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Impact of atrial fibrillation on in-hospital mortality of ischemic stroke patients and identification of promoting factors of atrial thrombi – Results from the German nationwide inpatient sample and a single-center retrospective cohort

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Abstract

Ischemic stroke is one of the leading causes of death and disability. Atrial fibrillation (AF) is a well-recognized risk factor for ischemic stroke.

We aimed to investigate the impact of AF on in-hospital mortality of ischemic stroke patients and to identify parameters associated with intra-cardiac thrombogenic material.

Patients were selected by screening the nationwide sample for ischemic stroke by ICD-Code (I63), stratified for AF. In this cohort, the association between in-hospital deaths and AF was investigated.

In a second study, we performed a retrospective analysis of patients who underwent transesophageal echocardiography (TEE) for various reasons, assigned these to 2 groups based on the heart-rhythm (sinus-rhythm[SR] vs AF) and examined associations between clinical and echocardiographic parameters and intra-cardiac thrombogenic material.

The Nationwide sample comprised 292,401inpatients (48.5%females) with ischemic stroke. Incidence was 360per 100,000citizens, with an age-dependent increase. In-hospital mortality rate was 8.2%; AF patients had 1.85-fold higher mortality rate (12.1% vs 6.5%).

In the retrospective study,219patients (median age 67[59.1–77.3]years, 39.3%females) were included: 115patients with AF (median age 71[59.0–78.0]years, 41.7%females) and 104patients (median age 68[56.3–76.8]years, 36.5%females) with SR. Solid thrombus or spontaneous-echo-contrast) was detected in 16 TEEs. Atrial dimensions were significantly enlarged in AF patients. Age, blood-flow velocity in LAA, LAA diameters, atrial areas, AF, and CHA2DS2-VASc-score were associated with thrombogenic material.

Incidence of ischemic stroke increased with age. AF was connected with higher stroke mortality. Presence of intra-cardiac thrombogenic material was associated with AF and most CHA2DS2-VASc-score factors. AF was associated with larger atrial dimensions and larger cavities favored thrombogenic material.

Abbreviations: AF = atrial fibrillation, BMI = body mass index, CI = confidence intervall, DRG = diagnosis related groups, ICD-10-GM = International Classification of Diseases, 10th Revision with German Modification, IQR = interquartile range, LA = left atrium, LAA = left atrial appendage, LVEF = left ventricle ejection fraction, OR = odds ratio, SEC = spontaneous echo contrast, SR = sinus rhythm, TIA = transient ischemic attack, TTE = transesophageal echocardiography, VTE = venous thromboembolism.

Keywords: atrial fibrillation, echocardiography, intracardiac thrombogenic material, left atrial appendage, mortality, stroke

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KK and MG contributed equally and should both be considered as first authors.

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1. Introduction

With an overall prevalence of 1% to 2%, an age-dependent increase and a trend to double in the next 50years,[3,12,13] atrial fibrillation (AF) is a well-recognized cause of ischemic stroke and one of the leading causes of death and disability.[3,6,9,17,19,27] Patients with AF have a 3- to 5-fold elevated relative risk for the occurrence of stroke in comparison to individuals without.[17,19] The hypothesis that AF produces stasis of blood resulting in thrombogenic material formation and thromboembolism to the brain has been proposed more than 100 years ago, but is still the most frequently suggested pathomechanism.[17,19] Thromboembolic strokes due to AF are common and frequently devastating, leading to severe impairment or death in 3/4 of the patients.[10,28] If rhythm control with an early cardioversion of AF patients in sinus rhythm (SR) is the strategy of choice, transesophageal echocardiography (TEE) has been shown to be suitable to exclude the majority of left atrial thrombi.[4,20] The left atrial appendage (LAA) is a blind pouch of the left atrium (LA), accounting for approximately 90% of intra-cardiac thrombi in AF.[8]

The objectives of our study were to investigate the impact of AF on the in-hospital mortality of ischemic stroke in a nationwide inpatient sample and to identify parameters associated with intracardiac thrombogenic material formation in patients examined with TEE in a retrospective cohort at the University Medical Center Mainz.

