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ORIGINAL PAPER

Types and outcomes of cardioversion in patients admitted to hospital for atrial fibrillation: results of the German RHYTHM-AF Study

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Abstract
Background Atrial fibrillation (AF) accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances. Little is known about the characteristics of current use of cardioversion (CV) and its success rates in clinical practice in Germany.
Methods As part of the international RHYTHM-AF Study, 655 consecutive patients with documented AF (mean age 68.3 ± 10.5 years, 64.9 % males) who were considered candidates for CV were prospectively enrolled in 22 German hospitals (21 academic/teaching and 1 non-teaching). CV was considered successful if sinus rhythm or atrial rhythm was obtained within 1 day after start of pharmacological CV (PCV) or if sinus rhythm was achieved and maintained for at least 10 min after electrical CV (ECV).

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Results Patients with AF considered for CV had ECG in 94.4 %, Holter ECG in 25.8 %, and transesophageal echocardiography (TEE) in 73.1 % of cases. They underwent ECV (after mean 16 h, range 4–48), in 65.3 % and PCV in 6.7 % of patients (amiodarone in 47.7 %, flecainide in 27.3 %, propafenone in 2.3 %) as first CV procedure. No CV was performed in 27.9 %, mainly due to spontaneous CV or pathologic TEE. Primary success rates were 86.7 % for electrical CV and 54.5 % for pharmacological CV. More patients in the ECV group compared to the PCV group received oral anticoagulation at discharge (79.2 vs. 59.1 %, $p < 0.001$), and at 60 days (77.5 vs. 56.8 %, $p < 0.001$). Further, at 60 days the proportion of patients in sinus rhythm was not different between groups (ECV 76.8 % vs. PCV 77.3 %).
Conclusions In large academic centres in Germany, the preferred CV method is electrical, mainly due to its easy access and to its higher success rate for the initial restoration of sinus rhythm. Considering the limitations of the open-label, non-randomised study design, overall short-term success rates appeared higher after ECV compared to PCV during hospitalisation, but not after 60 days.

Keywords Atrial fibrillation · Observational · Registry · Pharmacological conversion · Electrical conversion · Outcomes

Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice [1]. The condition is frequently managed by emergency physicians, and accounts for approximately one-third of hospitalizations due to cardiac rhythm disturbances [2]. The majority of patients

experience distressing symptoms leading to substantially reduced quality of life [3]. Further, AF is associated with increased risk of cardiovascular events, in particular stroke, and premature death [4, 5].

According to current guidelines at the time of data collection, a clinical approach is taken to distinguish AF types by presentation and duration of the arrhythmia [6]. Paroxysmal AF is self-terminating within 7 days, but usually after 2 days the likelihood of spontaneous conversion is substantially reduced [6]. In persistent AF (lasting >7 days) and in long-standing persistent AF (>1 year) there is the option of cardioversion (CV) to restore sinus rhythm either with drugs (pharmacological conversion, PCV) or by direct current CV (electrical conversion, ECV). In contrast, in permanent AF, the presence of the arrhythmia is accepted by both the patient and the physician, and a rate control strategy is pursued.

CV can be done in patients with recent-onset AF using intravenous antiarrhythmic drugs with various electrophysiological properties (flecainide, ibutilide, propafenone, vernakalant; or amiodarone in the presence of structural heart disease). PCV does not require sedation or anaesthesia, and may facilitate the choice of antiarrhythmic drug therapy to prevent recurrent AF. However, success rates are lower than with ECV. The latter is primarily recommended in haemodynamically unstable patients [6].

Data on the success rates of CV have primarily been collected in randomised trials or studies in special settings, while data in the clinical practice setting are limited. The current AF guidelines by the European Society of Cardiology recommend an individualised approach to treatment, which will likely translate into heterogeneous approaches to CV with possible differences across patient profiles, regions, and health care settings [6].

Against this background, the observational RHYTHM-AF Study was set up as a multi-national project to document selection of patients with AF for the two approaches of CV, their hospital-based management and associated short-term outcomes of the procedure. Here, we describe the data of the German cohort of patients.

Methods

Design

RHYTHM-AF was a prospective, open, observational, non-randomised study in 10 countries (Australia, Brazil, France, Germany, Italy, Netherlands, Poland, Spain, Sweden and the United Kingdom), performed between May and December 2010 in Germany. The rationale, design, and aims of the study have been described in greater detail previously [7]. In brief, participating centres were selected with the aim to be representative of those treating AF in the individual countries by size, type, availability of specialty care units, and location of the institution. This study was conducted in accordance with the EU Note for Guidance on Good Clinical Practice CPMP/ECH/135/95 and the Declaration of Helsinki. It was only initiated at the site level after local and ethics approval requirements were obtained. The study was planned, steered, and its data interpreted and disseminated by a scientific committee (11 members), consisting of one representative from each country, as well as one representative from the coordinating centre (Institut für Herzinfarktforschung in Ludwigshafen, Germany). The study is registered in ClinicalTrials.gov under the identifier NCT01119716.

Patients

Patients were eligible for participation if they met the following criteria: (1) at least 18 years old; (2) documented AF in the hospital setting as confirmed by electrocardiogram; (3) CV was one of the planned therapeutic options (scheduled CV, anticoagulation, oral loading); (4) written informed consent. Exclusion criteria were enrolment in a separate trial, and atrial flutter. Emphasis was put on consecutive enrolment of patients at each site.

Data collection

Data were collected at two time points, namely at the time of presentation of the patient with AF in the hospital and follow-up at 60 days (±10 days). Country-specific electronic case report forms (eCRF) were used.

