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FASTTRACK CLINICAL RESEARCH
Arrhythmia/electrophysiology

In-hospital mortality of patients with atrial arrhythmias: insights from the German-wide Helios hospital network of 161 502 patients and 34 025 arrhythmia-related procedures

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Aims Atrial fibrillation (AFib) and atrial flutter (AFlut) are common arrhythmias with increased use of invasive procedures. A steady re-evaluation of relevant safety endpoints is recommended and both quality management and pay-for-performance programs are evolving. Therefore, the aims of this study were (i) to investigate and report overall in-hospital mortality and mortality of invasive arrhythmia-related procedures and (ii) to identify mortality predictors in a German-wide hospital network.

Methods and results Administrative data provided by 78 Helios hospitals between 2010 and 2017 were examined using International Statistical Classification of Diseases and Related Health Problems- and Operations and Procedures-codes to identify patients with AFib or AFlut as main discharge diagnosis or secondary diagnosis combined with invasive arrhythmia-related interventions. In 161 502 patients, in-hospital mortality was 0.6% with a significant decrease from 0.75% to 0.5% ($P < 0.01$) during the observational period. In multivariable analysis, age [odds ratio (OR) 2.69, 95% confidence interval (CI) 2.36–3.05; $P < 0.01$], high centre volume (OR 0.57, 95% CI 0.50–0.65; $P < 0.01$), emergency hospital admission (OR 1.57, 95% CI 1.38–1.79; $P < 0.01$), and Charlson Comorbidity Index (CCI, OR 4.95, 95% CI 4.50–5.44; $P < 0.01$) were found as independent predictors of in-hospital mortality. Mortality rates were 0.05% for left atrial catheter ablation (CA, $n = 21\,744$), 0.3% for right atrial CA ($n = 9972$), and 0.56% for implantation of a left atrial appendage occluder ($n = 2309$), respectively.

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Conclusion We analysed for the first time in-hospital mortality rates of patients with atrial arrhythmias in a German-wide, multi-centre administrative dataset. This allows feasible, comparable, and up-to-date performance measurement of clinically important endpoints in a real-world setting which may contribute to quality management programs and towards value-based healthcare.

Keywords Atrial fibrillation • Atrial flutter • In-hospital mortality • Catheter ablation

Introduction

Atrial fibrillation (AFib) and atrial flutter (AFlut) are common arrhythmias with increasing incidences and arrhythmia-related hospitalization rates.[1,2] Corresponding to demographic changes, patients with AFib are becoming older and suffer from a growing number of comorbidities.[3] On the other hand, AFib itself is associated with the development of congestive heart failure, cerebrovascular events, and mortality.[4–6] Even AFlut can contribute relevantly to morbidity by the induction of tachycardiomyopathy.[7] Due to evolved therapeutic strategies, the outcome of patients with atrial arrhythmias has improved over the last years.[8] Besides restoring sinus rhythm, additional procedures like interventional implantation of a left atrial appendage occluder (LAAO) are performed with rising popularity to prevent secondary disorders. The growing number of interventions related to atrial arrhythmias necessitates a continual evaluation of procedure-related adverse events. Although mortality rates were described in the setting of different interventional procedures, real-life data regarding in-hospital mortality in patients with AFib and AFlut are rare for Germany. Therefore, we analysed a multi-centre, German-wide database to determine the in-hospital mortality of patients with main diagnosis of AFib or AFlut.

Methods

Data source

Between 1 January 2010 and 31 December 2017, data of 1 135 697 hospitalized patients with atrial arrhythmias were collected in an administrative database (according to Sec 21 KHEntgG) of 85 hospitals of the Helios group. All patients ($n = 159\,336$) with main discharge diagnosis of AFib and AFlut were identified for in-hospital mortality analysis using the encoded diagnoses of the International Statistical Classification of Diseases and Related Health Problems [ICD-10-GM (German Modification)]. This cohort has been expanded by patients with secondary diagnosis of AFib or AFlut and arrhythmia-related procedures during index hospitalization resulting in a total number of 161 502 patients for further analysis. Arrhythmia-related procedures were identified via the Operations and Procedures-codes [OPS (German adaptation of the International Classification of the Procedures in Medicine of the World Health Organization, version 2017)] within hospital discharge data. Numbers of consecutive implantations of LAAO and left atrial (LA), right atrial (RA), or biatrial catheter ablations (CA) were measured. If biatrial CA was performed, the left-sided procedure was considered more relevant to the risk of complications and mortality. Detailed information about ICD- and OPS-codes is listed in the Supplementary material online, *Tables S1 and S2*. In-hospital mortality was recorded on the basis of hospital discharge data. As no information regarding the cause of death was available due to data structure, ICD- and OPS-codes were analysed for indications of several acute cardiovascular diseases and other potential causes of death within patients who died during hospitalization (Supplementary material online, *Tables S3 and S4*). Nevertheless, no causal relationship can be derived from these administrative data. CHA_2DS_2-VASc score was estimated via specific ICD-codes as listed in the Supplementary material online, *Table S5*. Charlson Comorbidity Index (CCI) was calculated as described in previous publications in a slightly modified form (Supplementary material online, *Table S6*).[9] Patients undergoing CA in the context of cardiac surgery, patients with main diagnosis of atrial arrhythmias other than AFib or AFlut and patients younger than 20 years of age were excluded. The analysis was confirmed by the ethics committee of the University of Leipzig (128/17-ek) and complies to the Declaration of Helsinki. Patient data were stored in an anonymized form, and data use was approved by the Helios Kliniken GmbH data protection authority.