2. Methods and patients

Two separate patient cohorts were analyzed:

1. Analysis of incidence and in-hospital death in ischemic stroke patients: The German nationwide inpatient statistics (Diagnosis related groups [DRG statistics]) of the year 2015 was consulted for this analysis. Information includes treatment data from all inpatients processed according to the DRG system. In Germany, diagnoses of inpatients are coded according to ICD-10-GM (International Classification of Diseases, 10th Revision with German Modification). The DRG-coded diagnoses data of all hospital patients are gathered at the Federal Statistical Office in Germany (Statistisches Bundesamt, DEStatis). For our analysis, mortality data of in-patients diagnosed for ischemic stroke (ICD code I63) with and without additionally coded AF (ICD code I48) were obtained from the Federal Statistical Office of Germany (Statistisches Bundesamt, DEStatis, source: DRG-Statistik, Sonderauswertung des Statistischen Bundesamtes). Since this study did not involve direct access by the investigators to data on individual patients but only to summary results provided by the Research Data Center, approval by an ethics committee and informed consent were not required according to German law.
2. Correlation between echocardiographic parameters, clinical features, and stroke: Patients who underwent TEE in the Center of Cardiology at the University Medical Center Mainz (Mainz, Germany) were included in this retrospective analysis. This cohort included consecutive patients, aged ≥18 years, who were examined in the echocardiography department Center of Cardiology, University Medical Center Mainz by TEE (01/2013–03/2013). Patients were stratified by heart rhythm into 2 groups either SR or AF (all different clinical patterns of AF were assigned to the AF group). Patients which could not clearly be assigned to one group were excluded from analysis. We assessed patients' characteristics, comorbidities, and echocardiographic parameters and calculated the CHA_2DS_2-VASc-score.[25] Echocardiographic measurements were obtained by evaluation of 2- and 3-dimensional TEE loops stored on the clinic's server in DICOM-standard and assessment via Philips Xcelera and Qlab software (trademark by Philips healthcare). All echocardiographic analysis was performed and confirmed by at least 2 experienced echocardiographers. The echocardiographic measurements comprised evaluation of solid thrombogenic material or spontaneous echo contrast (SEC) in the LAA, blood flow velocity in LAA detected by Pulsed-waved (PW-) Doppler as well as the spatial dimensions of the LAA in kind of width (septal-lateral diameter obtained in short axis view/ 45° angulation) and length (aperture-apex) of the LAA in TEE (Fig. 1). Confirmation or exclusion of thrombogenic material (solid thrombi as well as the assessment of SEC) was performed in all recorded angulations and 3-dimensional reconstructions, if available. Left ventricle ejection fraction (LVEF), left and right septal-lateral and longitudinal diameters, as well as atrial areas and systolic pulmonary artery pressure, were measured, if a TTE was available from the same hospital visit. Ventricular dimensions, ejection fraction and atrial areas were determined in apical 4 chamber view using Simpson's method according to the EACVI- and ASE-recommendations on cardiac chamber quantification.[22] Proposed systolic artery pressure was estimated from Doppler regurgitation velocity on tricuspid regurgitation (Fig. 1). Since the study involved an anonymous, retrospective analysis of diagnostic standard data, ethics approval was not required according to German laws.

3. Statistics

First, we calculated the incidence of ischemic stroke in Germany (2015) in the nationwide sample. Total numbers of inpatients with ischemic stroke with and without AF as well as the relative mortality of AF related to no AF was computed.

In the second retrospective study cohort, we compared patients with thrombogenic material, defined as detected solid thrombus or SEC in the left atrium and especially in the LAA with those without these findings to identify factors associated with thrombogenic material.

Descriptive statistics for the relevant baseline comparison of both groups are provided with mean ± standard deviation, median and interquartile range (IQR), depending on Gaussian or skewed distribution, or absolute numbers and corresponding percentages. Continuous variables found not to follow a normal distribution, when tested with the modified Kolmogorov–Smirnov test, were compared using the Wilcoxon-Whitney *U* test. Normal distributed continuous variables were compared using the Students *t* test and categorical variables with Fisher exact or Chi^2 test, as appropriate.

We calculated univariate logistic regression models to examine different parameters as predictors for thrombogenic material. Additionally, multivariate logistic regression analyses adjusted for age an AF were performed for predictors. For the association of the comorbidity AF with thrombogenic material, multivariate logistic regression adjusted for age and congestive heart failure was used.

Parameters associated with thrombogenic material were entered in a receiver operating characteristics (ROC) analysis.

The software SPSS (version 22.0; SPSS Inc., Chicago, Illinois) was used for the majority of computerized analysis. For the

