCD. Furthermore, beyond a structured training at the WCD initiation, it is important to keep in contact with the patient by reviewing adherence and ECG recordings via the tele monitoring network.

Conclusion

The WCD is an effective and safe treatment option in patients at either transiently elevated risk of VT/VF or mandated postponed ICD implantation. WCD shock rate overall was 2.5% over a median 54 days WCD period. However SCD risk varied between different aetiologies, with patients post ICD explantation having a high (8.7%) risk of VT/VF events, patients post MI (3.4%) and myocarditis patients (2.2%) having a lower risk. A nurse-based training program and ECG review and follow up led to excellent wearing adherence despite a prolonged WCD wearing duration.

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LEGENDS

Figure 1. Temporal distribution of VT/VF events during WCD period
VT= ventricular tachycardia, VF= ventricular fibrillation

Figure 2. Reason for WCD termination
NICMP = non ischemic cardiomyopathy; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; other= patient desire, ablation, PCI/CABG, side effects, terminal disease, monitoring at intensive care unit, death, heart transplantation

Table 1. Patient characteristics at baseline/ WCD[1] prescription.

Variables	**ALL**	**NICMP[5]**	**Stable CAD[6] + recent PCI[7]/CA BG[8]**	**Post MI[9] + PCI[7]**	**Myocardi-tis[10]**	**ICD[11] explantation**	**Acute infec-tion[12]**	**Bridge to ablation[13]**	**Delayed ICD implanta-tion[14]**	**Other[15]**
N	**448**	94	62	88	45	46	18	11	54	30
Age (years)	**59 ± 14**	58 ± 13	64 ± 12	59 ± 12	48 ± 12	60 ± 13	64 ± 15	58 ± 15	62 ± 17	59 ± 15
Female gender (%)	**24**	25	14	18	29	30	11	46	27	34
VT[2]/VF [3]event before WCD (%)	**48**	17	53	40	62	39	6	73	63	83
Arterial hypertension (%)	**74**	68	91	92	29	67	72	55	75	56
CAD[6] (%)	**52**	22	100	100	2	44	50	27	94	42

Atrial fibrillation (%)	**24**	29	33	18	9	20	28	36	31	17
LVEF[4] baseline (%)	**33 ± 15**	24 ± 12	30 ± 14	33 ± 10	30 ± 15	33 ± 12	40 ± 16	47 ± 15	37± 18	49 ± 17

[1]wearable cardioverter defibrillator, [2]ventricular tachyarrhythmia, [3]ventricular fibrillation, [4]left ventricular ejection fraction,

[5]non ischemic cardiomyopathy: Newly diagnosed non-ischemic cardiomyopathy with left ventricular ejection fraction (LVEF) <35% within 90 days of the start/optimization of heart failure therapy.

[6]coronary artery disease + [7]percutaneous coronary intervention/ [8]coronary artery bypass graphting: Patients with severe ischemic cardiomyopathy (LVEF <35%) due to stable coronary artery disease within 90 days after revascularization and/or start/optimization of medical therapy

[9]myocardial infarction +PCI: Patients with a recent myocardial infarction (MI) <40 days undergoing PCI[3] and LVEF <35%.;

[10]myocarditis: Patients with acute myocarditis and a decreased LVEF and/or documented VT/VF

[11]implantable cardioverter defibrillator explantation: Patients with previously implanted ICD, which had to be temporarily removed due to an ICD associated infection,

[12]acute infection: Patients, who meet indications for an ICD, but implantation has to be delayed due to a systemic acute infection;

[13] bridge to ablation: Patients with documented VT events prior and/or post VT ablation;

[14]delayed ICD: Patients in whom an ICD is indicated, but immediate implantation is currently not possible due to comorbidities or other reasons;

[15]other: This category summarizes all other rare WCD indications, i.e. Brugada syndrome, long QT syndrome, post-partum cardiomyopathy or patients waiting for heart transplantation

