

# The Registry of the German Competence NETwork on Atrial Fibrillation: patient characteristics and initial management

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## Aims

The aim of this study was to describe the characteristics of patients with atrial fibrillation (AF) enrolled in the Central Registry of the German Competence NETwork on Atrial Fibrillation (AFNET) and to assess current medical practice in patients treated at various levels of medical care in Germany.

## Methods and results

From February 2004 to March 2006, 9582 ambulatory and hospitalized patients with ECG-documented AF were enrolled by 194 participating study centres from all levels of medical care in Germany. Clinical type of AF was reported as paroxysmal in 2893, persistent in 1873, and permanent in 3134 patients or classified as a first episode in 1035 patients. Predisposing conditions were common and present in 87.6% of the patients. Most patients were symptomatic with AF (75.1%). Rhythm control in persistent AF was provided to 53.4% of the symptomatic patients and to 47.8% of the patients without symptoms. Anticoagulation for stroke prevention was given to 71.4% of the patients considered eligible by applicable guidelines and to 48.4% of patients with low risk where guidelines do not recommend anticoagulation.

## Conclusion

This registry provides insight into current medical care of patients with AF in Germany. The use of oral anticoagulation in eligible patients was among the highest reported, whereas decisions on rate and rhythm control often do not follow current recommendations.

## Keywords

Atrial fibrillation • German AFNET Registry • Guidelines • Rate control • Rhythm control • Anticoagulation

## Introduction

Atrial fibrillation (AF) is the most frequent sustained arrhythmia in clinical practice and associated with a high risk of stroke, heart failure, and hospitalization.<sup>1–3</sup> Ageing of the population and the accumulation of predisposing conditions will cause the prevalence

of AF to rise by at least 2.5-fold by the year 2050.<sup>4</sup> For optimized diagnostic and therapeutic management, patient characteristics and determinants of clinical course and complications will be essential.

Clinical studies over the last 20 years have provided a framework for guidelines on care in AF.<sup>5–8</sup> However, it is difficult to establish the level of adherence to guidelines in every day clinical

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practice, given, among other things, the often limited feasibility of diagnostics and treatment in a preferentially elderly population or constraints such as patient preference and compliance. A limited number of previous national and international surveys and registries have provided information on the management of patients with AF,<sup>9–13</sup> usually focusing on specific patient subsets such as those cared for by cardiologists<sup>9,10,14</sup> or general practitioners.<sup>15,16</sup> There has been increasing awareness of recent guidelines and clinical trials on AF, importantly of the ACC/AHA/ESC guidelines published in 2001,<sup>5</sup> updated in 2006,<sup>6</sup> which may have influenced diagnostic and therapeutic decision-making, even though the impact of such guidelines on clinical practice has been disputed.

The German Competence NETwork on Atrial Fibrillation (AFNET), established in 2003 and funded by the Federal Ministry for Education and Research (BMBF), has initiated a large nationwide patient registry to evaluate current daily care of patients with AF in Germany. The study included patients with AF recruited by general practitioners, internists, and cardiologists, all office-based, as well as by community hospitals and tertiary care or specialized referral centres. This is the first report on characteristics and initial management of the patients in the central registry of the German AFNET.

## Methods

The central patient registry of the German AFNET is a multicentre prospective observational study designed to enrol patients at all levels of medical care. The project is organized as a network consisting of 13 regional coordinating centres (10 university departments of cardiology and 3 academic hospitals), each coordinating the activities in the regional hospital departments (59) and in the practices of office-based cardiologists (63), internists (36), and general practitioners (23). The central administrative office of the network is located at the University of Münster, Germany (for details see: [www.kompetenznetz-vorhofflimmern.de](http://www.kompetenznetz-vorhofflimmern.de)).

Enrolment sites were selected to provide a representative picture of current medical practice throughout Germany and include all levels of medical care (see Appendix 3 for participating centres, affiliation, and status). Patients were recruited from medical wards, outpatient clinics, and by office-based physicians (cardiologists, internists, and general practitioners). Management of patients was according to local medical practice. All participating centres agreed to consecutive enrolment of all patients with AF to minimize patient selection bias.

Patients were included in the registry if they were 18 years or older and had AF documented on ECG or Holter ECG recording, either at the time of enrolment or during the preceding 12 months. Patients with atrial flutter as the sole arrhythmia were not included. Informed consent was obtained in written form from all patients included in the registry. Patient follow-up is planned for up to 5 years after enrolment.

## Data collection

The web-based electronic data capture system MARVIN was managed by the Institute for Clinical Cardiovascular Research (IKKF, Munich, Germany; [www.ikkf.de](http://www.ikkf.de)). The primary route of data entry was via the internet. The data-cleaning process included automated range checks, with change requests displayed immediately to the user. A two-step query process included automated queries related to single data fields (edit checks) and manually created queries. The programme

was managed to comply with data protection requirements and security standards (FDA 21, CFR part 11). All information was kept confidential and data transmission was encrypted.

## Data analysis

Data analysis was performed at the 'Institut für Herzinfarktforschung Ludwigshafen an der Universität Heidelberg' (Institute for Research in Myocardial Infarction Ludwigshafen of the University of Heidelberg; [www.herzinfarktforschung.de](http://www.herzinfarktforschung.de)), located in Ludwigshafen/Rhein, Germany. The data are presented as absolute numbers and percentages. Unless otherwise stated, mean values and standard deviations are given. Dichotomous variables were compared by the  $\chi^2$  test (Pearson) and continuous variables by the Mann–Whitney *U*-test. A two-sided alpha level of 0.05 was considered statistically significant. Multivariate analysis was used to adjust for differences in patient characteristics at various levels of medical care on anticoagulation strategy. The statistical computations were performed using SAS, version 9.1 (Cary, NC, USA).