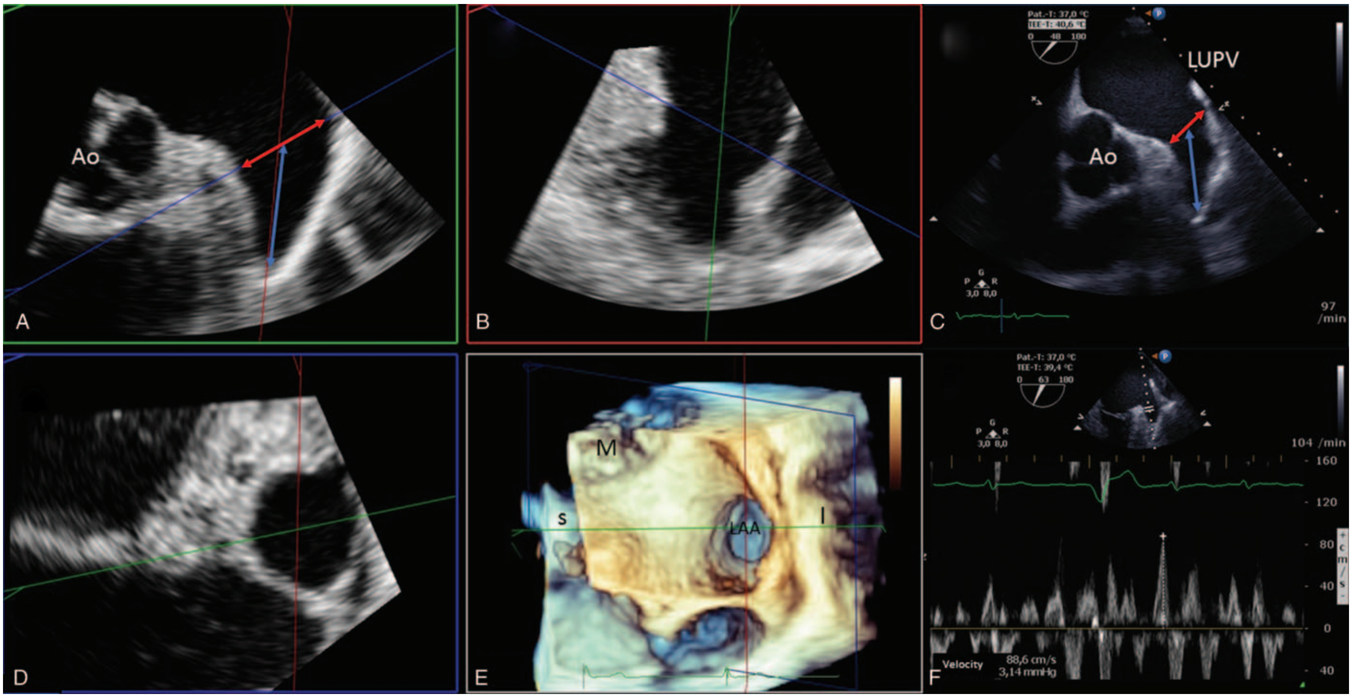

Figure 1. Assessment of LAA diameters and LAA velocity. LAA expansions were measured by determining orifice width and LAA depth. LAA orifice width (marked as red arrow) was estimated by measuring septo-lateral diameter in short axis view (SAX) as an approximated plane from the left coronary height (septal) to 1 to 2 cm below the highest point of the LUPV (left upper pulmonary vein)-limbus ("rim" / lateral); LAA depth (marked as blue arrow) was determined as distance from orifice plane to the deepest point of the LAA. If available, measurements were performed by multi-planar reconstruction of three-dimensional echo loops (Panels A, B, D: Panel A shows a reconstructed plane resembling SAX-view in left upper quadrant, Panel B another reconstructed longitudinal plane orthogonal on Panel A, Panel D the reconstructed "orifice" of the LAA). Panel C demonstrates measurements in "conventional" 2-dimensional TEE at about 45° resembling SAX-view. Panel E shows spatial relations in the LA in a 3-dimensional overview in "non-surgical" orientation. Panel F shows the determination of blood velocity in the LAA via PW-doppler in a patient with present atrial fibrillation (obviously shown by PW-curve demonstrating rapid and irregular LAA contractions). Ao = indicates aortic valve, l = lateral orientation, LAA = left atrial appendage, LUPV = left upper pulmonary vein, M = mitral valve, s = septal orientation.

calculation of the Youden cut-off values, specificity, sensitivity, and rate of misclassification in ROC analyses, BIAS (version 10.04; epsilon press, Frankfurt, Germany) was used. Only *P* values of $<.05$ (two-sided) were considered to be statistically significant.

4. Results

4.1. Analysis of the predictors of death in ischemic stroke patients

The nationwide sample comprised 292,401 inpatients (48.5% females) with ischemic stroke in Germany 2015. Calculated incidence for ischemic stroke was 360.1/100,000 citizens with an age dependent increase (Fig. 2A). Similarly, total numbers of ischemic stroke events increased up to the age-group ≥75years <80years (Fig. 2C).

In total, 24,054 patients with ischemic stroke died in-hospital (8.2%). The stroke-attributable mortality was 29.6/100 000 inhabitants, whereas the mortality-to-incidence ratio was 0.082. Ischemic stroke patients' mortality rate stratified for age groups increased distinctly in age groups >60years (Fig. 2B). Stroke patients with AF had a higher in-hospital mortality rate compared to those without (12.1% vs 6.5%). Highest relative mortality rates in ischemic stroke patients with additional AF compared to those without AF, could be detected in the age group ≥20 years up to <50years, with exception of stroke patients between ≥30 to <35years (Fig. 2D).