Hospitals ($n = 78$), of which patients were included into this registry, are listed in the Supplementary material online, *Table S7*. Centre volume was defined separately for the total study population and for each subgroup of arrhythmia-related procedures via the upper quartile of contributed patients per centre as a division by medians would have led to a 10:1 proportion of patient numbers in high- vs. low-volume centres. This definition was chosen as there are no consistently valid definitions for the different procedures being examined except from LA CA. In consequence, 20 hospitals were considered high-volume centres for overall mortality analysis which included at least 320 patients on average per year into the database (64.7% of all patients). For LAAO procedures, LA and RA CAs, 6, 7, and 9 centres were labelled as high-volume centres with a minimum of 12 (average $n = 30$), 104 (average $n = 304$), and 52 (average $n = 87$) interventions per year, respectively. This corresponds to earlier definitions of high-volume centres in comparable studies.[10,11]

Statistical analysis

Administrative data were extracted from QlikView (QlikTech, Radnor, Pennsylvania, USA). Statistical analysis was performed using SPSS version 17.0 (IBM Deutschland GmbH, Ehningen, Germany). Baseline characteristics were compared between patient groups with Student's t-test (for continuous variables) or with Fisher's exact probability test (for dichotomous variables). To identify possible reasons for a change of in-hospital mortality rates over time, a stepwise approach was used. First, a trend analysis during the inclusion period was performed for each variable of the baseline characteristics using Jonckheere-Terpstra-test. Effect size was measured via Kendalls-Tau-test. Covariates with significant results in trend analysis and time intervals were included in a logistic regression model to identify independent predictors of changing mortality rates. Kruskal-Wallis test was used to compare the three subgroups of arrhythmia-related procedures. To identify baseline variables with a significant association with in-hospital mortality, univariable odds ratios (OR) were calculated and tested with the use of Fisher's exact probability test. Exact 95% confidence intervals (CI) for these ORs were calculated. To identify independent baseline predictors for in-hospital mortality, we next performed a stepwise forward selection logistic regression analysis including variables with a significant association according to univariable analysis ($P < 0.10$). The entry criterion was set at $P < 0.05$ and the exit criterion was set at $P > 0.10$. CHA_2DS_2-VASc score was not taken into account for

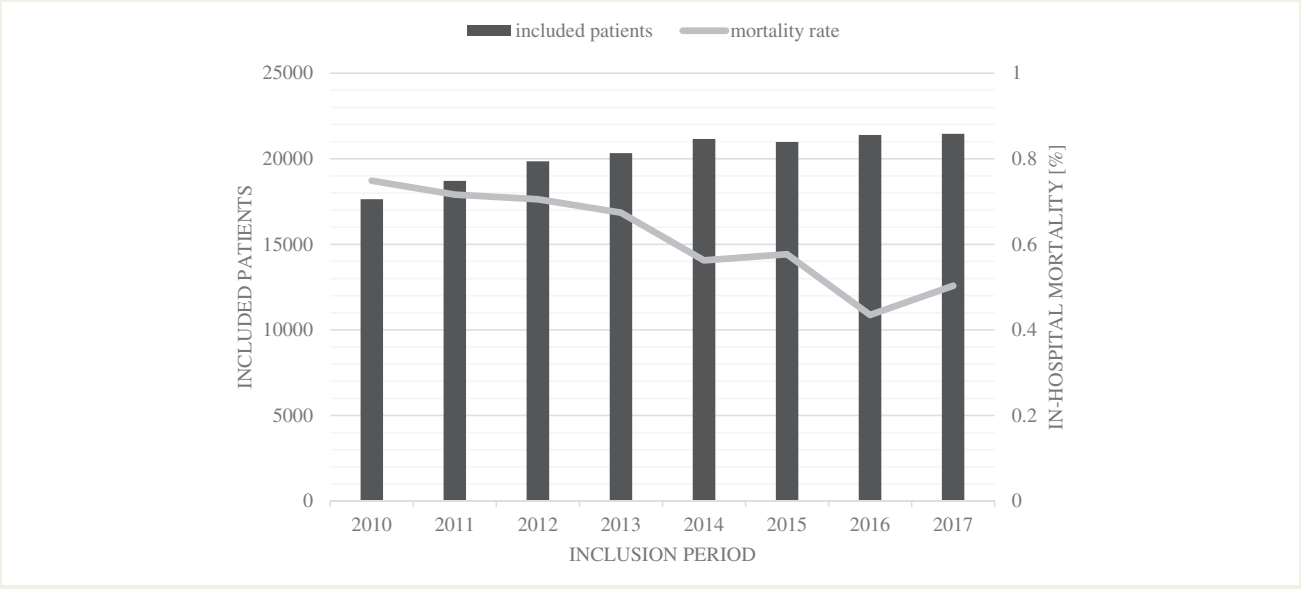

Figure 1 Numbers of included patients and mortality rates per year.

multivariable analysis to avoid interferences with CCI due to overlapping components. A double-sided $P \leq 0.05$ was considered statistically significant.