Data were collected from all cumulative medical records created between entry and follow-up during routine medical visits. If no visits occurred by day 60, patients (or their next of kin) were contacted over the phone to obtain follow-up information on the patient's vital status, clinical events, hospitalizations, or changes in treatment.

Outcomes

The primary success rate of CV without recurrence of AF was a major outcome. A PCV procedure was considered successful if sinus rhythm or atrial rhythm with a rate <100 beats/min was obtained within 1 day after the start of pharmacological treatment. An ECV was defined as successful if sinus rhythm was obtained and maintained for at least 10 min after the cardioversion procedure. Recurrence was defined as AF or atrial flutter following successful CV. In addition, the following major adverse events and complications of CV procedures were documented: major and minor bleeding complications, torsades de pointes tachycardia, heart failure, and hypotension.

Statistical considerations

Sample size calculations were based on the objective to document the success rate of different CV procedures. Within each country, patient sample sizes were broadly based on the relative population of each country. In the present analysis of data from Germany, a subset of 22 centres and 655 patients was used.

Continuous variables were summarised with descriptive statistics (absolute numbers *n*, means, standard deviation (SD), or medians, with 25th and 75th percentile as appropriate). Categorical data were described by the number (*n*) and percentage (%) of subjects in each category. Subgroups were formed according to the primary CV procedure in the hospital (no CV, ECV, and PCV). In an ancillary analysis, patients were categorised according to AF duration ($\leq$48 h, >48 h) to assess the use of TEE. Variables were compared using Chi-square tests (categorical variables) and Kruskal–Wallis tests (continuous variables). Statistical significance was assumed for $p < 0.05$. No Bonferroni adjustments were made for multiple comparisons. Percentages were calculated based on patients with data for each respective parameter (i.e. no percentages for missing values are provided). The Statistical Analysis System (SAS), release 9.2 was used for analysis.

Results

Sites

In Germany, 22 hospitals participated in the study, and all but one were academic/teaching hospitals. Mean number of beds in the cardiology department was 81 (70–100), in the cardiac care unit/intensive care unit 20 (12–30). The preferred type of ECV in all but one centre was biphasic direct current cardioversion, and the mean number of ECV was 300 (150–500). All participating sites (100 %) offered the capacity for transesophageal echocardiography (TEE), pacemaker or implantable cardioverter/defibrillator (ICD), 82 % of them had catheter ablation, and 50 % surgical therapy for AF available.

Patient characteristics

A total of 655 patients were enrolled, 64.9 % were male. The mean age was 68.3 ± 10.5 years. The primary reason for the admission to hospital were AF (81.8 %) and atrial flutter (2.9 %), and all AF diagnoses were confirmed by ECG (Table 1). With respect to the clinical type of AF, 30.5 % had the first detected AF episode, 28.1 % had paroxysmal, 34.7 % had persistent, and 3.4 % had permanent AF. Among patients undergoing ECV, the majority (38.3 %) had persistent AF. In patients undergoing PCV, 40.9 % had first detected AF (Fig. 1).

All patients were considered by the treating physicians to undergo cardioversion. During the index hospital stay, CV was not performed in 183 patients (27.9 %) for the following reasons: 100 patients (55.6 relative %) experienced spontaneous restoration of sinus rhythm, 31 had left atrial thrombus (17.2 relative %), and 14 (7.8 relative %) spontaneous echo contrast detected by TEE. About two-thirds of the patients (65.3 %) underwent ECV, and 6.7 % PCV. CV was planned for the same day in 45.3 % of patients, for the next day in 35.7 %, or for a later date in 18.9 % of patients. Patients undergoing PCV were more likely to be female and more often had been admitted to hospital for acute coronary syndromes. No further differences in comorbidities were found (Table 1).

Two-thirds of patients (67.6 %) reported AF symptoms in the past. Only 11.0 % of patients had no symptoms at time of AF episode. Shortness of breath, palpitations were most frequent, followed by fatigue and chest pain (Fig. 2). Mean $CHADS_2$ score (1.5 ± 1.1) and mean CHA_2DS_2-VASc score (2.9 ± 1.7) did not differ across groups.

During the time of the index hospitalisation, the majority of patients underwent a resting ECG (94.4 %), followed by TEE (73.1 %), chest X-ray (28.5 %), Holter ECG (28.5 %), stress test (5.3 %), computer tomography (4.9 %), and magnetic resonance imaging (2.3 %).

TEE was more frequently performed in the ECV group compared with the PCV group (82.5 % vs. 38.6 %, $p < 0.0001$). Even within the 140 patients with AF duration less than 48 h, 76 patients (54 %) underwent TEE. Atrial thrombi were found in 6.7 % (32 patients; Fig. 3).

Medication

Table 2 shows antithrombotic treatment reported at the enrolment visit. Most patients received oral anticoagulation (vitamin K antagonist VKA 51.6 %, specifically, fenprocoumon in all but four cases). In the breakdown by $CHADS_2$ score groups, there were no significant differences in the VKA rates, in contrast to the breakdown by CHA_2DS_2-VASc score ($p < 0.01$; Fig. 4, top).

With respect to antiarrhythmic or rate control drugs, beta blockers were most frequently used, followed by amiodarone and dronedarone and digitalis (few differences between groups, Fig. 5). For other cardiac or anti-diabetic treatments, there were no statistically significant differences between groups (details not presented).