## Results

### Patient enrolment

Between 16 February 2004 and 31 March 2006, a total of 9582 patients were enrolled by 194 participating study centres (for a list of centres, see Appendix 3). 3785 patients (39.5%) were enrolled by the 13 regional coordinating centres. Community hospitals (59 sites) enrolled 2348 (24.5%) patients, office-based cardiologists 2638 (27.5%, 63 sites), and internists and general practitioners 811 (8.5%, 59 sites). Therefore, the survey represents patients treated at all levels of medical care from large university medical centres to office-based general practitioners.

### Patient characteristics on admission or at consultation

Characteristics of the 9582 patients included in the registry are shown in Table 1. Age of the patients ranged from 18 to 98 years (mean age  $68.4 \pm 11.0$ ; 29.2% 75 years or older), and women were older than men (Figure 1), consistent with later onset of AF in women as observed in epidemiological studies.<sup>17</sup> At the time of enrolment into the registry, 1035 patients (10.8%) presented with their first episode of AF, 2893 (30.2%) with paroxysmal AF, 1873 (19.5%) with persistent AF, and 3141 (32.8%) with permanent AF [unknown type of AF in 640 (6.7%) patients, Table 1].<sup>5,18</sup>

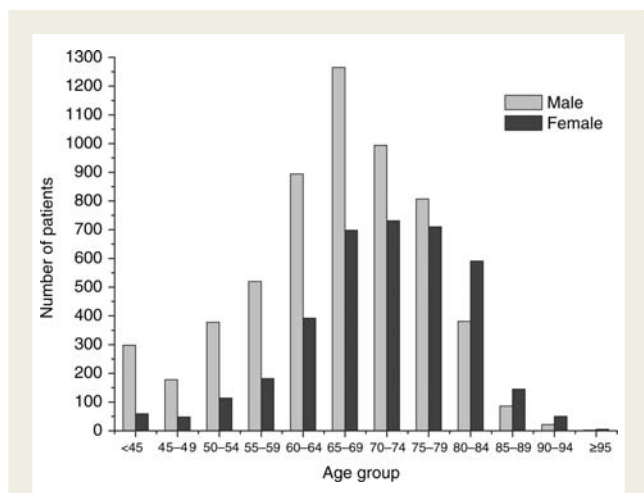
Only 12.4% of the patients were diagnosed to have 'lone AF', implying the absence of detectable concomitant disease known to promote AF. By far the most prevalent concomitant condition was arterial hypertension (69.2% of patients). Other cardiac diseases commonly present were valvular heart disease (36.3%; only 3.7% of which were rheumatic in origin), coronary artery disease (28.1%), symptomatic heart failure [New York Heart Association (NYHA) II to NYHA IV, 29.0%], and various forms of cardiomyopathy (10.7%), all of which tended to be more prevalent in patients with permanent AF compared with paroxysmal or persistent AF (Table 1). The high proportion of patients with valvular heart disease was mostly due to a high prevalence of mitral valve regurgitation, which was reported to be present in 29.1% of the patients, preferentially in patients with persistent (30.3%)