Results

In-hospital mortality

Of 1 135 697 patients with main or secondary diagnosis of AFib or AFlut, 161 502 patients fulfilled the inclusion criteria. Overall in-hospital mortality was 0.6% with a significant decrease within the inclusion period (0.75% in 2010 vs. 0.5% in 2017, $P < 0.01$, *Figure 1*). Several variables within the baseline characteristics including CCI and almost all of its components, age, and the proportions of high-volume centre treatment and emergency hospital admission revealed significant trends of either increasing or decreasing frequency over time. Detailed information about trend analysis and effect size is provided in the Supplementary material online, *Table S8*. However, in regression analysis, none of those variables was associated with changes in annual mortality rates. Patients with main diagnosis of AFlut had a lower in-hospital mortality than those with main diagnosis of AFib (0.3% vs. 0.61%, $P < 0.01$). Baseline characteristics are summarized in *Table 1*.

Predictors of overall in-hospital mortality

In univariable analysis, in-hospital mortality was associated with higher age, female gender, and a higher CCI (*Table 2*). In detail, almost every component of CCI was over-represented in patients of the mortality-group except of rheumatic disease and AIDS/HIV infection. Multivariable analysis was performed for the total study cohort using two different models. A first model included age, gender, centre volume, the way of hospital admission, and CCI. In a second analysis, the individual CCI components were investigated. In both models, a higher age, emergency hospital admission, and treatment in a low-volume centre were significantly associated with an increased in-hospital mortality rate (*Figure 2*). Several components of CCI (*Table 3*) and CCI itself remained as independent predictors for in-hospital mortality (*Figure 2*). All results of univariable and multivariable analysis are listed in *Tables 2* and *3*.

Arrhythmia-related procedures

A subgroup analysis for each arrhythmia-related procedure was performed. In total, 34 025 invasive arrhythmia-related procedures including 21 744 LA CAs (21.8% in low-volume centres), 9972 RA CAs (36.9% in low-volume centres) and 2309 LAAO procedures (36.4% in low-volume centres) were identified. There were relevant differences with a lower age and less common comorbidities in the group of LA CA compared to the groups of RA CA and LAAO procedures (*Table 1*). The number of procedures per year was constant for RA CAs but increased significantly for LA CAs ($n = 1521$ in 2010 to $n = 3977$ in 2017, $P < 0.01$) and LAAO procedures ($n = 66$ in 2010 to $n = 401$ in 2017, $P < 0.01$) during the inclusion period. Baseline characteristics for the subgroups are listed in *Table 1*.

In-hospital mortality in arrhythmia-related procedures

Mortality rates were 0.05% for LA CA, 0.30% for RA CA, and 0.56% for LAAO procedures, respectively. For each procedure, there was a numerically higher mortality rate in low-volume compared to high-volume centres with a statistically significant difference for LA CA (0.11% vs. 0.03%, $P = 0.03$) but not for RA CA (0.33% vs. 0.29%, $P = 0.73$) and LAAO procedures (0.83% vs. 0.41%, $P = 0.19$).

Predictors of overall in-hospital mortality in arrhythmia-related procedures

Similar to the analysis of the entire study cohort, two different multivariable models were used. In patients who underwent LA CA, centre volume, CCI, and its components chronic kidney disease and