Cardioversions and other interventions related to AF

In the ECV group, time elapsed from admission until first electrical conversion was 16 h (range 4–48), and the

Table 1 Demographics, concomitant diseases and risk factors

Characteristics	Total 655 (100 %)	No CV 183 (27.9 %)	ECV 428 (65.3 %)	PCV 44 (6.7 %)	*p* value
Demographic					
Age	68.3 ± 10.5	67.7 ± 11.2	68.6 ± 9.9	67.7 ± 13.3	0.66
Gender, female	35.1 (230)	37.7 (69)	32.5 (139)	50.0 (22)	<0.05
Primary admission reason					
Atrial fibrillation	81.8 (536)	84.2 (154)	81.1 (347)	79.5 (35)	0.61
Atrial flutter	2.9 (19)	2.2 (4)	3.5 (15)	0.0 (0)	0.33
Acute coronary syndrome	2.1 (14)	2.7 (5)	1.2 (5)	9.1 (4)	<0.01
Heart failure	4.4 (29)	2.7 (5)	5.6 (24)	0.0 (0)	0.10
Stable coronary artery disease	1.8 (12)	2.2 (4)	1.9 (8)	0.0 (0)	0.62
History of cardiovascular disease					
Prior myocardial infarction	12.5 (82)	16.9 (31)	11.0 (47)	9.1 (4)	0.10
Prior PCI	15.9 (104)	15.3 (28)	16.1 (69)	15.9 (7)	0.97
Prior CABG	7.6 (50)	7.1 (13)	8.2 (35)	4.5 (2)	0.65
Valvular heart disease	19.0 (121)	17.2 (31)	20.8 (86)	9.5 (4)	0.16
Prior surgery for AF	3.2 (21)	3.3 (6)	3.0 (13)	4.5 (2)	0.86
Cardiomyopathy	13.4 (88)	15.8 (29)	12.9 (55)	9.1 (4)	0.42
Chronic heart failure	17.7 (116)	15.8 (29)	18.7 (80)	15.9 (7)	0.66
Ischemic stroke	3.5 (22)	3.4 (6)	3.7 (15)	2.5 (1)	0.92
Transient ischemic attack	1.4 (9)	1.1 (2)	1.5 (6)	2.5 (1)	0.80
$CHADS_2$ score, 0–6	1.5 ± 1.1	1.4 ± 1.1	1.5 ± 1.0	1.4 ± 1.1	0.75
CHA_2DS_2VASc score, 0–9	2.9 ± 1.7	2.8 ± 1.7	2.9 ± 1.6	3.0 ± 1.9	0.85
Cardiovascular risk factors					
Family history of premature CHD	29.4 (131)	32.5 (39)	28.8 (87)	21.7 (5)	0.53
Diabetes mellitus	19.5 (128)	20.8 (38)	19.4 (83)	15.9 (7)	0.76
Arterial hypertension	74.4 (480)	72.9 (132)	76.0 (319)	65.9 (29)	0.30
Hyperlipidaemia	42.3 (268)	42.0 (74)	42.8 (178)	38.1 (16)	0.84
Smoking, current	7.9 (52)	7.7 (14)	7.0 (30)	18.2 (8)	<0.05
Comorbidities					
COPD	7.6 (49)	7.7 (14)	7.6 (32)	7.0 (3)	0.99
Peripheral vascular disease	7.6 (49)	9.9 (18)	6.1 (26)	11.4 (5)	0.17
Chronic renal failure	13.1 (85)	17.6 (32)	11.1 (47)	13.6 (6)	0.10
Anaemia	5.1 (33)	5.5 (10)	4.8 (20)	7.0 (3)	0.80

Values are % (number of patients) or mean ± standard deviation. *p* values for comparison between groups from χ^2 or Kruskal–Wallis test

AF atrial fibrillation, *CABG* coronary artery bypass graft, *CHD* coronary heart disease, *COPD* chronic obstructive pulmonary disease, *CV* cardioversion, *ECV* electrical cardioversion, *ICD* implantable cardioverter defibrillator, *PCI* percutaneous coronary intervention, *PCV* pharmacological cardioversion

hospital stay was 52 h (range 24–147). Almost all patients (98 %) received external ECV; 2 % received ECV by ICD. No transvenous or transesophageal ECV procedures were reported. Handheld paddles were used in 64.1 %, and adhesive pads in 35.4 % (other types of electrodes in 0.5 %). The anterior posterior pad/paddle position was more often used compared to the anterior lateral (77.5 vs. 20.9 %). Mean number of shocks was 1.7 ± 5.7, the energy used for the first shock was 152 ± 68 J, and for the last shock 163 ± 85 J. Biphasic wave was used in 92 %, and monophasic wave in 8 %. In the subgroup of patients without symptoms, 11.2 % (52 of 463 patients) were converted and 10.4 % (20 of 192) were not. The primary ECV was successful in 86.7 %, while multiple ECV were needed in 3.7 % (Fig. 6).

Mean time to PCV was 16 h (range 1.5–47), and the hospital stay was 72 h (range 29–189), and thus longer than in ECV (probably due to the higher rate of patients with acute coronary syndrome in this group, 9.1 % PCV vs. 1.2 % ECV). Primary PCV was successful in 54.5 %, while multiple PCV were needed in 2.3 %, and a change to ECV in 38.6 % (Fig. 6). Drugs used for PCV were