**Table 1** Patient characteristics

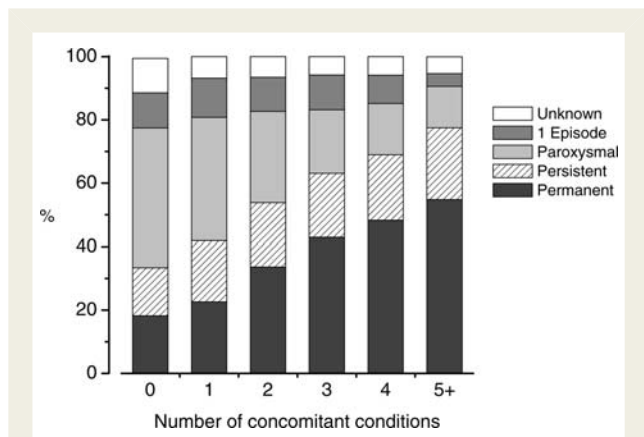
	First detected 10.8% (n = 1035)	Paroxysmal 30.2% (n = 2893)	Persistent 19.5% (n = 1873)	Permanent 32.8% (n = 3141)	P-value
Demographics					
Age (years)	67.0 ± 12.3	65.5 ± 11.3	67.6 ± 11.2	71.7 ± 9.2	*
Female gender (%)	40.1	41.2	35.2	38.7	*
Concomitant disease					
Hypertension (%)	68.9	65.9	70.6	71.1	*
Coronary artery disease (%)	26.8	25.0	28.4	31.0	*
Old infarction (%)	14.5	11.2	14.0	14.5	
Previous PCI/CABG (%)	14.7	16.7	16.6	17.6	
Angina (%)	15.5	12.9	13.2	13.1	
Heart failure (%)	31.6	24.1	41.4	45.2	*
Valvular heart disease (%)	27.7	25.1	37.0	48.1	*
Rheumatic origin (%)	3.1	2.5	3.3	5.3	*
Non-rheumatic origin (%)	24.6	22.6	33.7	42.7	*
Valve replacement (%)	2.4	3.9	4.3	7.6	*
Cardiomyopathy (%)	7.2	6.8	13.6	13.8	*
Tachycardiomyopathy (%)	0.3	0.2	1.0	0.2	*
Hypertrophic (%)	1.7	1.0	1.4	0.7	
Dilated (%)	4.2	3.5	7.2	9.5	*
Other type (%)	1.1	2.0	3.4	3.1	*
Sick sinus syndrome (%)	3.9	8.8	5.3	6.7	*
Chronic obstructive pulmonary disease (%)	10.4	10.2	10.6	13.5	*
Hypothyroidism (%)	5.0	5.7	5.1	5.5	
Overt hyperthyroidism (%)	3.9	3.3	5.1	4.0	
Subclinical hyperthyroidism (%)	3.5	2.8	2.6	2.5	
Idiopathic AF (%)	13.9	17.0	10.0	9.3	*
Cardiovascular risk factors					
Diabetes mellitus (%)	20.5	15.8	21.3	27.6	*
Hyperlipidaemia (%)	48.3	46.8	44.7	45.8	
Current smoker (%)	11.6	8.7	7.4	5.2	*
Previous smoker (%)	32.4	33.9	38.4	37.9	*
No regular exercise (%)	44.6	41.5	46.7	53.3	*
Family history of CAD (%)	27.5	34.2	31.0	27.1	*
Comorbidities					
Previous thrombo-embolism (%)	8.1	11.9	13.8	16.0	*
Stroke (%)	3.7	5.0	6.7	8.5	*
TIA (%)	2.1	3.3	4.0	4.1	
Other thrombo-embolism (%)	2.7	4.3	4.3	5.3	
Prior major bleeding (%)	0.9	1.5	2.2	2.8	*
Malignancy (%)	7.2	7.4	7.3	9.6	*
Peripheral vascular disease (%)	5.2	5.3	6.7	8.7	*
Renal failure (%)	9.2	9.6	11.2	14.5	*
Previous interventions					
Pharmacological conversion (%)	11.1	16.2	8.9	2.6	*
Electrical cardioversion (%)	9.5	17.1	22.7	6.9	*
Catheter ablation (%)	1.1	7.5	3.3	1.9	*
Pacemaker implantation (%)	1.7	7.5	5.2	9.2	*
ICD implantation (%)	1.0	1.3	2.6	2.6	*
Surgery for AF (%)	0.1	0.2	0.1	0.3	

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CAD, coronary artery disease; TIA, transient ischaemic attack; ICD, implantable cardioverter defibrillator.

\*Difference with  $P < 0.001$  among the four AF types.



**Figure 1** Age distribution for men and women enrolled in the central patient registry of the German AFNET. The male/female ratio was 1.6; 22.2% of men and 40.1% of women were 75 years or older.



**Figure 2** Shift of atrial fibrillation type from paroxysmal to permanent in relation to concomitant conditions known to promote atrial fibrillation. Factors counted were age  $\geq 75$  years, hypertension, diabetes, cardiomyopathy, heart failure, valve disease or replacement.

and permanent (39.7%) AF. Diabetes mellitus (21.7%) and lack of regular physical activity (47.4%) were frequently reported and more common in patients with permanent AF (Table 1).

Non-cardiac diseases frequently present were chronic obstructive pulmonary disease, increasing in prevalence from paroxysmal (10.2%) to permanent AF (13.5%), and renal failure, also more common in permanent (14.5%) than paroxysmal (9.6%) AF. This contrasts with thyroid disease, which was distributed equally in all clinical types of AF (11.8–12.8%; Table 1). Previous thromboembolic events were common and present with increasing frequency from first episodes (8.1%) to permanent AF (16.0%). Approximately half of the events were strokes (Table 1).

Permanent AF was strongly associated with the presence of concomitant cardiac and non-cardiac disease and with risk factors for stroke (Figure 2). In the absence of concomitant disease, only 18.7%

of the patients had permanent AF, increasing to 54.8% in patients with five or more concomitant diseases. The increase in permanent AF with the accumulation of co-morbidities was almost exclusive at the cost of paroxysmal AF, with the fraction of patients in persistent AF remaining essentially constant (15.2–22.7%).

There was no relationship between the presence of hyperlipidaemia, angina pectoris, or history of percutaneous coronary intervention or bypass surgery and the clinical type of AF. Current smoking was reported with decreasing frequency in persistent (7.4%) and permanent forms (5.2%) of AF when compared with those presenting with a first episode (11.6%) or paroxysmal AF (8.7%). Previous smoking was reported to be most prevalent in persistent (38.4%) and permanent (37.9%) AF when compared with those presenting with a first episode (32.4%, Table 1;  $P < 0.001$ ).

Symptoms were assessed on the basis of the presence or absence of palpitations, dyspnoea, chest pain, dizziness, or fatigue (see Appendix 1) and NYHA functional class. Symptoms reported most frequently were palpitations, especially in paroxysmal AF (54.9%) or during a first episode (54.3%), which were also the most symptomatic types of AF. Dyspnoea was a frequently reported symptom and most prevalent in persistent (47.5%) and permanent AF (47.5%). Higher degrees of heart failure were much more common in patients with permanent AF (37.3% were classified at least NYHA class II and 13.3% at least NYHA class III) than with paroxysmal AF (18.4% at least NYHA class II and 6.8% at least NYHA class III). The lack of control of heart rate was evident in patients presenting with their first episode of AF (mean heart rate during AF,  $109 \pm 30$  bpm; 45.0% of the patients above 110 bpm) or with paroxysmal AF (mean heart rate,  $100 \pm 29$  bpm; 33.1% of the patients above 110 bpm), possibly also responsible for the more symptomatic nature of these conditions (Table 2).