4.2. Correlation between echocardiographic parameters, clinical features, and stroke

Overall, 225 consecutive patients who underwent TEE for various reasons were enrolled. Among these, 6 patients were excluded due to heart rhythm which could not be clearly assigned to one of the study groups. Therefore, 219 patients (median age 67years [59.1–77.3], 39.3% females) remained for analysis. The medical indication for TEE comprised evaluation regarding intracardiac thrombogenic material before planned cardioversion in 54.8%, further evaluation of valve disorders (including suspected endocarditis) in 26.0%, as well as other reasons in 19.2%. CHA_2DS_2-VASc-score of the whole study population regardless of underlying heart rhythm was 3points in median.

In total, 115 (52.5%) patients presented with AF and 104 (47.5%) patients with SR. Patients' characteristics did not differ significantly in age, most comorbidities and CHA_2DS_2-VASc-score (Table 1), but patients without AF were more likely to suffer from coronary artery disease.

Solid thrombus could be proven by TEE in only 4 (1.8%) patients, whereas relevant SEC was observed in 12 (5.5%) patients. The study groups differed significantly in identified thrombogenic material defined as solid thrombus and/or SEC (AF: 13.7% vs SR: 2.5%, $P=.007$)

Echocardiographic diameters were significantly larger in patients with AF compared to those with SR and PW-Doppler revealed lower blood flow velocity in AF patients (Table 1). Univariate logistic binary regression models demonstrated