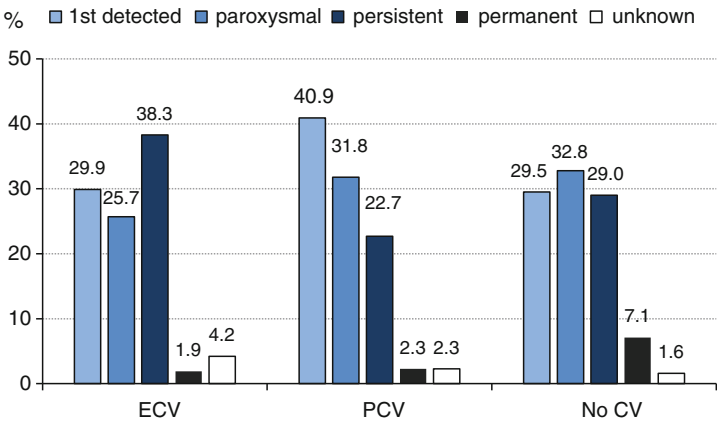

Fig. 1 Type of CV, by AF type. *ECV* electrical cardioversion, *CV* cardioversion, *PCV* pharmacological cardioversion

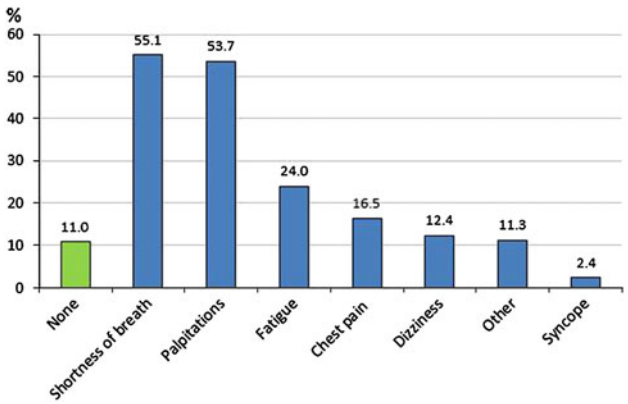

Fig. 2 Symptoms of AF in the total cohort during enrolment

amiodarone in 47.7 % (success rate 57.1 %, hospital stay 120 h), flecainide in 27.3 % (success rate 25.0 %, hospital stay 37 h), and propafenone in 2.3 % of patients (success rate 100 %, hospital stay 29 h). A switch to the ECV method was frequently reported (38.6 %).

Ablations were performed in six patients (3 in the ECV and 3 in the no CV group), a pacemaker was implanted in 8 patients (6 in ECV, 1 in PCV, 1 in the no CV group), and an ICD in three patients (2 ECV, 1 PCV).

Outcomes at discharge from hospital

At follow-up, data were available in 649 patients (99.1 %). The overall stay in hospital was 52 h (range 24–147) for ECV and 72 h (range 29–189) for PCV. Between enrolment and discharge, 3 (0.5 %) patients died, and 25 (3.8 %) reached a composite outcome of major adverse events, death or complication [statistically significantly more frequent in PCV (11.4 %) compared to ECV (4.0 %) and no CV (1.6 %), Table 3]. Patients who underwent ECV more often had sinus rhythm at discharge as compared to those who underwent PCV (87.8 % vs. 75.0 %, respectively).

At discharge more patients who underwent ECV compared to PCV were treated with oral anticoagulation (79.2 vs. 59.1 %). No differences were noted for VKA in the different $CHADS_2$ or CHA2DS2-Vasc groups (Fig. 4, bottom). Nearly all patients were discharged on antiarrhythmic drugs, a majority of patients on beta blockers (overall 78.3 %), followed by amiodarone (18.4 %), dronedarone (12.6 % overall, significantly more frequent in ECV) and flecainide (6.1 %). Types of antiarrhythmic therapy prescribed at discharge did not differ significantly between ECV and PCV patients.

Outcomes at 60 days

Information on outcomes at 60 days post-conversion was documented in 649 patients (99 %), mostly by phone calls (90.0 %), followed by chart review (10.0 %) and visits (4.3 %; several contact modes in individual patients possible). Results are summarised in Table 4. Between discharge and day 60, 5 (0.8 %) patients died, and 21 (3.2 %) reached a composite outcome of major adverse event, death or complication (with no statistically significant differences between ECV and PCV). Compared to discharge from hospital, at 60-day follow-up, fewer patients did receive anticoagulation treatment, with a higher rate in ECV patients than in PCV (77.5 vs. 56.8 %; Table 4).

The proportion of patients without any antiarrhythmic or rate control drugs increased without differences between ECV and PCV. There were no differences in the rate of self-reported sinus rhythm (76.8 % ECV and 77.3 % PCV, respectively; Fig. 7) or recurrences of AF (26.0 % ECV and 27.3 % PCV; respectively). Of note, only 65.7 % of patients who had not received CV were still in sinus rhythm.

Discussion

The present analysis provides a real-life picture of the current management of patients with AF considered for cardioversion when admitted to academic/teaching hospitals in Germany. The majority of patients received ECV,