Table 2. WCD use by gender, age and WCD indication

	Daily use (hours)	p values	Days of wear (days)	p values
WCD[7] use				
overall, median (range)	23.5 (1-24)		54(1-436)	
WCD use by gender				
Male, median (range)	23.4(1-23.9)	p=ns	54(1-436)	p=ns
Female, median (range)	23.7(9.7-23.9)		58(4-298)	
WCD use by age quartile				
<49 years, median (range)	22.9(0.3-23.9)	p=ns	63(1-248)	p<0.01
40 to 57 years, median (range)	23.3(0.1-24)		68(1-436)	
58 to 68 years, median (range)	23.5(0.1-23.9)		53(1-280)	
>68 years, median (range)	23.8(1-23.9)		43(1-179)	
WCD use by indication				
Post MI[1] + PCI[2]	23.5(0.1-23.9)	p<0.01	63(1-248)	p<0.01
Stable CAD[3] + recent PCI[2]/CABG[4]	23.7(9.6-23.9)		57(6-161)	
NICMP[5]	23.4(0.1-24)		77(3-298)	
ICD[6] explantation	23.8(0.1-24)		36(1-436)	
Myocarditis	22.7(0.3-23.9)		84(4-312)	
Acute infection	23.6(17.1-23.9)		41(6-182)	
Bridge to ablation	21.4(16.5-23.9)		47(32-244)	
other	22.8(6.9-23.9)		55(1-312)	
Delayed ICD[6] implantation	23.6(9.8-23.9)		28(3-283)	

Table 3. automatically and manually recorded WCD[1] ECGs[2]

Type of recorded ECG	Recorded ECGs n(%)	Patients n (%)
Automatic ECG	**10201 (100)**	**300 (100)**
appropriate	**165(1.6)**	**44 (10)**
Shocked VT[3]/VF[4] events	19(10)	11(25)
Sustained VT[3]	35(21)	15(34)
VF[4]	1(1)	1(2)
Non sustained VT[3]	107(65)	28(64)
Bradycardia	2(2)	2(5)
Asystole	1(1)	1(2)
inappropriate	**10036**	**290(97)**
artefacts	9731(97)	283
Suparventricular tachycardia	124(1)	19
Atrial fibrillation	110(1)	13
Pacemaker oversensing	71(1)	1
Manual ECG	**2787(100)**	**248(100)**
appropriate	**56(2)**	**20(8)**
Atrial fibrillation	23(41)	10(4)
Non sustained VT[3]	27(48)	7(3)
Slow sustained VT[3]	3(5.5)	2(1)
Bradycardia	3(5.5)	2(1)
inappropriate	**2731(98)**	**227(92)**
Ventricular extrasystole	16(0.6)	3(1)
Sinus tachycardia	2(0.1)	1(0.4)
Normal rhythm	2713(99.3)	223(90)

[1]wearable cardioverter defibrillator, [2] electrocardiogram, [3]ventricular tachyarrhythmia, [3]ventricular fibrillation,