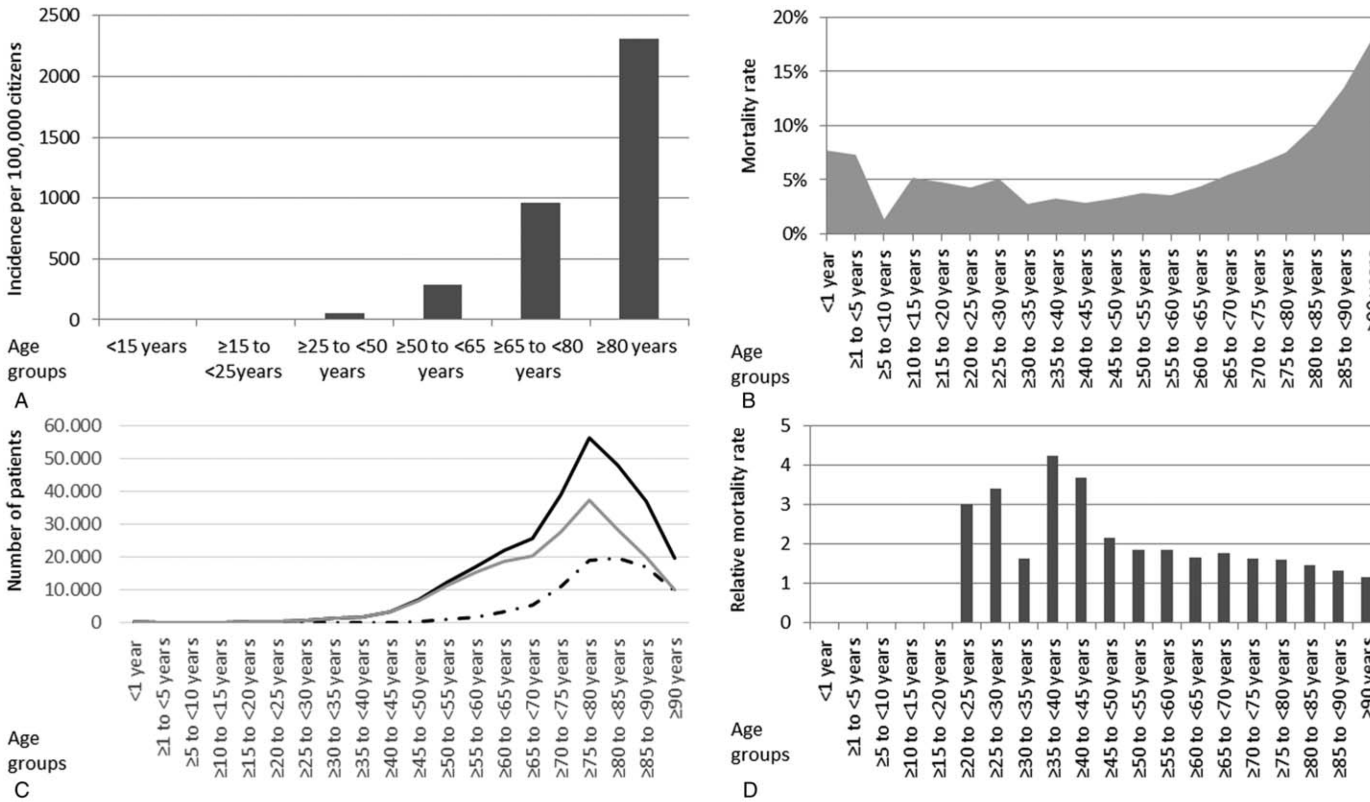

Figure 2. Incidence of ischemic stroke per 100,000 citizens (A), mortality rate (B), total numbers of ischemic stroke events (C) and relative mortality rate (D) stratified by different age groups in Germany in the year 2015. In Figure C the solid black line represents all ischemic stroke patients, the grey line those without AF and the dashed black line these with AF. In Figure D, the relative mortality rate in ischemic stroke patients with additional AF compared to those without AF is shown stratified for different age-groups (ischemic stroke patients without AF are the reference group and equated with 1). AF = atrial fibrillation.

Table 1

Clinical characteristics and echocardiographic parameters in patients with sinus rhythm and patients with atrial fibrillation.

Variable	Patients with sinus rhythm (n=104)	Patients with AF (n=115)	*P*-value
Age (years)	68.0 (56.3–76.8)	71.0 (59.0–78.0)	.124
Gender (females)	38 (36.5%)	48 (41.7%)	.824
Body height (m)	1.71±0.10	1.72±0.10	.754
Body weight (kg)	74.0 (65.0–89.5)	79.0 (69.0–92.5)	.182
BMI (kg/m^2)	26.4 (23.5–28.7)	26.8 (24.1–29.8)	.172
Comorbidities			
Heart failure	22 (21.2%)	27 (23.5%)	.680
Arterial hypertension	67 (64.4%)	85 (73.9%)	.128
Coronary artery disease	39 (37.5%)	28 (24.3%)	**.035**
Diabetes mellitus	19 (18.3%)	23 (20.0%)	.745
History of stroke or TIA	16 (15.4%)	10 (8.7%)	.126
History of myocardial infarction	8 (7.7%)	12 (10.4%)	.482
Peripheral artery disease	16 (15.4%)	14 (12.2%)	.490
History of VTE	9 (8.7%)	9 (7.8%)	.824
CHA_2DS_2-VASc-Score (points)	3 (2–4)	3 (2–4)	.423
Echocardiographic parameters			
Thrombus or spontaneous echo contrast	2 (2.5%)	14 (13.7%)	**.007**
Thrombus without spontaneous echo contrast	2 (2.5%)	2 (2.0%)	.815
Left ventricle ejection fraction (%)	55.0% (40.0–55.0)	50.0% (40.0–55.0)	.096
Left atrial longitudinal diameter (cm)	5.8 (5.0–6.5)	6.4 (5.8–7.0)	**.001**
Left atrial septal-lateral diameter (cm)	4.2 (3.8–4.5)	4.5 (4.0–4.9)	**.015**
Left atrial area (cm^2)	20.2±6.4	24.1±6.6	**<.001**
Right atrial septal-lateral diameter (cm)	3.8±0.9	4.2±0.7	**.018**
Right atrial longitudinal diameter (cm)	5.2 (4.6–5.7)	5.9 (5.3–6.3)	**<.001**
Right atrial area (cm^2)	16.0 (12.7–19.6)	21.3 (16.0–24.6)	**<.001**
Systolic pulmonary artery pressure (mmHg)	40.8±11.4	37.6±9.8	.155
Blood flow velocity in the LAA detected by Pulsed-waved Doppler (cm s^{-1})	50.0 (35.9–64.3)	41.9 (27.5–59.9)	**.035**
LAA width (septal-lateral diameter) (cm)	1.5 (1.2–2.0)	1.8 (1.6–2.1)	**.002**
LAA longitudinal diameter from aperture to apex (cm)	3.1±0.8	3.4±0.6	**.028**

BMI=body mass index, LAA=indicates left atrial appendage, TIA=transient ischemic attack, VTE=venous thromboembolism.

Table 2

Univariate regression analyses for the associations between several parameters and intra-cardiac thrombus formation in kind of solid thrombi and spontaneous echo contrast.