Table 1 Baseline characteristics of the total study cohort

Variable	Total	LA catheter ablation (1)	RA catheter ablation (2)	LAAO (3)	*P*-value 1 vs. 2	*P*-value 1 vs. 3	*P*-value 2 vs. 3
n	161 502	21 744	9972	2309	—	—	—
Female (%)	45.7	39.0	26.8	41.3	<0.01	0.09	<0.01
Age (years)	69.3 ± 11.8	63.3 ± 10.3	67.8 ± 10.9	75.0 ± 7.8	<0.01	<0.01	<0.01
CHA_2DS_2-VASc score	3 (IQ 2–4)	2 (IQ 1–3)	3 (IQ 2–4)	4 (IQ 3–5)	<0.01	<0.01	<0.01
0 (%)	5.8	10.4	7.0	0.2	—	—	—
1 (%)	12.9	20.1	15.0	2.9	—	—	—
2 (%)	17.9	23.9	19.3	10.4	—	—	—
3 (%)	21.8	21.8	22.2	18.5	—	—	—
4 (%)	21.5	15.0	19.8	26.7	—	—	—
≥5 (%)	20.1	8.8	16.7	41.3	—	—	—
Charlson Comorbidity Index	1 (IQ 0–2)	1 (IQ 0–2)	1 (IQ 0–3)	3 (IQ 1–4)	<0.01	<0.01	<0.01
01 Myocardial infarction (%)	4.7	3.9	7.3	10.8	<0.01	<0.01	<0.01
02 Congestive heart failure (%)	32.4	27.8	37.7	43.8	<0.01	<0.01	<0.01
03 Peripheral vascular disease (%)	6.8	7.9	8.0	19.9	0.97	<0.01	<0.01
04 Cerebrovascular disease (%)	3.8	2.1	3.7	13.1	<0.01	<0.01	<0.01
05 Dementia (%)	2.4	0.1	0.7	3.2	<0.01	<0.01	<0.01
06 Chronic pulmonary disease (%)	7.9	4.5	9.3	12.3	<0.01	<0.01	<0.01
07 Rheumatic disease (%)	1.0	0.8	0.7	1.1	0.12	0.11	0.15
08 Peptic ulcer disease (%)	0.5	0.5	0.2	0.9	<0.01	0.01	<0.01
09 Mild liver disease (%)	1.6	1.2	1.5	4.0	0.18	<0.01	<0.01
10 Diabetes - chronic complications (%)	14.4	10.4	16.1	17.1	<0.01	<0.01	0.09
11 Diabetes + chronic complications (%)	5.4	3.3	7.1	18.7	<0.01	<0.01	<0.01
12 Hemiplegia or paraplegia (%)	1.1	0.4	0.8	4.2	<0.01	<0.01	<0.01
13 Chronic kidney disease (%)	23.7	17.1	23.9	53.4	<0.01	<0.01	<0.01
14 Any malignancy (%)	1.8	0.6	2.1	2.3	<0.01	<0.01	0.76
15 Moderate or severe liver disease [%]	0.2	0.2	1.0	1.7	0.39	<0.01	<0.01
16 Metastatic solid tumour (%)	0.4	<0.1	0.3	0.2	<0.01	<0.01	0.34
17 AIDS/HIV (%)	<0.1	0	0	0	1.00	1.00	1.00
Centre volume					<0.01	<0.01	0.67
Low-volume centre (%)	35.3	21.8	36.9	36.4	—	—	—
High-volume centre (%)	64.7	78.2	63.1	63.6	—	—	—
Death (%)	0.60	0.05	0.30	0.56	<0.01	<0.01	0.11

IQ, interquartile range; LA, left atrial; LAAO, left atrial appendage occlude; RA, right atrial.

hemiplegia/paraplegia were significantly associated with fatal outcomes in univariable analysis. In multivariable analysis, only CCI remained as an independent predictor of in-hospital mortality (*Table 4*). In patients who underwent RA CA, age, and CCI were found to be significantly predictive in univariable analysis. Moreover, several CCI components were associated with in-hospital death (*Table 5*). In the first multivariable model, CCI remained highly predictive for in-hospital mortality, mainly driven by its components of congestive heart failure, mild liver disease, peptic ulcer disease, and history of malignant diseases as shown in the second multivariable model (*Table 5*). In patients with LAAO procedures, female gender, CCI, a history of congestive heart failure, and several cerebral and cerebrovascular diseases were associated with fatal outcomes in univariable analysis. In multivariable analysis, CCI was significantly associated with in-hospital mortality. Marginal results were obtained for female gender in multivariable analysis. The CCI components of congestive heart failure and hemiplegia/paraplegia were associated with mortality in the second multivariable model of patients who underwent LAAO procedures (*Table 6*).

Discussion

Atrial arrhythmias are of rising medical and socio-economic relevance and a constant re-evaluation of outcomes and success rates of arrhythmia-related procedures is necessitated.[12,13] In this study, we investigated overall in-hospital mortality and mortality related to invasive procedures in patients with AFib and AFlut and identified characteristics associated with fatal outcomes. To the best of our knowledge, this is the largest real-life dataset of patients with atrial arrhythmias in Germany and the first to show an association of CCI with in-hospital mortality in a cohort of patients with AFib and AFlut as well as in subcohorts undergoing AFib/AFlut-related procedures.