## Diagnostic procedures used

Transthoracic echocardiography was used preferentially in patients presenting with a first episode of AF (74.0%) and with permanent AF (68.2%, Table 3; only echocardiography performed within 3 months before inclusion was an accepted entry). Chest X-rays were used only in a few patients (18.9%). Thyroid function was reported to be studied in the majority of the patients (57.5% of all patients, usually within the preceding 6 months) and in 64.5% of patients on amiodarone at the time of inclusion.

## Drug therapy

Drug therapy was evaluated at the end of the enrolment visit (discharge from hospital or end of outpatient visit). Information on medication was available for 8962 of 9582 (93.5%) patients (Table 4). Beta-blockers and digitalis were the rate control drugs used most frequently in the overall population (65.7 and 35.5%, respectively). In permanent AF, beta-blockers (59.2%) and digitalis (50.9%) were used more frequently than calcium channel blockers (verapamil 10.2% and diltiazem 1.0%). In the other types of AF, the use of beta-blockers was even more common, ranging from 67.4% in paroxysmal AF to 73.7% in patients with a first detected episode of AF. Digitalis was used less frequently in these types of AF (paroxysmal AF 21.4% and persistent AF 35.2%; Table 4).

**Table 2 Admission/consultation information**

	<b>First detected 10.8% (n = 1035)</b>	<b>Paroxysmal 30.2% (n = 2893)</b>	<b>Persistent 19.5% (n = 1873)</b>	<b>Permanent 32.8% (n = 3141)</b>	<b>P-value</b>
Reason for admission/consultation					
AF (%)	71.7	71.4	66.0	46.5	*
Other cardiovascular disease (%)	22.0	23.3	26.4	43.4	*
Non-cardiovascular disease (%)	6.3	5.3	7.6	10.1	*
Symptoms					
Current AF symptoms (%)	82.6	78.7	76.7	69.6	*
Palpitations (%)	54.3	54.9	41.4	26.1	*
Chest pain (%)	22.7	21.2	18.8	15.1	*
Dyspnoea (%)	44.3	38.7	47.5	47.5	*
Dizziness (%)	27.2	28.7	24.9	21.9	*
Fatigue (%)	49.5	47.6	49.0	38.4	*
No symptoms (%)	17.4	21.3	23.3	30.4	*
Heart failure NYHA class III/IV (%)	11.6	6.8	14.8	13.3	*
Physical examination					
BMI (kg/m <sup>2</sup> )	27.6 ± 4.7	27.5 ± 4.6	27.8 ± 4.6	27.8 ± 4.8	
Systolic BP (mmHg)	132.5 ± 19.8	130.4 ± 18.7	130.3 ± 19.8	133.7 ± 20.3	*
Diastolic BP (mmHg)	78.8 ± 11.9	78.2 ± 10.9	78.8 ± 11.6	80.2 ± 12.2	*
ECG					
Atrial fibrillation (%)	75.4	58.4	88.1	94.7	*
Heart rate in AF (bpm)	108.6 ± 30.2	100.2 ± 28.7	88.0 ± 25.0	79.9 ± 19.9	*
Heart rate in AF >110 bpm (%)	45.0	33.1	15.8	7.4	*
Left BBB (%)	6.0	6.2	8.0	8.8	*
Right BBB (%)	5.5	6.5	9.1	8.2	*
QRS duration (ms)	94.5 ± 23.5	98.5 ± 27.7	102.0 ± 28.0	104.6 ± 30.5	*

BMI, body mass index; BP, blood pressure; BBB, bundle branch block; TTE, transthoracic echocardiography.

\*Difference with  $P < 0.001$  among the four AF types.

The concomitant use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists was very common. In the total study cohort, 47.0% of the patients were treated with ACE inhibitors and 16.2% of the patients were treated with AT II antagonists (Table 4).

## Rate and rhythm control

Rhythm control with electrical or pharmacological cardioversion or ablation was performed in 53.4% of the patients with persistent AF and current AF-related symptoms (details in Appendix 1) and in 47.8% of the patients in persistent AF not reporting AF-related symptoms. However, the use of electrical or pharmacological cardioversion or ablation in patients with persistent AF increased with the number of reported symptoms from 40.8% (no symptoms) to 49.5% (one symptom reported) and 60.6% (all five symptoms present), suggesting a relevant impact of symptom burden on treatment strategy.

Anti-arrhythmic drugs (classes I and III) were given to 21.3% of the patients, primarily to patients with paroxysmal (flecainide, 14.7%; propafenone, 2.9%; sotalol, 5.3%; amiodarone, 13.8%) and persistent AF (flecainide, 7.9%; propafenone, 1.2%; sotalol, 2.0%; amiodarone, 13.1%). In contrast, anti-arrhythmic drugs were

given only occasionally to patients with permanent AF (flecainide, 1.1%; propafenone, 0.5%; sotalol, 2.3%). Amiodarone was given to 4.4% of the patients with permanent AF.