Variable	Odds Ratio	(95% CI)	*P*-value
Age (per year)	1.065	1.010–1.125	**.021**
Male gender	1.985	0.706–5.582	.194
Blood flow velocity in the LAA detected by Pulsed-waved Doppler (per cm s^{-1})	0.955	0.925–0.986	**.005**
LAA longitudinal diameter (per cm)	3.472	1.653–7.246	**.001**
LAA septal-lateral diameter (per cm)	2.500	1.133– 5.495	**.023**
Left ventricle ejection fraction (per %)	0.982	0.937–1.030	.460
Right atrial septal-lateral diameter (per cm)	1.848	0.847–4.032	.123
Right atrial longitudinal diameter (per cm)	1.010	0.866–1.178	.900
Right atrial area (per cm^2)	1.157	1.041–1.289	**.007**
Left atrial septal-lateral diameter (per cm)	1.026	0.827–1,272	.819
Left atrial longitudinal diameter (per cm)	1.021	0.820–1,272	.850
Left atrial area (per cm^2)	1.129	1.007–1.264	**.038**
Systolic pulmonary artery pressure (per mmHg)	0.996	0,931–1.065	.914
BMI (per kg/m^2)	1.004	0.907–1.125	.934
Body weight (per kg)	0.991	0,959–1.026	.662
Body length (per m)	0.059	0.00017–20.408	.342
Presence of Atrial Fibrillation	6.289	1.385–28.571	**.017**
History of VTE	0.702	0.087–5.682	.741
Heart failure	4.237	1.484–12.195	**.007**
Arterial Hypertension	1.965	0.538–7.194	.306
Coronary artery disease	1.808	0.640–5.128	.263
Diabetes mellitus	3.861	1.332–11.236	**.013**
History of stroke or TIA	2.873	0.837–9.804	.094
Peripheral artery disease	3.289	1.041–10.417	**.043**
History of myocardial infarction	2.119	0.548–8.197	.277
CHA_2DS_2-VASc-Score (per point)	1.664	1.248–2.220	**.001**

BMI = body mass index, LAA = indicates left atrial appendage, TIA = transient ischemic attack, VTE = venous thromboembolism.

associations of the parameters age, blood flow velocity in the LAA detected by PW- Doppler, LAA longitudinal and septal-lateral diameter, right and left atrial areas, presence of AF, diabetes mellitus, heart failure, peripheral artery disease, and CHA_2DS_2-VASc-score with thrombogenic material. The presence of AF and heart failure were associated with 6.2- and 4.2-fold risk of intra-cardiac thrombogenic material, respectively (Table 2). Each additional point in the CHA_2DS_2-VASc-score was accompanied by 66% increase in the risk of developing thrombogenic material.

After adjustment for age and AF, blood flow velocity in the LAA detected by PW-Doppler (OR 0.948 (95% CI 0.910–0.988, $P=.011$)), LAA longitudinal (OR 4.708 (95% CI 1.757–12.616, $P=.002$) and septal-lateral (OR 3.670 (95% CI 1.402–9.604), $P=.008$) diameter, right (OR 1.125 (95% CI 1.003–1.262), $P=.045$) atrial area, presence of heart failure (OR 4.845 (95% CI 1.546–15.184), $P=.007$), diabetes mellitus (OR 3.121 (95% CI 1.024–9.515), $P=.045$), and peripheral artery disease (OR 3.537 (95% CI 1.013–12.347), $P=.048$) remained significantly associated with thrombogenic material in multivariate regression analysis. In addition, AF was also still associated with thrombogenic material in multivariate logistic regression model after adjustment for age and heart failure (OR 7.557 (95% CI 1.542–37.021), $P=.013$).

The ROC curves identifying the thresholds as best cut-off for the prediction of the presence of thrombogenic material are shown in Figures 3 and 4. These cut-offs were associated with a sensitivity >65% and a specificity >61% in the prediction of SEC. The highest accuracy was observed for blood flow velocity determination in LAA by PW-Doppler with an area under the curve of 0.799 (Table 3).

5. Discussion

Ischemic stroke, one of the leading causes of death and disability worldwide,[1,15,19,27] shows large differences in incidence, prevalence, and mortality between different regions, especially between Eastern and Western Europe.[1,21,30] The calculated incidence of ischemic stroke in Germany was 360/100,000 citizens and therefore lower than in Eastern Europe but distinctly higher than in other parts of the world.[21] Importantly, the incidence of stroke appears thus to be increasing as compared to earlier years.[21,30]

The stroke-attributable mortality was 29.6/100,000 persons (2015) in Germany, lower than in Russia,[21] but similar to the USA and France.[30] Hence, the higher incidence in comparison to former years and other countries detected by national coding system might be driven by coding differences.

The mortality-to-incidence ratio was very low, similar to the high-income regions of North America and east Asia.[21] The mortality rate increased from <4% in patients aged younger than 50years to >13% in those ≥85years old, presumably attributable to the growing number of comorbidities.

In accordance with previous studies, the results of the German nationwide sample demonstrated an increase of the stroke incidence with growing age[8,29,30] and a 1.85-fold higher case fatality rate during in-hospital stay in those stroke patients with a comorbidity of AF in comparison to those without.[16,23,29] This fatal correlation proved to be most pronounced in the relatively young group of ischemic stroke patients younger than 45years of age.