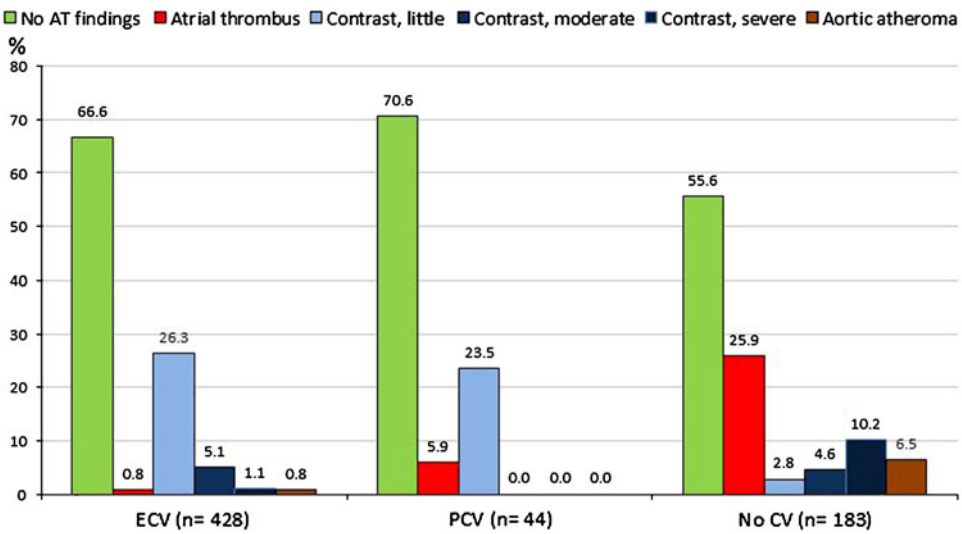

Fig. 3 Findings of transesophageal echocardiography. *AT* atherothrombotic, *TEE* transesophageal echocardiography. TEE was performed in 478 patients overall (73.1 %): in 108 patients (59.3 %) of the No CV group, in 353 (82.5 %) in the ECV group, and in 17 patients (38.6 %) in the PCV group (p between groups <0.0001)

Table 2 Anticoagulation and antiarrhythmic medication at baseline

	Total 655 (100 %) % (*n*)	No CV 183 (27.9 %) % (*n*)	ECV 428 (65.3 %) % (*n*)	PCV 44 (6.7 %) % (*n*)	*p* value
Drug class prior to entry					
Antithrombotic treatment					
Vitamin K antagonist	51.6 (338)	37.7 (69)	58.6 (251)	40.9 (18)	<0.0001
Other antithrombotic treatment					
No other antithrombotic	52.6 (344)	43.4 (79)	57.0 (244)	47.7 (21)	<0.01
Unfractionated heparin	2.9 (19)	2.7 (5)	3.0 (13)	2.3 (1)	0.95
LMWH	21.3 (139)	26.4 (48)	19.4 (83)	18.2 (8)	0.14
ASA	31.3 (205)	37.4 (68)	28.0 (120)	38.6 (17)	<0.05
Clopidogrel	4.7 (31)	6.6 (12)	4.0 (17)	4.5 (2)	0.38
Antiarrhythmic or rate control drugs					
Beta blocker	66.5 (435)	58.8 (107)	69.4 (297)	70.5 (31)	<0.05
Amiodarone	11.3 (74)	7.7 (14)	13.3 (57)	6.8 (3)	0.08
Dronedarone	8.4 (55)	8.2 (15)	8.6 (37)	6.8 (3)	0.91
Digitoxin	6.0 (39)	6.6 (12)	6.1 (26)	2.3 (1)	0.55
Digoxin	4.6 (30)	5.5 (10)	4.4 (19)	2.3 (1)	0.64
Flecainide	3.4 (22)	3.3 (6)	3.3 (14)	4.5 (2)	0.90

p values for comparison between groups from χ^2 or Kruskal–Wallis test

ASA acetylic salicylic acid, *CV* cardioversion, *ECV* electrical cardioversion, *LMWH* low molecular weight heparin, *PCV* pharmacological cardioversion

while PCV played a minor role. Success rates were higher after ECV compared to PCV during the hospital stay, but the proportion of patients maintaining sinus rhythm did not differ after 60 days.

Overall, data on CV under real-life conditions are sparse. According to a recent report on a subset of patients of the multi-centre prospective Euro Heart Survey on AF, 33.8 % of the 5,333 patients underwent CV in 2003/2004. Sinus rhythm was restored by ECV in 88 % of patients, by intravenous PCV in 71 %, and at 1-year follow-up, 81 % of ECV patients and 67 % of PCV patients were still in sinus rhythm [8].

In Germany, in recent years, few observational studies described the management of AF under practice conditions. In the MOVE registry, which documented 3,354 AF patients (34 % paroxysmal, 27 % persistent, 39 % permanent) primarily treated by office-based cardiologists, 18.2 % had received PCV in the 12 months prior to inclusion in both ambulatory or hospital settings, and ECV in 17.5 % [9]. During a 1-year follow-up period, 23.6 %