Table 2 Event rates and univariable analysis of the total study cohort

Variable	In-hospital death		*P*-value
	% (*n*/*N*)	OR (95% CI)	
Gender			
Male	0.5 (403/87 753)		
Female	0.8 (581/73 749)	1.72 (1.52–1.96)	<0.01
Age (years)			
≤64	(52/49 286)		
65–74	0.3 (132/52 796)	2.37 (1.72–3.27)	<0.01
≥75	1.3 (800/59 420)	12.9 (9.76–17.1)	<0.01
CHA_2DS_2-VASc score			
0–1	0.1 (29/30 218)		
2–3	0.4 (250/64 208)	4.07 (2.77–5.98)	<0.01
≥4	1.1 (705/67 076)	11.1 (7.63–16.0)	<0.01
Charlson Comorbidity Index			
0–1	0.1 (72/101 752)		
2–4	1.0 (517/5087)	14.7 (11.5–18.9)	<0.01
≥5	4.1 (395/9663)	60.2 (46.8–77.4)	<0.01
01 Myocardial infarction			
No	0.6 (884/153 891)		
Yes	1.3 (100/7611)	2.30 (1.87–2.84)	<0.01
02 Congestive heart failure			
No	0.3 (327/109 402)		
Yes	1.3 (657/52 100)	4.26 (3.73–4.87)	<0.01
03 Peripheral vascular disease			
No	0.6 (883/150 443)		
Yes	0.9 (101/11 059)	1.56 (1.27–1.92)	<0.01
04 Cerebrovascular disease			
No	0.5 (826/155 305)		
Yes	2.5 (158/6197)	4.89 (4.12–5.81)	<0.01
05 Dementia			
No	0.5 (768/157 651)		
Yes	5.6 (216/3851)	12.1 (10.4–14.2)	<0.01
06 Chronic pulmonary disease			
No	0.6 (825/148 739)		
Yes	1.2 (159/12 763)	2.26 (1.91–2.68)	<0.01
07 Rheumatic disease			
No	0.6 (974/159 846)		
Yes	0.6 (10/1656)	0.99 (0.53–1.85)	0.98
08 Peptic ulcer disease			
No	0.6 (965/160 691)		
Yes	2.3 (19/811)	3.97 (2.51–6.29)	<0.01
09 Mild liver disease			
No	0.6 (954/158 938)		
Yes	1.2 (30/2564)	1.96 (1.36–2.83)	<0.01
10 Diabetes - chronic complications			
No	0.6 (815/138 184)		
Yes	0.7 (169/23 318)	1.23 (1.04–1.45)	0.02
11 Diabetes + chronic complications			
No	0.6 (883/152 701)		
Yes	1.1 (101/8801)	1.99 (1.62–2.46)	<0.01
12 Hemiplegia or paraplegia			
No	0.6 (911/159 725)		

Continued

Table 2 *Continued*

Variable	In-hospital death		*P*-value
	% (*n*/*N*)	OR (95% CI)	
Yes	4.1 (73/1777)	7.47 (5.86–9.52)	<0.01
13 Chronic kidney disease			
No	0.4 (544/123 159)		
Yes	1.1 (440/38 343)	2.62 (2.31–2.97)	<0.01
14 Any malignancy			
No	0.6 (892/158 526)		
Yes	3.1 (92/2976)	5.64 (4.53–7.01)	<0.01
15 Moderate or severe liver disease			
No	0.6 (976/161 183)		
Yes	2.5 (8/319)	4.22 (2.09–8.54)	<0.01
16 Metastatic solid tumour			
No	0.6 (945/160 893)		
Yes	6.4 (39/609)	11.6 (8.32–16.1)	<0.01
17 AIDS/HIV			
No	0.6 (984/161 496)		
Yes	0.0 (0/6)	0.99 (0.99–1.00)	1.00
Centre volume			
Low	1.0 (543/57 013)		
High	0.4 (441/104 489)	0.44 (0.39–0.50)	<0.01
Type of hospital admission			
Non-emergency	0.4 (409/96 258)		
Emergency	0.9 (575/65 244)	2.08 (1.84–2.37)	<0.01
Arrhythmia-related procedure during hospitalization			
No	0.7 (913/127 486)		
Yes	0.2% (53/34 025)	0.21 (0.16–0.28)	<0.01

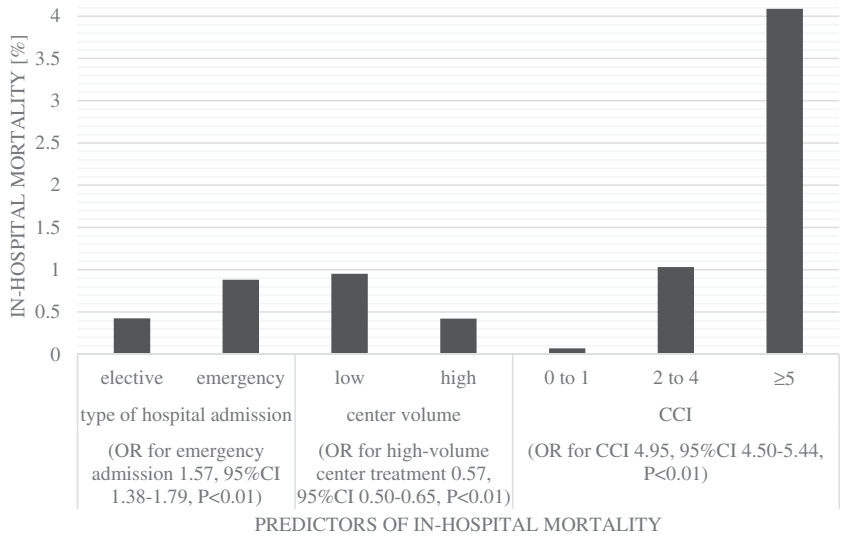

Figure 2 In-hospital mortality rates of the total study cohort in dependence of the way of hospital admission, centre volume, and Charlson Comorbidity Index.

