


Anticoagulation practices in adults with congenital heart disease and atrial arrhythmias in Switzerland

Ketina Arslani MD^{1*} | Lukas Notz^{1*} | Marzena Zurek MD¹ |
Matthias Greutmann MD² | Markus Schwerzmann MD³ | Judith Bouchardy MD⁴ |
Reto Engel MD⁵ | Christine Attenhofer Jost MD⁶ | Daniel Tobler MD¹  |

On behalf of the SACHER investigators

¹Department of Cardiology, University Hospital of Basel, University of Basel, Switzerland

²Department of Cardiology, University Heart Center, University of Zurich, Switzerland

³Department of Cardiology, Center for Congenital Heart Disease, Inselspital, University of Bern, Switzerland

⁴Department of Cardiology and Cardiac Surgery (CHUV), Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

⁵Cardiology, Kantonsspital St. Gallen, St. Gallen, Switzerland

⁶Klinik im Park, Zurich, Switzerland

Correspondence

Daniel Tobler, MD, Department of Cardiology, University Hospital Basel, Petersgraben 4; CH-4031 Basel.
Email: daniel.tobler@usb.ch

Abstract

Background: In adults with congenital heart disease (CHD) and atrial arrhythmias, recommendations for thromboprophylaxis are vague and evidence is lacking. We aimed to identify factors that influence decision-making in daily practice.

Methods: From the Swiss Adult Congenital HEart disease Registry (SACHER) we identified 241 patients with either atrial fibrillation (Afib) or atrial flutter/intraatrial reentrant tachycardia (Aflut/IART). The mode of anticoagulation was reviewed. Logistic regression models were used to assess factors that were associated with oral anticoagulation therapy.

Results: Compared with patients with Aflut/IART, patients with Afib were older (51 ± 16.1 vs 37 ± 16 years, $P < .001$) and had a higher CHA₂DS₂-VASc ($P < .001$) and HAS-BLED scores ($P = .005$). Patients with Afib were more likely on oral anticoagulation than patients with Aflut/IART (67% vs 43%, $P < .001$). In a multivariate logistic regression model, age [odds ratio (OR) 1.03 per year, 95%CI (1.01-1.05), $P = .019$], atrial fibrillation [OR 2.75, 95%CI (1.30-5.08), $P = .007$], non-paroxysmal atrial arrhythmias [OR 5.33, 95%CI (2.21-12.85)], CHA₂DS₂-VASc-Score >1 [OR 2.93, 95%CI (1.87-4.61), $P < .001$], and Fontan palliation [OR 17.5, 95%CI (5.57-54.97), $P < .001$] were independently associated with oral anticoagulation treatment, whereas a HAS-BLED score >1 was associated with absence of thromboprophylaxis [OR 0.32, 95%CI (0.17-0.60), $P < .001$].

Conclusions: In this multicenter study, age, type, and duration of atrial arrhythmias, CHA₂DS₂-VASc and HAS-BLED scores as well as a Fontan palliation had an impact on the use of thromboprophylaxis in adult CHD patients with atrial arrhythmias. In daily practice, anticoagulation strategies differ between patients with Afib and those with Aflut/IART. Prospective observational studies are necessary to clarify whether this attitude is justified.

KEYWORDS

anticoagulation, atrial arrhythmia, congenital heart disease, thromboprophylaxis

1 | BACKGROUND

Atrial arrhythmias are the most frequent complications in adults with congenital heart disease (CHD) and are associated with increased

morbidity and mortality.^{1,2} Intraatrial reentrant tachycardia (IART), atrial flutter, and atrial fibrillation have been identified as the most common atrial arrhythmias.³

In contrast to patients with acquired heart disease, only few studies explored the association between thromboembolic events and atrial arrhythmia in CHD patients.^{1,4} Moreover, there is lack of evidence

*Ketina Arslani and Lukas Notz contributed equally to this study.

about who may benefit from anticoagulation therapy in order to prevent thromboembolic events. Simple extrapolation from guidelines developed for patients with atrial arrhythmias^{5,6} in the setting of acquired heart disease may not be appropriate. Patients with CHD are typically younger than patients with acquired heart disease and comprise substantial heterogeneity in terms of clinical presentation, and the variety of underlying anatomical characteristics, sometimes with unique lesions- and patient-specific hemodynamics (eg, in patients with a Fontan procedure for palliation of a single ventricle physiology). Current recommendations are thus based on limited retrospective analysis and mainly expert opinions.^{7,8}

The aim of this study was to characterize the clinical spectrum of adult CHD patients with atrial arrhythmias, to review the mode of anticoagulation therapy and to analyze factors that influence the decision-making whether or not a patient with atrial arrhythmias was put on oral anticoagulation.