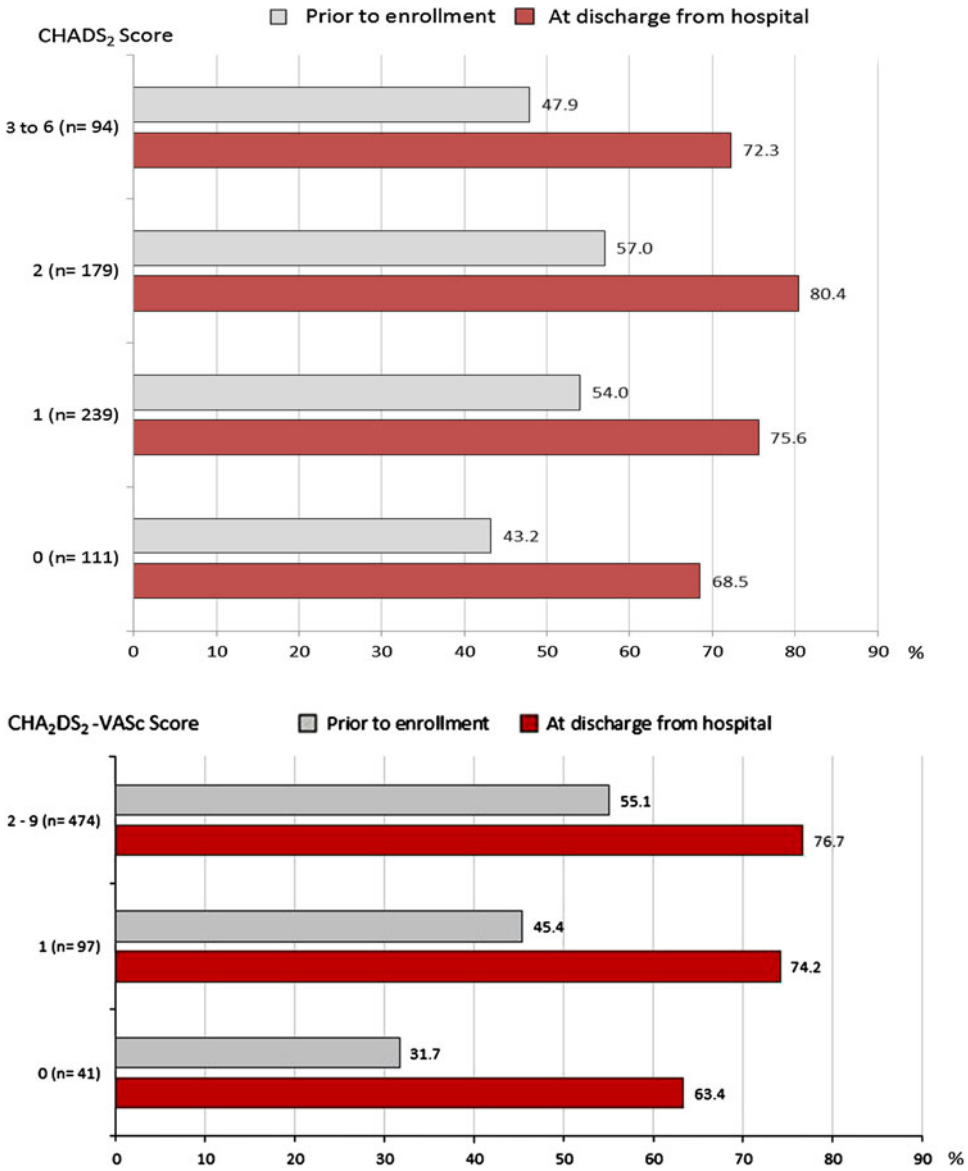

Fig. 4 Use of vitamin K antagonists at entry and at discharge, by $CHADS_2$ score (*top*) and CHA_2DS_2-VASc score (*bottom*). There were no significant differences with regard to VKA use between the categorical $CHADS_2$ groups at entry ($p = 0.10$) nor at discharge ($p = 0.12$). There were differences with regard to VKA use between categorical CHA_2DS_2-VASc groups at baseline ($p < 0.01$), but not at discharge ($p = 0.16$)

received any cardioversion, while 5.8 % underwent an ablation procedure [10]. Success rates on cardioversion were not published to date. In the German AFNET registry (primarily centres with special expertise in the management of AF) ECV/PCV/catheter ablation was applied in 24.4 %/13.2 %/1.5 % in first detected AF, in 14.0 %/9.3 %/11.9 % in paroxysmal AF, in 24.1 %/6.2 %/5.7 % in persistent AF, and in 2.9 %/0.7 %/1.7 % in permanent AF [11]. Success rates for CV were high in patients with a first episode of AF, irrespective of whether pharmacological or electrical conversion was applied, but in patients with persistent AF, PCV had a much lower success rate (55.9 %) than ECV (86.8 %) [11].

RHYTHM-AF provides further details on current practice of CV in large academic hospitals. In contrast to the reported data of other observational studies, the great majority of patients in RHYTHM-AF in Germany received ECV as first-line treatment (also in paroxysmal AF, likely to obtain fast relief of symptoms) and the low use of PCV distinguishes Germany from other countries. The high initial success rate of ECV (86 %) is in line with prior reports from the Euro Heart Survey on AF and other studies [12, 13]. For ECV, almost all centres used biphasic external defibrillators, which require less energy and have greater efficacy compared to monophasic defibrillators [6, 14, 15]. Anteroposterior electrode placement was preferred, consistent with findings that it is more effective than anterolateral placement [16].

Among patients with PCV, amiodarone was frequently used despite the fact that the drug has distinct disadvantages due to its slow onset of action and therefore low conversion success rates as well as slow metabolism [11].

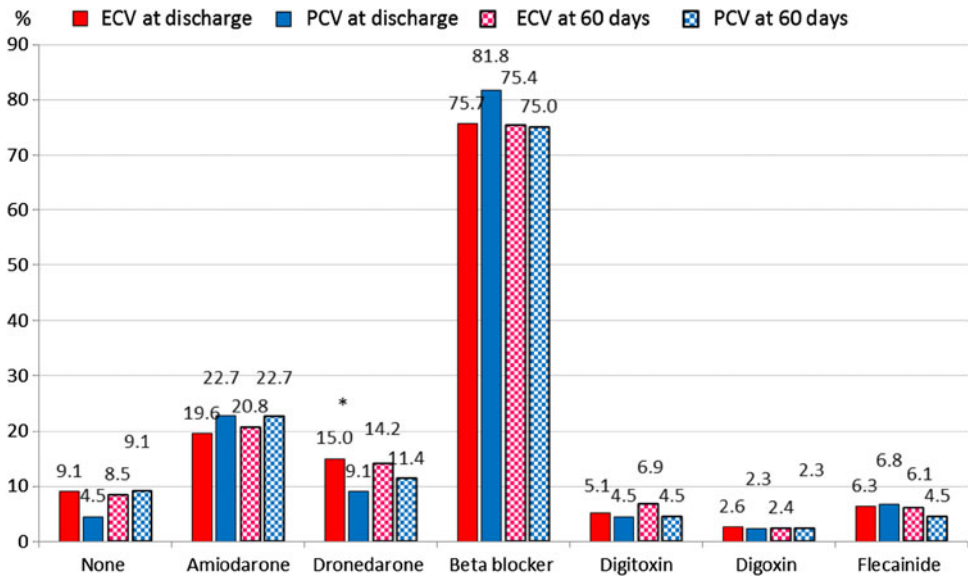

Fig. 5 Medication for AF at discharge and at follow-up at 60 days in patients who had undergone cardioversion. *ECV* electrical cardioversion, *PCV* pharmacological cardioversion. *$p < 0.05$ between ECV and PCV discharge from hospital