Rhythm control drugs were usually combined with rate control drugs, and 63.4% of the patients on class I agents also received beta-blockers or calcium channel blockers (verapamil or diltiazem). Flecainide was more frequently combined with rate control drugs (66.5%) than propafenone (50.0%). Similarly, the class III drug amiodarone was frequently combined with rate control drugs (beta-blockers, 62.3%; verapamil or diltiazem, 2.5%).

After electrical cardioversion, 16.5% of the patients received class I anti-arrhythmic drugs (flecainide, 14.6% and propafenone, 1.9%), 3.5% sotalol, and 22.9% amiodarone to prevent recurrences of AF. Beta-blockers only were given to 47.8% of the patients after cardioversion, calcium antagonists (verapamil or diltiazem) to 2.5%. In only 8.3% of the patients, no anti-arrhythmic drugs, beta-blockers, or calcium antagonists, were given after electrical cardioversion. Only a rare patient (15/9582) with a risk profile for class I anti-arrhythmic drugs (defined as previous myocardial infarction or coronary bypass surgery or severe LV dysfunction on echocardiography) received class I anti-arrhythmic drugs.



**Table 3** Diagnostics and interventions

	First detected 10.8% (n = 1035)	Paroxysmal 30.2% (n = 2893)	Persistent 19.5% (n = 1873)	Permanent 32.8% (n = 3141)	P-value
Diagnostics <sup>a</sup>					
TTE (%)	74.0	60.3	61.4	68.2	*
Chest X-ray (%)	30.2	17.9	22.3	15.7	*
Holter monitoring (%)	20.2	19.0	17.6	11.3	*
Exercise test (%)	10.7	10.1	12.0	12.4	
TEE (%)	19.6	18.0	20.0	9.0	*
Electrophysiology (%)	1.9	6.7	3.4	1.2	*
Serum TSH measurement (%)	75.8	63.8	66.7	41.9	*
Interventions <sup>b</sup>					
Pharmacological conversion (%)	13.2	9.3	6.2	0.7	*
Electrical cardioversion (%)	24.4	14.0	24.1	2.9	*
Catheter ablation (%)	1.5	11.9	5.7	1.7	*
Pacemaker implantation (%)	2.1	4.8	3.7	2.4	*
ICD implantation (%)	1.4	1.0	0.9	1.1	
AF surgery (%)	0.6	0.8	1.0	0.4	

TTE, transthoracic echocardiography; TEE, transoesophageal echocardiography; ICD, implantable cardioverter defibrillator.

<sup>a</sup>Prior to or during qualifying admission or consultation.

<sup>b</sup>During qualifying admission or consultation.

\*Difference with  $P < 0.001$  among the four AF types.

## Interventions

Ablation procedures for AF have been used frequently even before inclusion into the registry, with 7.5% of the patients in paroxysmal AF and 3.3% of patients in the persistent AF treated previously with an ablation procedure. After enrolment, patients in paroxysmal AF were treated with an ablation procedure in 11.9%, in persistent AF in 5.7%, and in permanent AF in 1.7%. Patients with a first episode received an ablation procedure in only 1.5%. Considering all ablations performed, most of them were applied to patients with paroxysmal AF (64.6%) and persistent AF (20.0%), and only a few (10.3%) were in patients with permanent AF ('long-lasting persistent AF'<sup>19</sup>) or after a first episode (2.9%). Ablation procedures were almost exclusively performed at the regional coordinating centres (10 university departments of cardiology and 3 academic hospitals).

## Anti-thrombotic treatment

Stroke prevention remains one of the primary treatment goals in patients with AF. On the basis of the stroke risk stratification of the ACC/AHA/ESC 2001 Guidelines, 90.8% of the patients in the registry would be considered to be at high or very high risk for stroke, mandating anticoagulation. This includes patients undergoing a cardioversion or ablation procedure. After excluding patients with documented potential contraindications (prior major bleeding or haemorrhagic stroke, 2.5% and malignancy, 8.1%), 67.5% of the 7194 patients requiring anticoagulation did receive oral anticoagulants. A further 3.9% received low-molecular-weight heparin (LMWH), with the intention to provide adequate anticoagulation, resulting in a total of 71.4% of

the eligible patients on anticoagulation therapy (Figure 3 and Table 5). Antiplatelet drugs were given in 16.9% of the patients as the only anti-thrombotic treatment (Figure 3). Still, 11.2% of the patients eligible for anticoagulation received no anti-thrombotic treatment. Of the 710 patients not considered candidates for anticoagulation, 351 (49.4%) received oral anticoagulation (46.2%) or LMWH (3.2%) for anticoagulation purposes, indicating that a significant portion of low-risk patients may be overtreated.

## Discussion

The age distribution of the patients with AF highlights the upcoming dimension of this disease in an ageing population (Figure 1).<sup>1,4,20</sup> With 40.1% of women and 22.2% of men 75 years or older, special requirements and limitations in care for these patients will apply, also pertaining treatment with oral anticoagulants. Rheumatic valvular heart disease, which used to be an important underlying disease for the development of AF,<sup>9,20</sup> was present in only 3.7% of the patients, reflecting a change in the cardiac disease. The contemporary patients with AF are likely to have multiple comorbidities, most importantly hypertension, diagnosed in almost 70% of the patients in this registry, as opposed to 50% in the general population in Germany.<sup>21</sup> Usually, hypertension was accompanied by other cardiac and non-cardiac diseases. The absence of predisposing cardiac diseases resulting in classification as 'lone AF'<sup>5,6,22</sup> was only seen in a small percentage of patients (12.4% of all patients), similar to earlier estimates<sup>23</sup> and results from the Euro Heart Survey (10.2%).<sup>10</sup>