Table 3 Multivariable regression analysis of the total study cohort

Variable	Multivariable analysis (including CCI)		Multivariable analysis (including CCI components)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Gender (female)	1.17 (1.02–1.33)	0.02	1.11 (0.97–1.27)	0.13
Age	2.69 (2.36–3.05)	<0.01	2.88 (2.53–3.27)	<0.01
Charlson Comorbidity Index	4.95 (4.50–5.44)	<0.01	—	—
01 Myocardial infarction	—	—	1.59 (1.28–1.97)	<0.01
02 Congestive heart failure	—	—	2.94 (2.56–3.38)	<0.01
03 Peripheral vascular disease	—	—	1.12 (0.91–1.39)	0.29
04 Cerebrovascular disease	—	—	1.61 (1.29–2.01)	<0.01
05 Dementia	—	—	4.47 (3.78–5.28)	<0.01
06 Chronic pulmonary disease	—	—	1.53 (1.28–1.82)	<0.01
08 Peptic ulcer disease	—	—	2.36 (1.47–3.79)	<0.01
09 Mild liver disease	—	—	1.55 (1.05–2.27)	0.03
10 Diabetes - chronic complications	—	—	0.98 (0.83–1.17)	0.83
11 Diabetes + chronic complications	—	—	0.94 (0.75–1.17)	0.56
12 Hemiplegia or paraplegia	—	—	2.54 (1.86–3.48)	<0.01
13 Chronic kidney disease	—	—	1.11 (0.97–1.28)	0.13
14 Any malignancy	—	—	3.12 (2.37–4.11)	<0.01
15 Moderate or severe liver disease	—	—	2.19 (1.03–4.67)	0.04
16 Metastatic solid tumour	—	—	3.81 (2.49–5.82)	<0.01
High-volume centre treatment	0.57 (0.50–0.65)	<0.01	0.62 (0.54–0.70)	<0.01
Emergency hospital admission	1.57 (1.38–1.79)	<0.01	1.59 (1.39–1.82)	<0.01

Table 4 Univariable and multivariable regression analysis of patients who underwent left atrial catheter ablation

Variable	Univariable analysis			Multivariable analysis (including CCI)		Multivariable analysis (including CCI components)	
	Mortality % (*n*/*N*)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Charlson Comorbidity Index							
0–1	<0.1 (2/15 902)						
2–4	0.1 (7/5273)	10.6 (2.19–50.89)	<0.01				
≥5	0.2 (1/569)	13.9 (1.27–154.6)	0.10	3.98 (1.61–9.84)	<0.01	—	—
12 Hemiplegia or paraplegia							
No	<0.1 (9/21 744)						
Yes	1.1 (1/88)	27.6 (3.47–220.6)	0.04	—	—	19.2 (0.42–877.5)	0.13
13 Chronic kidney disease							
No	<0.1 (5/18 033)						
Yes	0.1 (5/3711)	4.87 (1.41–16.8)	0.02	—	—	3.72 (0.93–14.8)	0.06
High-volume centre treatment							
Low	0.1 (5/4745)						
High	<0.1 (5/16 999)	0.28 (0.08–0.96)	0.04	0.35 (0.09–1.22)	0.09	0.12 (0.08–1.15)	0.08

A wide range of in-hospital mortality rates in patients with atrial arrhythmias has been reported in the literature, most likely as a consequence of different study designs and heterogeneous cohorts.[14,15] Observational registries using administrative data and comparable methods reported an in-hospital mortality of 0.9–2.2%.[15,16] The lower mortality rate in our cohort may be explained by the higher age in one of the previous cohorts and the higher prevalence of diabetes mellitus and chronic pulmonary diseases which were known to be independent risk factors for adverse outcomes in general. However, assessment and comparability of such mortality rates must be done with caution, since

Table 5 Univariable and multivariable regression analysis of patients who underwent right atrial catheter ablation