2 | METHODS

2.1 | Study population

We identified all patients of the Swiss Adult Congenital HEart disease Registry (SACHER, ClinicalTrials.gov Identifier NCT 2258724) enrolled from May 2014 to August 2016 with a history of atrial arrhythmia. The structure of SACHER has been described previously.⁹ At inclusion into SACHER, previous or concurrent atrial arrhythmias are classified as either atrial fibrillation or as atrial flutter/intraatrial reentrant tachycardia (IART) or as other supraventricular tachycardia (SVT). Other SVT include atrioventricular nodal re-entrant tachycardia, accessory-pathway mediated tachycardia, automatic focal atrial tachycardia, or junctional tachycardia. The type of arrhythmias was determined by the treating cardiologists. Atrial arrhythmias less than 48 hr was defined as paroxysmal; if greater than 48 hr it was defined as nonparoxysmal.

For the purpose of this study, patients with atrial fibrillation and concomitant other types of atrial arrhythmias (eg, atrial fibrillation and atrial flutter) were classified as "atrial fibrillation" and patients with atrial flutter or IART and other SVT were classified as atrial flutter/IART. All patients participating in SACHER have given written informed consents for analysis of their data.

2.2 | Data collection

Patient characteristics including age at inclusion, sex, cardiac diagnosis, and previous surgical history were obtained from SACHER. In all patients with a history of atrial fibrillation or atrial flutter/IART the following variables were collected at the time of inclusion: weight, height, oxygen saturation at rest, the presence of pulmonary hypertension, the components of the CHA₂DS₂-VASc,¹⁰ and HAS-BLED scores,¹¹ the underlying rhythm (sinus rhythm, atrial fibrillation, atrial flutter, paced rhythm, and other) at the time of inclusion as well as the mode of oral anticoagulation therapy (defined as being either on vitamin K antagonists or on novel oral anticoagulation therapy [NOAC]). The etiology of stroke was obtained by chart review and defined as either cardio-

embolic, paradoxical, peri-interventional, or due to other reasons. Patients with mechanical heart valves were excluded from analysis. Given that there is no indication for preventive anticoagulation in patients classified as other SVT (atrioventricular nodal reentrant tachycardia or accessory pathway-mediated tachycardia) without concomitant atrial fibrillation or atrial flutter they were excluded from analysis as well.

2.3 | Statistics

Data analysis was performed using SPSS software (Version 22.0, SPSS Inc., Chicago, Illinois). Data were described as medians with ranges or means with standard deviations, as appropriate. Comparisons of continuous or categorical variables were performed with Student's test or Mann-Whitney test, and chi-square tests or Fisher's exact test, as appropriate. The *P* values <.05 were considered significant. Binomial logistic regression with backward selection was used to determine factors associated with oral anticoagulation therapy in patients with atrial fibrillation or atrial flutter/IART. The following variables were entered into the model: sex, age at inclusion, time interval between date of first onset of the qualifying atrial arrhythmia and date of inclusion, the presence of prior cardiac intervention, subsequent interventions after the main repair (more than one cardiac surgery), the presence of atrial fibrillation, the presence of nonparoxysmal atrial arrhythmia at the time of inclusion, a CHA₂DS₂-VASc score ≥ 2 , a HAS-BLED score ≥ 2 , and all cardiac diagnoses with more than 10 cases of atrial arrhythmias (repaired tetralogy of Fallot, transposition of the great arteries after an atrial switch operation, Fontan palliation, atrial septal defects (repaired and unrepaired, excluding patients with Eisenmenger physiology), atrioventricular septal defect (repaired and unrepaired, excluding patients with Eisenmenger physiology), and hypertrophic cardiomyopathy).