**Table 4 Drug therapy at discharge/end of visit**

	<b>First detected 10.8% (n = 1035)</b>	<b>Paroxysmal 30.2% (n = 2893)</b>	<b>Persistent 19.5% (n = 1873)</b>	<b>Permanent 32.8% (n = 3141)</b>	<b>P-value</b>
<b>Anti-thrombotic</b>					
Low-molecular-weight heparin (%)	12.2	10.1	10.7	5.1	*
Heparin (%)	1.1	0.6	1.3	0.6	<0.05
Oral anticoagulation (%)	47.8	55.6	74.4	70.7	*
Aspirin (%)	30.0	25.8	16.1	20.6	*
Clopidogrel (%)	8.8	6.3	5.9	5.0	*
Combination of the above (%)	17.2	14.2	14.8	9.0	*
None (%)	20.5	17.9	9.0	8.6	*
<b>Anti-arrhythmic/rate control</b>					
<b>Class I (%)</b>					
Quinidine (%)	0.0	0.1	0.1	0.0	
Disopyramide (%)	0.0	0.0	0.1	0.0	
Other class IA (%)	0.0	0.0	0.1	0.0	
Flecainide (%)	3.5	14.7	7.9	1.1	*
Propafenone (%)	0.9	2.9	1.2	0.5	*
Verapamil and quinidine (%)	0.0	0.1	0.1	0.0	
Beta-blocker (class II) (%)	73.7	67.4	70.8	59.2	*
<b>Class III (%)</b>					
Sotalol (%)	1.9	5.3	2.0	2.3	*
Amiodarone (%)	7.1	13.8	13.1	4.4	*
<b>Class IV (%)</b>					
Diltiazem (%)	0.2	0.6	0.7	1.0	
Verapamil (%)	4.8	4.4	5.2	10.2	*
Other class IV (%)	0.0	0.0	0.0	0.0	
Digitalis (%)	28.6	21.4	35.2	50.9	*
<b>Other medication</b>					
ACE inhibitor (%)	48.8	39.1	51.0	51.5	*
AT II antagonist (%)	13.5	15.3	15.5	17.6	<0.01
Dihydropyridine (%)	16.2	12.8	12.0	13.8	
Diuretics (%)	49.1	41.7	57.8	64.7	*
Nitrate (%)	4.8	4.3	6.1	10.9	*
Statin (%)	8.0	10.5	10.2	9.4	
Insulin (%)	2.4	1.7	2.6	3.0	
Oral antidiabetic drugs (%)	5.7	4.2	5.7	7.8	*
Thyroid hormone therapy (%)	7.5	10.6	9.7	8.7	

\*Difference with  $P < 0.001$  among the four AF types.  
Classification of anti-arrhythmic drug according to Vaughan Williams.<sup>34</sup>

### Clinical type of atrial fibrillation

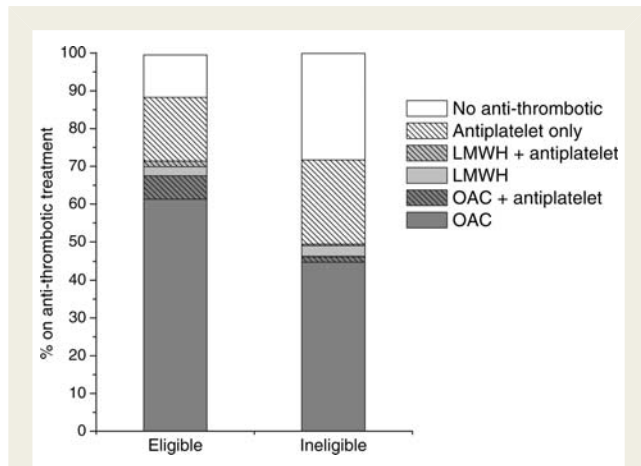
Although classification of AF into different types is clinically useful to select for the appropriate treatment, the shortcomings of such classifications becomes obvious when applied at a single point in time such as at study entry. The later course of the disease or further information emerging might require different treatment decisions or suggests that a different classification may be more appropriate than the one initially attributed. For example, patients initially classified to have permanent AF were at times treated with a successful cardioversion later during their hospital stay. Conflicts in the assignment to the different clinical entities

appear unavoidable from a retrospective point of view, especially as current treatment options have the potential to alter the natural course of the disease. This is highlighted by current catheter ablation techniques, which may provide ‘cure’ from ‘long-lasting persistent’ AF, a path not considered in the current AF classification.

### Rate vs. rhythm control

Current guidelines recommend the decision to treat with either rate or rhythm control to be guided by the symptomatic status of the patient, as no survival benefit of a rhythm control strategy

has been observed.<sup>24–26</sup> In daily clinical practice, other factors appear to importantly influence the treatment strategy. Focusing on the subgroup of patients with persistent AF, the impact of AF-related symptoms on the treatment given appears limited, as



**Figure 3** Anti-thrombotic treatment of patients eligible and ineligible for oral anticoagulation according to the ACC/AHA/ESC Guidelines 2001, applicable during recruitment of the patients. Stroke risk factors are given in Appendix 1. Overall, 71.4% of the eligible patients received anticoagulation (oral anticoagulation or low-molecular-weight heparin for anticoagulation purposes). In patients not eligible, anticoagulation was given in 49.4%. OAC, oral anticoagulation; LMWH, low-molecular-weight heparin; antiplatelet, aspirin, clopidogrel, or ticlopidine.