Variable	Univariable analysis			Multivariable analysis (including CCI)		Multivariable analysis (including CCI components)	
	Mortality % (*n*/*N*)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age							
≤64	0.1 (4/3377)						
65–74	0.3 (11/3517)	2.65 (0.84–8.32)	0.12				
≥75	0.5 (15/3078)	4.13 (1.37–12.5)	<0.01	0.87 (0.37–2.05)	0.75	1.49 (0.89–2.50)	0.13
Charlson Comorbidity Index							
0–1	0.0 (0/6022)						
2–4	0.4 (12/3211)	1.04 (1.02–1.06)	<0.01				
≥5	2.4 (18/739)	1.03 (1.01–1.04)	<0.01	10.1 (5.42–18.9)	<0.01	—	—
01 Myocardial infarction							
No	0.2 (22/9246)						
Yes	1.1 (8/726)	4.67 (2.07–10.5)	<0.01	—	—	2.38 (0.99–5.73)	0.05
02 Congestive heart failure							
No	0.1 (4/6212)						
Yes	0.7 (26/3760)	10.8 (3.77–30.9)	<0.01	—	—	6.39 (2.12–19.3)	<0.01
03 Peripheral vascular disease							
No	0.3 (25/9174)						
Yes	0.6 (5/789)	2.31 (0.88–6.04)	0.09	—	—	0.94 (0.32–2.71)	0.90
04 Cerebrovascular disease							
No	0.3 /25/9599)						
Yes	1.3 (5/373)	5.20 (1.98–13.7)	<0.01	—	—	1.34 (0.55–6.83)	0.31
06 Chronic pulmonary disease							
No	0.3 (23/9044)						
Yes	0.8 (7/928)	2.98 (1.28–6.97)	0.02	—	—	1.95 (0.79–4.78)	0.15
08 Peptic ulcer disease							
No	0.3 (28/9955)						
Yes	11.8 (2/17)	47.3 (10.3–216.4)	<0.01	—	—	27.2 (4.97–149.4)	<0.01
09 Mild liver disease							
No	0.3 (26/9821)						
Yes	2.6 (4/151)	10.3 (3.53–29.7)	<0.01	—	—	4.79 (1.36–16.9)	0.02
11 Diabetes + chronic complications							
No	0.3 (24/9262)						
Yes	0.8 (6/710)	3.28 (1.34–8.05)	0.02	—	—	1.28 (0.47–3.44)	0.63
12 Hemiplegia or paraplegia							
No	0.3 (28/9890)						
Yes	2.4 (2/82)	8.81 (2.06–37.59)	0.03	—	—	4.01 (0.62–25.9)	0.15
13 Chronic kidney disease							
No	0.2 (14/7592)						
Yes	0.7 (16/2380)	3.66 (1.79–7.52)	<0.01	—	—	1.69 (0.74–3.82)	0.21
14 Any malignancy							
No	0.2 (24/9767)						
Yes	2.9 (6/205)	12.2 (4.95–30.3)	<0.01	—	—	8.39 (3.15–22.3)	<0.01
15 Moderate or severe liver disease							
No	0.3 (29/9962)						
Yes	10.0 (1/10)	38.1 (4.67–310.1)	0.03	—	—	11.8 (0.87–158.6)	0.06

relevant information such as the cause of death are not available due to data structure. Nevertheless, baseline characteristics concerning age, gender distribution, cardiovascular comorbidities, and thrombo-embolic risk factors were similar to previously published datasets.[3,17]

Almost all registered comorbidities were over-represented in the mortality-group in our study. Regarding possible risk factors for fatal outcomes, reference must be made to the low event rate which is reflected in partly high ORs. The presence of congestive heart failure

Table 6 Univariable and multivariable regression analysis of patients who underwent left atrial appendage occluder procedures

Variable	Univariable analysis			Multivariable analysis (including CCI)		Multivariable analysis (including CCI components)	
	Mortality % (*n*/*N*)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Gender							
Male	0.3 (4/1355)						
Female	0.9 (9/954)	3.22 (0.99–10.5)	0.05	3.33 (1.01–10.9)	0.04	3.29 (0.98–11.1)	0.05
Charlson Comorbidity Index							
0–1	0.1 (1/675)						
2–4	0.5 (6/1123)	3.62 (0.43–30.1)	0.27				
≥5	1.2 (6/511)	8.01 (0.96–66.7)	0.05	2.69 (1.16–6.20)	0.02	—	—
02 Congestive heart failure							
No	0.2 (3/1298)						
Yes	1.0 (10/1011)	4.31 (1.18–15.7)	0.02	—	—	4.23 (1.14–15.7)	0.03
04 Cerebrovascular disease							
No	0.4 (8/2007)						
Yes	1.7 (5/302)	4.21 (1.37–12.9)	0.02	—	—	1.73 (0.35–8.53)	0.50
05 Dementia							
No	0.5 (11/2234)						
Yes	2.7 (2/75)	5.54 (1.21–25.4)	0.05	—	—	3.14 (0.60–16.3)	0.17
12 Hemiplegia or paraplegia							
No	0.4 (9/2213)						
Yes	4.2 (4/96)	10.6 (3.22–35.2)	<0.01	—	—	6.58 (1.19–36.2)	0.03

and diabetes mellitus as well as a resulting higher CHA_2DS_2-VASc score are known to be predictors for in-hospital death in patients with AFib.[18,19] Inconclusive results concerning the role of diabetes mellitus may be explained by the division of patients with diabetes within the CCI and the resulting lower number of patients in each subgroup, which may lead to a non-significant effect. Notably, mortality was higher in female patients in our cohort even if multivariable analysis revealed inconclusive results for gender. Although secondary disorders and especially thrombo-embolic events in patients with AFib are known to be gender-associated, data regarding the impact on mortality are inconclusive.[20–22] Concerning the encoded main diagnosis, we found a significant association of in-hospital mortality with the type of atrial arrhythmia (AFib vs. AFlut), which is in line with findings of other databases.[4,23] In a nationwide US-registry of patients with AFib, O'Neal *et al.* reported of higher in-hospital mortality depending on the treatment in a rural institution compared to urban hospitals. The authors considered a connection to the lower number of patients with AFib and the resulting missing routine.[16] To transfer these results to our findings with a higher mortality in so defined low-volume centres is possible only to a limited extent because of different definitions of centre volume. Nevertheless, the positive effect of higher numbers of treated patients on outcome is well described for numerous cardiovascular disorders.[24–26] We found a decrease of in-hospital mortality over time. This change could not be explained by any of the baseline characteristics. General improvements in inpatient treatment may contribute to the decrease of in-hospital mortality. Nevertheless, due to available data, this observation cannot be conclusively explained and therefore deserves further investigation.