FIGURES

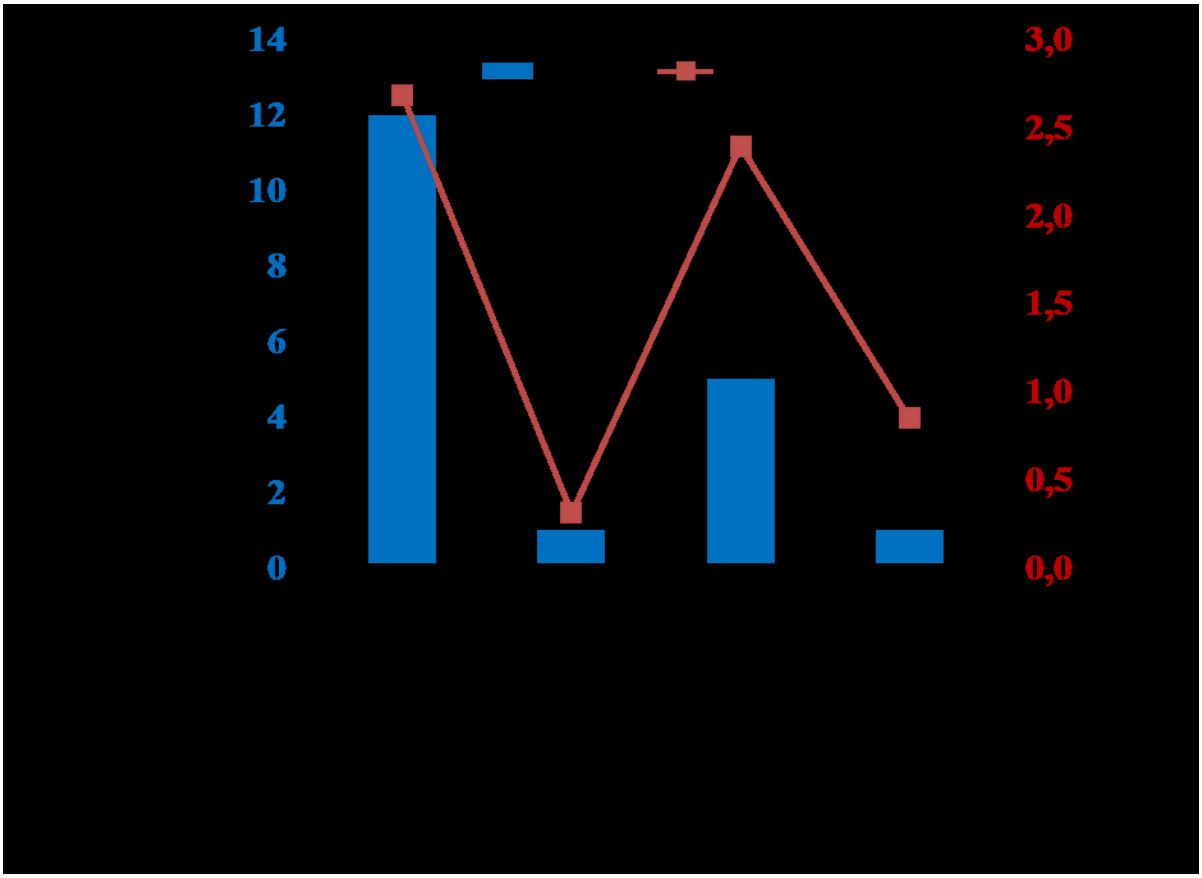

Figure 1. Temporal distribution of VT/VF events during WCD period

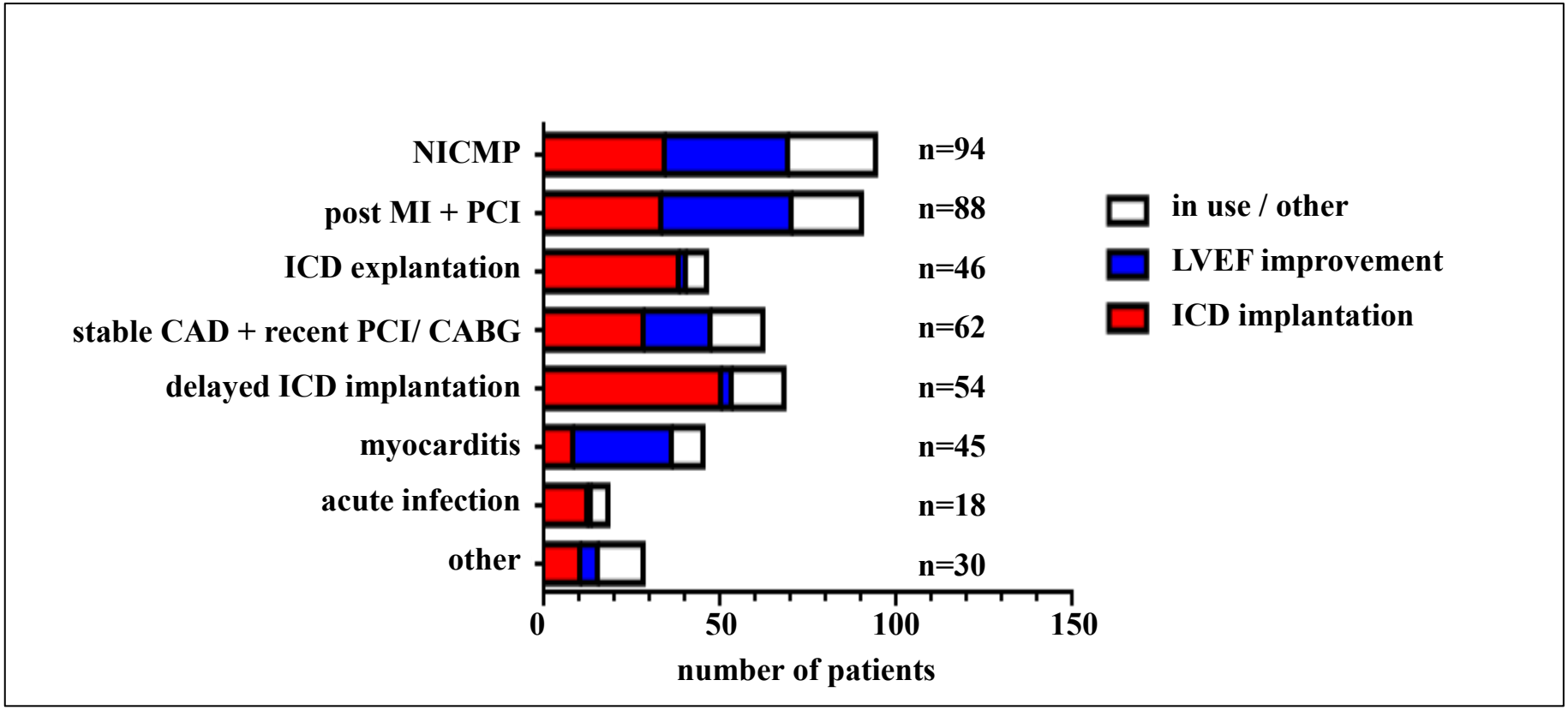

Figure 2. Reason for WCD termination

Appendix 1: Structured educational interactive nurse- based training program for patients with wearable cardioverter defibrillator (WCD)