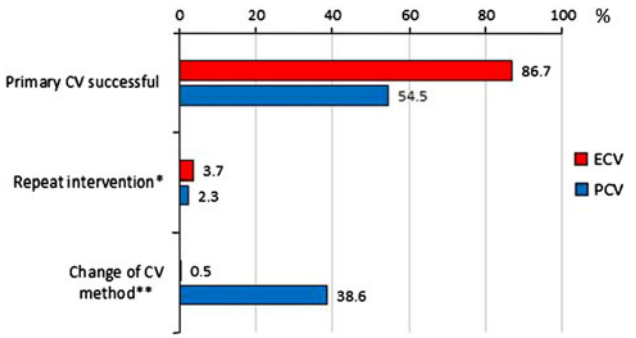

Fig. 6 Cardioversion success rates: ECV versus PCV. *ECV* electrical cardioversion, *CV* cardioversion, *PCV* pharmacological cardioversion. *Single asterisk* of the same type, *double asterisk* from ECV to PCV or vice versa

Usually the drug is used to lower heart rates and cardiovert patients with substantial heart disease such as chronic heart failure or coronary artery disease in whom an acute CV is not required, but early relief from symptoms is needed [7].

Of note, the rate of oral anticoagulation therapy in AF patients was 59 % in the ECV group and 41 % in the PCV group, and thus relatively low compared to other recent observational data in Germany. For example, in the ATRIUM registry on AF patients in the primary care setting, oral anticoagulants were administered in 83 % suggesting that stroke prevention is a firmly established goal in these patients [17]. The low rate of OAC in RHYTHM-AF is likely be due to the fact that nearly one-third of patients (31 %) had a newly detected episode, roughly another third (28 %) paroxysmal AF, and one-third (persistent or permanent). Overall stroke risk was lower in RHYTHM-AF, as evidenced by a $CHADS_2$ score of 1.5 (as compared to ATRIUM 2.2), which indicates that a substantial portion of patients was not (necessarily) eligible for OAC treatment. Nevertheless, a considerable proportion of patients with $CHAD_2$ or CHA_2DS_2-Vasc score of 0 (43 % and 32 % at discharge, respectively) actually received oral anticoagulation.

In nearly one-third of patients (29.3 %) considered for cardioversion by the treating physician, finally no CV was performed, with the most frequent cause being spontaneous cardioversion into sinus rhythm. Other reasons include the identification of thrombi as contrast by TEE prior to CV [18]. In our study, the high rate of atrial thrombi in patients undergoing electrical and pharmacological cardioversion deserves attention. The current ESC AF guidelines mandate the use of TEE in AF duration of >48 h or unknown duration as alternative to an at least 3-week anticoagulant pre-treatment of AF [6]. However, the duration of AF cannot be reliably determined by symptoms alone. In a recent series of 366 consecutive, unselected patients with short-term AF <48 h, TEE revealed left atrial thrombi in 1.4 % and left atrial dense spontaneous echo contrast in 10 % of patients with short-term AF, of whom 63 % were receiving anticoagulation therapy (patients without prior anticoagulation had a 4 % prevalence of left atrial thrombi) [19]. In line with the current literature [19–21], in RHYTHM-AF, 54 % of patients with AF ≤48 h received TEE, and the use of TEE was not guided by presence of pre-existing sufficient oral anticoagulant treatment that may indicate routine rather than indicated use. TEE use is also associated with and may predispose choice of electrical CV. Other factors like size of hospitals may also affect the use of TEE.

Methodological considerations

Patients were selected based on the physician intention to perform CV, which reflects the "real world" approach of

Table 3 Outcomes at discharge from the hospital

	Total 655 (100 %) % (*n*)	No CV 183 (27.9 %) % (*n*)	ECV 428 (65.3 %) % (*n*)	PCV 44 (6.7 %) % (*n*)	*p* value
Outcomes					
Death or complications, MAE	3.8 (25)	1.6 (3)	4.0 (17)	11.4 (5)	<0.01
Death	0.5 (3)	1.1 (2)	0.2 (1)	0.0 (0)	0.32
Complications and MAE	3.5 (23)	1.1 (2)	3.7 (16)	11.4 (5)	<0.01
Sinus rhythm	80.9 (524)	65.7 (117)	87.8 (374)	75.0 (33)	<0.0001
Atrial fibrillation	19.1 (124)	33.7 (60)	12.7 (54)	22.7 (10)	<0.0001
Atrial flutter	0.5 (3)	1.1 (2)	0.0 (0)	2.3 (1)	<0.05
Medication at discharge					
Oral anticoagulation (OAC)	74.5 (487)	67.0 (122)	79.2 (339)	59.1 (26)	<0.001
No other antithrombotic	41.0 (268)	24.3 (44)	48.8 (209)	34.1 (15)	<0.0001
Unfractionated heparin	3.1 (20)	5.5 (10)	1.9 (8)	4.5 (2)	<0.05
LMWH	36.1 (236)	46.4 (84)	32.5 (139)	29.5 (13)	<0.01
ASA	28.9 (189)	32.0 (58)	26.6 (114)	38.6 (17)	0.14

p values for comparison between groups from χ^2 or Kruskal–Wallis test

ASA acetylic salicylic acid, *CV* cardioversion, *ECV* electrical cardioversion, *LMWH* low molecular weight heparin, *MAE* major adverse event, *ECG* electrocardiogram, *PCV* pharmacological cardioversion