Several publications investigated fatal outcomes after specific arrhythmia-related procedures. For LA CA, in-hospital mortality rates of 0–0.5% have been reported. Since congestive heart failure, hypertension, previous cerebrovascular events, higher age, female sex, and other comorbidities as well as the CHA_2DS_2-VASc score were described to be predictive for in-hospital adverse events in general, no direct association with mortality has yet been reported.[21,22,27] As mortality rates were low, most analyses were underpowered concerning the identification of predictors for fatal outcomes. However, operator volume and centre experience are accepted predictors both for complications and mortality after CA for AFib.[10,27] This association cannot be conclusively confirmed by our data, since centre volume was predictive for in-hospital mortality in univariable but not in multivariable analysis. Data regarding in-hospital mortality after RA CA are rare, Brembilla-Perrot *et al.*[28] found a mortality rate of 0.22% in their rather small population of 883 patients which is comparable to the above mentioned rate of 0.3% in our cohort. Interestingly, in our population in-hospital mortality rate was higher in the subgroup with RA CA compared to LA CA despite the expected greater periprocedural risk caused, among others, by transseptal puncture. Once again, the limited comparability of mortality rates due to lacking information regarding the cause of death has to be mentioned. Probable explanations are higher age as well as higher proportions of existing comorbidities in the former

group. Comparing long-term outcomes after CA of AFib and AFlut, Vadmann *et al.*[29] found higher rates of comorbidities and an increased mortality in patients with AFlut. In our dataset, main diagnosis of AFlut was significantly over-represented in patients who underwent RA CA. Moreover, non-elective hospital admission was significantly more frequent in those patients which also may influence the risk for fatal outcomes. A correlation between centre volume and in-hospital mortality has been shown for ablation of AFlut.[11] As several cardiovascular comorbidities were predictive for a fatal outcome in our cohort of right sided atrial CA, centre volume was not. For LAAO procedures, several studies reported intervention-associated complications rates, but only small cohorts and case series were analysed for in-hospital mortality risk.[30–32] In a population of 83 patients, one procedure-related death has been described by Masoud *et al.*[33] resulting in a non-representative mortality rate of 1.2%. With fatal outcomes being observed in 0.56% in our population, we found a lower in-hospital mortality rate compared to the study mentioned above. Nevertheless, the mortality rate was rather high in contrast to the mortality rate especially in patients who underwent LA CA. Once more, differences in baseline characteristics are most likely causative for those observations. In the larger EWOLUTION trial with a comparable population regarding age and cardiovascular conditions, the investigators reported of mortality rates after LAAO procedures of 0.29% and 0.68% within 7 and 30 days, respectively.[34] Even if in-hospital mortality not specifically has been described, the mortality rates were similar to our results. Predictors for fatal outcomes were not reported. Regarding adverse events in general, neither CHA_2DS_2-VASc score nor HAS-BLED score were found to be predictive. ????CCI has not been measured in this population. As operator volume was shown to be associated with lower complication rates and specific requirements for hospitals and operators are recommended, data concerning an improvement of survival are lacking.[35,36] Despite a two-fold increase of in-hospital mortality in patients treated in low-volume centres, the analysis failed to reach statistical significance. Therefore, a further evaluation with an adequate powered group-size of this volume-dependence in LAA-occlusion procedures is required. Overall, the low event rates and concomitant limitations in the interpretation of mortality predictors should be considered for each group of arrhythmia-related procedure.

Limitations

This study analysed data from an administrative, multi-centre dataset. These data were not stored for research interests but for remuneration reasons which potentially could affect the encoded information.[37] Quality of the results depends to a large extent on the correct encoding of ICD- and OPS-codes.[9,38] Procedure- or operator-related data, which may have influenced outcome, were not available as well as information about the patients' laboratory results and medication. Although each of the examined procedures was connected to the case number of the index hospitalization, neither a specific cause of death nor a causal relationship to the intervention could be determined. We only included cases of in-hospital death in one of the participating centres into our analysis. An unknown number of cases in which patients with adverse events were being transferred to other institutions could led to an underestimation of in-hospital morality, but the probability of death after hospital transfer could not be derived from the available data. On the other hand, most of the procedures being examined are done electively and the performance of a CA for an atrial arrhythmia in a primarily unstable patient is likely to be rare.

Conclusions

In this study, we investigated the largest real-world dataset of patients with AFib and AFlut in Germany by now. We showed a significant decrease of overall in-hospital mortality as the most important safety parameter of arrhythmia-related procedures during the observational period. Moreover, we identified centre volume and several clinical parameters as relevant predictors for fatal outcome. Especially CCI seems to be an appropriate prognostic indicator for in-hospital mortality in patients with AFib and AFlut in general and those undergoing invasive arrhythmia-related procedures. Further investigation is needed to identify specific causes of death within each cohort as this was not the main purpose of this study. The assessment of administrative data of multi-centre hospital networks allows feasible, comparable, and up-to-date performance measurement of clinically important endpoints in a real-world setting which may contribute to quality management programs in atrial arrhythmias and towards value-based healthcare.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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