The WCD training program for patients consists of a structured educational interactive lesson of about 2 hours, held on day of prescription of the WCD. All teaching personal had undergone dedicated training regarding WCD application. This consists of 3 hours training before being allowed to teach and provide advice regarding WCDs to the patients. Furthermore all had to teach 5 patients under supervision of a WCD expert.

Before direct contact with a patient is made, information about the individual situation, medical history and therapy plan is collected via medical charts and/or the treating healthcare professionals. The patient's history, WCD indication, and patient-specific issues are discussed with the responsible cardiologist.

The treating cardiologist informs the patient prior to the training lesson about the indication for and the basic principles of the WCD. The lesson takes part after prescription of the WCD. An appointment is made with the patient at a time point close to the discharge date, as patients are usually still admitted to the hospital. Furthermore one close relative (usually the partner) of the patient is invited to this appointment if possible. An appropriate environment is considered for the appointment to ensure privacy and enable full concentration on the topic of SCD and use of WCD.

The following topics are addressed at the session, which is held together with the treating cardiologist as needed:

4) General information about SCD, individual risk of SCD depending on the underlying disease of the patient, the WCD in general as a bridging option, as well as the WCD in the individualised situation of the patient
5) Information about the components of the WCD
    a. Monitoring function:
        - Introduction to the sequence of alarms released by the WCD in case of automatically detected ventricular arrhythmias.
        - Function of the response button which is pressed by the conscious patient in case of siren alarms to abort the shock sequence.

- The patient has to proof that he is able to press the response buttons, which is checked several times during the training lesson.
- Information is given about what happens in case of unconsciousness and a release of a shock by the WCD
- Information and training of the change and recharge of the WCD battery, which is needed every 24 hours, is given
- Opportunity of inducing a manually stored ECG by pressing and holding the response buttons for 3 seconds in case of symptoms is trained
- Information is given about automatic and manual transmission of all ECGs

b. Electrode belt and garment
   - Assembling of the electrode belt and garment: first the assembling is shown by the teaching person, afterwards this should be done by patient alone to ensure he will be able to do so at home
   - Instruction for change and washing of the garment are given
   - Chest circumference is measured and the an appropriate size of the garment is fitted

c. Charging station
   - Information about battery charging is given
   - Information about data transmission and positioning of the charging station is given

6) Use of the WCD in daily life
   a. Information is given about how to handle the WCD when showering or bathing
   b. Information about time point of changing the battery is given. Therefore a plan is made with the patient considering his daily routines at home, which time he/she is mostly at home and therefore the best time point to change the battery
   c. Information about how often and how to change and wash the garment is given
   d. The patient is informed that he should only take off the WCD (for showering or changing the garment) in attendance of a second person
   e. In case of attendance of relatives at the initial teaching lesson information is given about different possible situations, such as shock of the WCD, unconsciousness of the patient when not wearing the WCD (i.e. during shower) and how to support the patient in general. If none of the relatives are able to join

this session an additional appointment is made for the relatives. Information is given about journeys abroad with the WCD, especially for flights.

f. Information is given about movement and sports with WCD
g. Possible questions of the patient are answered
h. A 24 hour available hotline number is given in case of further question or technical problems with WCD

Follow up of the patients and remote monitoring is individualised and done as needed. The WCD has the ability to capture information about patient arrhythmic events. This information is uploaded to Lifevestnetwork database in an automatically. The responsible health care professionals have access to this database and are able to see all automatically and manually recorded ECGs of their patients as well as the patients' wearing adherence. Alerts and notifications can be tailored so that the healthcare professionals can choose which events to be notified for, such as WCD treatments, patient-recorded ECGs, and detected arrhythmia events in which no treatment is given, such as a short run of VT as well as wearing adherence (i.e. less than 20 hour per day). The notification and alerts are automatically sent by email to all treating health care professionals (nurses and physicians). Individualised phone or personal contact is made with the patient as needed to optimise treatment pathways and to improve compliance.

In order to improve compliance, the same health care professional / nurse serves as the primary contact person for the patient. In addition, all ECGs were analysed independently of two members of the research team (one nurse and one physician). ECGs of all shock events recorded by the WCD were reviewed by three members of the research team (one nurse, one physician and one consultant specialised in electrophysiology.