Table 4 Outcomes at follow-up after 60 days

	Total 649 (100 %) % (*n*)	No CV 181 (27.9 %) % (*n*)	ECV 424 (65.3 %) % (*n*)	PCV 44 (6.8 %) % (*n*)	*p* value
Outcomes					
Death or complications, MAE	3.2 (21)	3.3 (6)	3.5 (15)	0.0 (0)	0.45
Death	0.8 (5)	1.7 (3)	0.5 (2)	0.0 (0)	0.26
Sudden cardiac death	**(4)**	**(3)**	**(1)**	**(0)**	
Non-cardiac thromboembolic	**(1)**	**(0)**	**(1)**	**(0)**	
Patients with complications and MAEs	2.5 (16)	1.7 (3)	3.1 (13)	0.0 (0)	0.33
Heart failure	**(4)**	**(1)**	**(3)**	**(0)**	
Major bleeding	**(1)**	**(1)**	**(0)**	**(0)**	
Minor bleeding	**(1)**	**(0)**	**(1)**	**(0)**	
Recurrence of atrial fibrillation	**(4)**	**(0)**	**(4)**	**(0)**	
Recurrence of atrial flutter	**(2)**	**(0)**	**(2)**	**(0)**	
Torsade de pointes	**(1)**	**(0)**	**(1)**	**(0)**	
Bradycardia	**(1)**	**(1)**	**(0)**	**(0)**	
Hypotension	**(1)**	**(0)**	**(1)**	**(0)**	
Other	**(5)**	**(0)**	**(5)**	**(0)**	
Sinus rhythm	75.9 (491)	73.3 (132)	76.8 (325)	77.3 (34)	0.64
Atrial fibrillation	21.9 (142)	24.4 (44)	21.0 (89)	20.5 (9)	0.63
Other rhythm	2.2 (14)	2.2 (4)	2.1 (9)	2.3 (1)	1.00
Recurrence of AF	26.1 (169)	26.1 (47)	26.0 (110)	27.3 (12)	0.98
Rehospitalisation	20.6 (133)	24.4 (44)	19.6 (83)	13.6 (6)	0.20
Medication at follow-up					
Oral anticoagulation (OAC)	72.2 (467)	63.3 (114)	77.5 (328)	56.8 (25)	<0.001
No other antithrombotic	46.1 (298)	35.6 (64)	51.1 (216)	40.9 (18)	<0.01
Unfractionated heparin	2.2 (14)	2.2 (4)	1.9 (8)	4.5 (2)	0.51
LMWH	27.5 (178)	33.9 (61)	25.5 (108)	20.5 (9)	0.06
ASA	30.4 (197)	32.2 (58)	28.6 (121)	40.9 (18)	0.20

Values for patients who had more than one event are shown in bold. *p* values for comparison between groups from χ^2 or Kruskal–Wallis test

ASA acetylic salicylic acid, *CV* cardioversion, *ECV* electrical cardioversion, *PCV* pharmacological cardioversion, *LMWH* low molecular weight heparin, *MAE* major adverse event

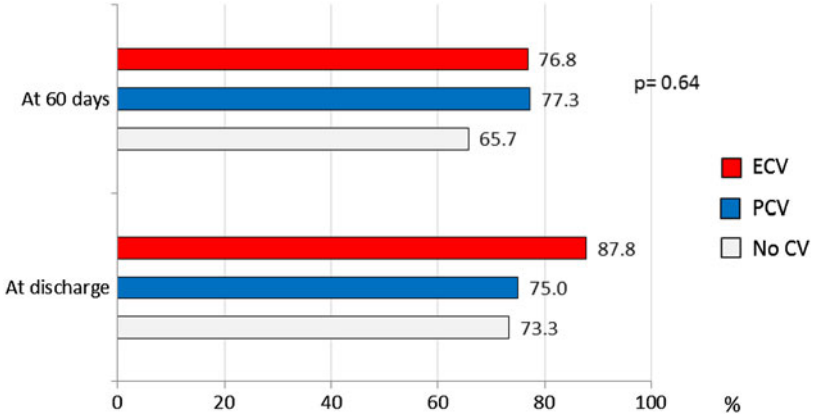

Fig. 7 Sinus rhythm at discharge from hospital and at 60-day follow-up. CV was considered successful if sinus rhythm or atrial rhythm was obtained within 1 day after start of pharmacological treatment (PCV) or if sinus rhythm was achieved and maintained for at least 10 min after electrical CV (ECV). According to the intent-to-treat principle, in the PCV group also patients were analysed who switched to ECV during hospitalisation

the study concept. While the selection process of centres aimed to provide a representative sample for the hospital-based management of centres throughout the participating countries in RHYTHM-AF, in Germany the majority of centres were academic and specialised AF centres which are known to probably have better outcomes and less AF-related events [22]. The experience of centres and various quality assurance measures contributed to a low number of missing data for the inclusion and the follow-up visit. However, clinical events were not adjudicated, and therefore under-reporting or misclassification of events cannot be fully excluded. This is particularly important, as only a minority of patients presented personally for the documentation of the follow-up visit.

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Conflict of interest A.K.G. has been a consultant for and served on the speakers' bureau of MSD. D.P. and T.L. have provided consultancy for MSD and other manufacturers of cardiovascular drugs. W.S. and G.M. are full-time employees of MSD Germany. A.B. states that there is no conflict of interest.

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