53.4% of the patients with AF-related symptoms and 47.8% of the patients without symptoms received a rhythm control strategy. Nevertheless, increasing symptom burden clearly favoured a rhythm control strategy. Similar observations were made in the Euro Heart Survey, in which 44% of the patients in the absence of symptoms and 67% with symptoms received rhythm control treatment.<sup>10</sup> Follow-up data from the AFNET registry will allow assessment of long-term effects of treatment strategies on outcome including complications.

## Interventions

Acute success of cardioversions strongly depends on the type of AF, which is very high in patients with a first episode of AF, irrespective of whether pharmacological or electrical conversion was applied. In patients with persistent AF, pharmacological conversion had a much lower success rate (55.9%) than electrical cardioversion (86.8%). The success rate of electrical cardioversion compares well with the success rates in controlled trials,<sup>27,28</sup> suggesting that the results of these trials can be transferred into routine care.

The frequency of catheter ablation applied to patients in this registry already reflects the recent surge in AF ablation procedures in daily clinical practice.<sup>29</sup> This relates to procedures performed before enrolment as well as after inclusion in the registry. In fact, the rate of AF ablation is more in line with the latest version of the ACC/AHA/ESC guidelines on AF<sup>6</sup> published after the patient enrolment ended. This indicates a rapid communication of novel

**Table 5** Stroke risk factors

	First detected 10.8% (n = 1035)	Paroxysmal 30.2% (n = 2893)	Persistent 19.5% (n = 1873)	Permanent 32.8% (n = 3141)	P-value
Stroke risk factors					
Age ≥75 years (%)	27.7	19.9	26.3	39.0	*
Heart failure or LVEF ≤35% or severely impaired systolic LV function on TTE (%)	28.4	18.8	35.7	36.8	*
Hypertension (%)	68.9	65.9	70.6	71.1	
Mitral stenosis (%)	0.9	1.2	2.2	3.3	*
Valve replacement (%)	2.4	3.9	4.3	7.6	*
Stroke/TIA (%)	5.4	7.8	9.8	11.6	*
Age 60–74 years and diabetes or CAD (%)	13.6	15.5	18.0	17.1	
At least one of the above (%)	82.5	77.4	86.3	90.2	*
Overt hyperthyroidism (%)	3.9	3.3	5.1	4.0	
Mean CHADS <sub>2</sub> score	1.6 ± 1.1	1.4 ± 1.1	1.8 ± 1.2	2.0 ± 1.3	*
CHADS <sub>2</sub> score ≥2 (%)	49.4	38.8	53.4	62.1	*
CHADS <sub>2</sub> score ≥3 (%)	20.0	15.5	26.8	32.7	*
Contraindications					
Major bleeding (%)	0.9	1.5	2.2	2.8	*
Prior cerebral haemorrhage (%)	0.1	0.4	0.5	0.6	
Malignancy (%)	7.2	7.4	7.3	9.6	*

LVEF, left ventricular ejection fraction; TTE, transthoracic echocardiography; TIA, transient ischaemic attack; CAD, coronary artery disease; CHADS<sub>2</sub>, stroke-risk index: recent congestive heart failure, history of hypertension, age ≥75 years, diabetes mellitus (1 point each), and prior cerebral ischaemia (2 points).<sup>35</sup>

\*Difference with  $P < 0.001$  among the four AF types.



therapeutic modalities within the AFNET study centres to provide optimal care to the patients.

## Anticoagulation

Prevention of stroke remains a major treatment goal in AF and is usually achieved by the administration of oral anticoagulants to patients considered at high risk for stroke.<sup>5,7,30,31</sup> Reports from the last 15 years, however, indicate that oral anticoagulation remains significantly underused in AF.<sup>32,33</sup> Based on the ACC/AHA/ESC 2001 guidelines,<sup>5</sup> effective throughout enrolment of the patients in this registry, 90.8% of the patients included would be considered at high or very high risk for stroke, mandating anticoagulation therapy (Figure 3). Of 7194 patients eligible, 5136 (71.4%) received anticoagulation (oral anticoagulation or LMWH for anticoagulation purpose), which ranks among the highest rates reported. It is similar to the anticoagulation rate reported in the Euro Heart Survey (67%), which was conducted primarily among specialized centres of cardiology in Europe, most of them supported by an anticoagulation clinic to monitor the INR.<sup>10</sup> The similarity in the rate of anticoagulation may relate to the fact that the majority of the patients in this registry were also recruited by specialized university hospitals and cardiologists (together 67.0%).

Considering that 28.4% of the patients eligible for oral anticoagulation did not receive such a treatment, it has to be kept in mind that in clinical practice, anticoagulation treatment is highly dependent on the individual patient and takes into account factors such as age, feasibility of adequate monitoring of therapy, co-morbidities, and the patient's lifestyle and personal preference. Thus, the decision not to give anticoagulant therapy for a patient eligible for anticoagulation may still be the most appropriate strategy for that individual.