It is well known that patients with AF are at increased risk for stroke.[3,5,11,24,25,27,29] Overall, 15% to 30% of all strokes are due to AF - presumably this rate is even underestimated due to unidentified “silent” or paroxysmal AF.[7,9,19,26,27]

The LAA is the primary localization for intra-cardiac thromboembolic material in non-valvular AF and the primary cause of cardioembolic strokes with approximately 90% of intra-cardiac thrombi.[7,8,24] TEE is the standard procedure for the diagnosis or exclusion of intra-cardiac thrombi in AF

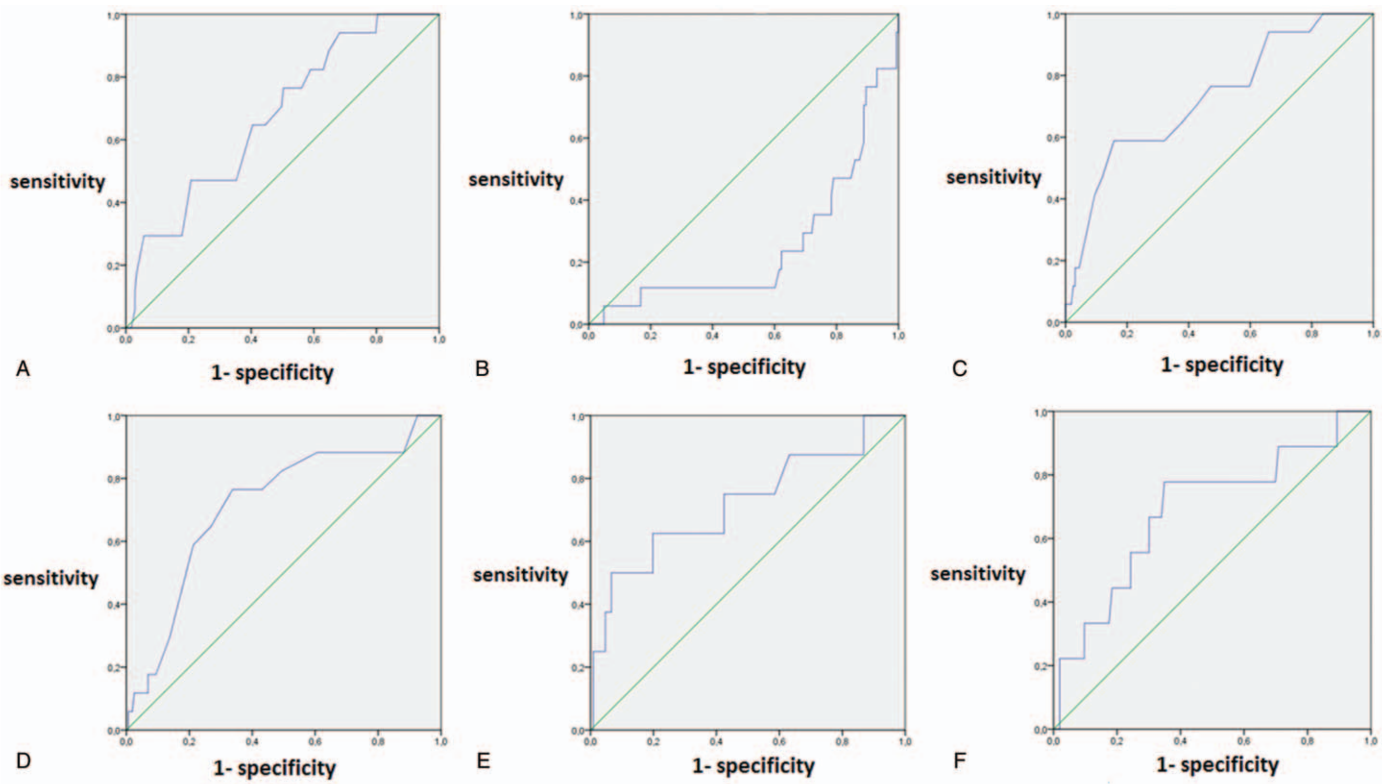

Figure 3. ROC curves for age (A), Pulsed-waved Doppler (B), Left atrial appendage longitudinal diameter (C), Left atrial appendage septal-lateral diameter (D), Right atrial area (E), and Left atrial area (F) as predictors of intra-cardiac thrombogenic material (solid thrombus and spontaneous echo contrast).

patients.[2,7,14] In accordance with the literature we found larger atrial diameters and areas including larger LAA diameters in AF patients in comparison to those with SR.[8,18] In this context, the blood flow velocity in the LAA measured by PW-Doppler was also lower in AF patients.