In contrast, anticoagulation therapy (oral anticoagulation or LMWH) was also given to 351 of the 710 (49.4%) patients with a low or very low risk of stroke when anticoagulation is not recommended by ACC/AHA/ESC 2001 guidelines. Even though half of the patients at low or very low risk of stroke received oral anticoagulation, this is, by absolute numbers, only a small fraction of the patients. In some of these patients, diseases other than AF (e.g. prior pulmonary embolism or deep venous thrombosis, pulmonary hypertension) may have justified oral anticoagulation. Still, some of them appear to have been exposed to the inconvenience of oral anticoagulation, along with the risk of bleeding, without any foreseeable benefits.

## Limitations

The inclusion of various levels of medical care is a major advantage of this registry and will help gain a more representative picture of patients with AF than previous registries focusing on selected patients from specialized centres of cardiology.<sup>9,10</sup> Although a balanced recruitment of patients for this registry was intended, university and academic medical centres contributed slightly more patients than smaller hospitals and practising cardiologists. Compared with these three groups, patients cared for by internists and general practitioners were significantly underrepresented. This has to be taken into account when extrapolating from these data to the general population.

## Conclusions

Most patients included in the registry have AF associated with one or multiple concomitant conditions, most importantly hypertension. Although the sudden onset of AF may suggest it to be an acute disease, it has to be recognized that AF originates from long-term substrate alterations by cardiac and non-cardiac diseases. These data support current 'comprehensive' treatment strategies for the prevention of AF in general and for the prevention of progression to permanent AF. The use of oral anticoagulation in high-risk patients is among the highest reported, indicating that the need for anticoagulation in these patients is well established in daily medical care for patients with AF in Germany. In contrast, decisions on rate and rhythm control do not appear to be strictly guided by current guideline recommendations. Long-term follow-up of the patients in this registry will determine the consequences of guideline adherence on complications and survival.

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## Appendix 1: definitions

### First detected episode of atrial fibrillation

Episode of AF diagnosed for the first time, recognizing that there may be uncertainty about the duration of the episode and about previous undetected episodes.

### Paroxysmal atrial fibrillation

Recurrent AF that terminates spontaneously and generally lasts less than or equal to 7 days (usually <24 h).

### Persistent atrial fibrillation

Recurrent or sustained AF that does not terminate spontaneously and usually lasts more than 7 days; termination with pharmacological therapy or electrical cardioversion does not change the designation.

### Permanent atrial fibrillation

Long-standing AF in which cardioversion has failed or has not been attempted.

### Idiopathic/lone atrial fibrillation

Applies to young individuals under 60 years without clinical or echocardiographic evidence of cardiac disease.

## Symptomatic atrial fibrillation

The presence of one or more of the following symptoms: palpitations, chest pain, dyspnoea, dizziness, fatigue.

## Rhythm control strategy

A rhythm control strategy was assumed when pharmacological or electrical cardioversion was performed or planned, or ablation for AF performed or planned, or class IA, IC, or III anti-arrhythmic drugs (Vaughan Williams classification<sup>34</sup>) were prescribed.

## Rate control strategy

Patients were considered on rate control if no drugs or interventions used for rhythm control strategy were applied.

## Eligible for anticoagulation

Eligibility for anticoagulation was decided on the basis of the criteria of the ACC/AHA/ESC Guidelines 2001<sup>5</sup> and included the following risk factors for stroke: age  $\geq 60$  years and diabetes or coronary artery disease, age  $\geq 75$  years, heart failure, left ventricular ejection fraction  $\leq 0.35$ , overt hyperthyroidism, hypertension, mitral valve stenosis, valve replacement, or prior thrombo-embolism. Patients undergoing pharmacological or electrical cardioversion or catheter ablation were also considered to be eligible for anticoagulation. Patients with potential contraindications for oral anticoagulation, defined as prior cerebral haemorrhage, major bleeding, or malignancy were excluded.

## Not eligible for anticoagulation

If not meeting the above criteria for eligibility, patients were considered ineligible for oral anticoagulation.

## Low-molecular-weight heparin for anticoagulation

When low-molecular-weight heparin was used as bridging therapy with initiation of oral anticoagulation within 7 days, it was counted as oral anticoagulation therapy at the time of discharge.

## Mean New York Heart Association class

Only patients classified as NYHA class I–IV were included in the calculation.

## Appendix 2: organization of the AFNET registry

The German Competence Network on Atrial Fibrillation (AFNET)—founded in 2003—is an interdisciplinary national research network sponsored by the Federal Ministry of Education and Research (BMBF). The network currently consists of clinicians in more than 100 hospitals and more than 200 office-based cardiologists, internists, and general practitioners and university-based researchers coordinating the activities. AFNET aims at improving care of patients with AF by promoting research, medical services, and information in emerging diagnostic and therapeutic fields in AF.

*Board:* G.B. (Speaker), Münster; Thomas Meinertz, Hamburg; U.R., Dresden; G.S., Munich.

*Steering Committee:* Thomas Fetsch, München; Andreas Götte, Magdeburg; P.K., Münster; T.L., Bonn; M.O., Brandenburg; Karl Wegscheider, Hamburg; Thomas Weiß, Münster.

*Advisory Board:* Maurits Allesie (Maastricht, The Netherlands); Peter Bauer (Vienna, Austria); Stefan Gesenhues (Ochtrup, Germany); Robert Hatala (Bratislava, Slovakia); Lukas Kappenberger (Lausanne,

Switzerland); Ruth Strasser (Dresden, Germany); Hein J.J. Wellens (Maastricht, The Netherlands); Karl Werdan (Halle, Germany); Stefan Willich (Berlin, Germany).

## Appendix 3: contributing centres

### Reginal coordinating centres

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