Our study demonstrated that besides AF, a larger size of the atria and the LAA and lower blood flow velocity were associated with thrombogenic material defined as solid thrombi and SEC, which may reflect microthrombi development.[8] Of note, the present data do not allow a definite conclusion whether larger dimensions are direct causes of the thrombogenic material formation or if they are the consequence of AF and therefore only cofactors of AF in thrombogenic material formation. Additionally, diabetes, heart failure, peripheral artery disease, and advanced age were also associated with thrombogenic material occurrence. As expected, a CHA_2DS_2-VASc-score >2.5 was predictive for thrombogenic material.

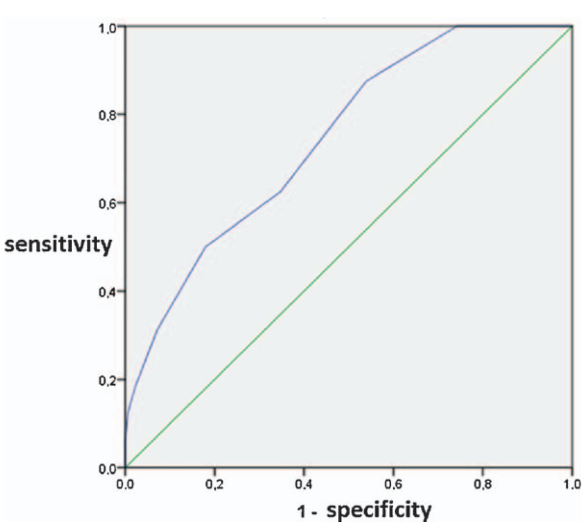

Figure 4. ROC curve for CHA_2DS_2-VASc-score as predictors of intra-cardiac thrombogenic material (solid thrombus and spontaneous echo contrast).

6. Limitations

Of course, our study has some limitations. The data of the nationwide sample from Federal Statistical Office of Germany (Statistisches Bundesamt, DEStatis) for this analysis are pooled/aggregated data. Therefore, we can only present a descriptive data analysis, without statistical testing for difference with *P*-values and without adjustment for age and other cofactors such as comorbidities (e.g., cardiovascular disease). Furthermore, only patients treated in-hospital were included.

The central limitations of the second study-part are the single-center design and the retrospective data assessment of a medium sized patient cohort. Follow-up examinations are missing. In addition, only a small number of *solid* thrombi could be detected in the patient cohort, not allowing for statistically significant evidence. Thus, we decided to analyze solid thrombi and SEC as equivalent for thrombogenic material, respectively intra-cardiac thrombus formation. The occurrence of SEC was assessed by at least 2 experienced echocardiographers. Despite these limitations, we were able to identify important factors of intra-cardiac formation of thrombogenic material.

Table 3

Prognostic performance for prediction of thrombogenic material (solid thrombus and spontaneous echo contrast). Risk of misclassification is defined as sum of false positive and false negative values.

Parameter	*P*-value	Area under the curve (95% CI)	Calculated cut-off value	Sensitivity	Specificity	Risk of miss-classification
Diabetes mellitus	.074	0.635 (0.479–0.791)	**Presence of diabetes mellitus**	0.438	0.832	0.365
Peripheral artery disease	.206	0.596 (0.437–0.754)	**Presence of peripheral artery disease**	0.313	0.880	0.404
Atrial fibrillation	**.022**	0.674 (0.554–0.794)	**Presence of atrial fibrillation**	0.875	0.473	0.326
Heart failure	**.041**	0.655 (0.502–0.807)	**Presence of heart failure**	0.500	0.808	0.346
CHA_2DS_2-VASc-score (points)	**.001**	0.746 (0.630–0.861)	**2.5 points**	0.781	0.612	0.340
Age (years)	**.018**	0.674 (0.549–0.799)	**61.5 years**	0.838	0.581	0.370
Blood flow velocity in the LAA detected by Pulsed-waved Doppler (cm s^{-1})	**.001**	0.799 (0.688–0.910)	**42.25cm/s**	0.906	0.702	0.231
LAA longitudinal diameter (cm)	**.002**	0.728 (0.599–0.858)	**3.95cm**	0.695	0.813	0.259
LAA septal-lateral diameter (cm)	**.004**	0.714 (0.581–0.846)	**1.85cm**	0.781	0.710	0.259
Right atrial area (cm^2)	**.038**	0.721 (0.508–0.934)	**27.60cm^2**	0.651	0.880	0.284
Left atrial area (cm^2)	.061	0.689 (0.496–0.882)	**23.15cm^2**	0.745	0.690	0.286

LAA = indicates left atrial appendage.

7. Conclusions

The incidence of ischemic stroke in the German nationwide sample of inpatients in 2015 was 360/100,000 citizens and increased with age. AF was connected to higher in-hospital mortality in ischemic stroke. AF was associated with 6-fold higher risk of thrombogenic material compared to SR.

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Conceptualization: Karsten Keller, Martin Geyer.
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Project administration: Karsten Keller.
Resources: Karsten Keller.
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