3 | RESULTS

3.1 | Baseline characteristics

From May 2014 to August 2016, 2602 patients have been enrolled in SACHER. Of these, we identified 344 patients with atrial arrhythmias. Thirty patients with a mechanical valve were excluded for further analysis. About 73 patients had isolated SVT and were also excluded. Compared with patients without atrial arrhythmias, patients with atrial arrhythmias were older and had a higher rate of previous surgical interventions (Table 1). A total of 241 patients either had atrial fibrillation or atrial flutter/IART as their main atrial arrhythmia and were analyzed for association between clinical characteristics and anticoagulation strategy. Of these, 144 patients were grouped as atrial fibrillation and 100 patients as atrial flutter/IART. The rhythm on ECG at the time of inclusion revealed sinus rhythm in 147 patients (61%) and atrial fibrillation or atrial flutter/IART in 56 patients (23%). Within patients with atrial fibrillation, 37 (26%) had nonparoxysmal atrial fibrillation; of those with atrial flutter/IART, 11 patients (11%) had nonparoxysmal atrial flutter/IART. The underlying cardiac diagnoses of these patients are illustrated in Figure 1.

TABLE 1 Patient characteristics

	All Patients (n = 2602)	Without AA ^a (n = 2288)	SVT (n = 73)	Afib (n = 141)	Aflutter/IART (n = 100)	P ^b
Male, n (%)	1434 (55)	1254 (55)	34 (47)	86 (61)	60 (60)	.160
Age at inclusion, y	33 ± 14	32 ± 13	36 ± 13	51 ± 16	37 ± 13	<.001
Caucasian, n (%)	2517 (97)	2209 (97)	68 (93)	140 (99)	100 (100)	.023
Additional lesions, n (%)	1597 (61)	1355 (59)	55 (76)	111 (79)	76 (76)	<.001
Prior cardiac surgery, n (%)	1835 (71)	1573 (69)	55 (75)	114 (81)	93 (93)	<.001
Prior palliative intervention, N (%)	499 (19)	391 (17)	24 (33)	36 (26)	48 (48)	<.001
>1 cardiac intervention, N (%)	868 (33)	677 (30)	37 (51)	76 (54)	78 (78)	<.001
Valve surgery, N (%)	397 (15)	349 (15)	10 (14)	26 (18)	12 (12)	<.001
Mechanical	140 (5)	140 (6)	0	0	0	
Bioprosthesis	175(7)	144 (6)	6 (8)	18 (13)	7 (7)	
Reconstruction	82 (3)	65 (3)	4 (6)	8 (6)	5 (5%)	
RV or LV to PA conduits, N (%)	274 (11)	230 (10)	8 (11)	19 (14)	17 (17)	.099
Prior device implantation, N (%)	203(7)	131 (6)	11 (15)	40 (28)	21 (21)	<.001
PM	138 (5)	90 (4)	6 (8)	26 (18)	16 (16)	
ICD/CRT	65 (3)	41 (2)	5 (7)	14 (10)	5 (5)	

Abbreviations: AA, atrial arrhythmia; Afib, atrial fibrillation; IART, intraatrial reentrant tachycardia; PM, pacemaker; RV or LV to PA, right ventricle or left ventricle to pulmonary artery; SVT, supraventricular tachycardia.

^aIncluding patients with AA and mechanical valve (n = 30).

^bP value between patients with and without AA.

3.2 | Risk factors for thromboembolic events

Patients with atrial fibrillation were significantly older compared with patients with atrial flutter/IART (age at first onset of the qualifying arrhythmia was 43 ± 16 years vs 30 ± 15 years, $P < .001$ and age at inclusion into SACHER was 51 ± 16 years vs 37 ± 16 years, $P < .001$). Patients with atrial fibrillation had a higher prevalence of arterial

hypertension (33% vs 12%, $P < .001$), diabetes mellitus type 2 (6% vs 0%, $P < .007$), and had a higher CHA₂DS₂-VASc score (CHA₂DS₂-VASc score ≥2: 46% vs 22%, $P < .001$). Of the 35 patients with previous stroke, the etiology of the stroke was cardio-embolic in 17 (49%), paradoxical emboli in 7 (20%), peri-interventional in 6 (17%), and of other etiology in 5 patients (14%), with septic emboli among others. In patients with atrial flutter/IART, the etiology of the stroke was cardio-embolic in 4 out of 12 (33%), whereas in patients with atrial fibrillation the etiology was cardio-embolic in 13 out of 23 (57%), $P = .17$. Risk factors for thromboembolic events are summarized in Table 2.

3.3 | Oral anticoagulation therapy

Overall, patients with atrial fibrillation were more likely on oral anticoagulation therapy compared with patients with atrial flutter/IART (67% vs 43%, $P < .001$). In patients with a CHA₂DS₂-VASc score ≥2, more patients with atrial fibrillation were on oral anticoagulation compared with patients with atrial flutter/IART (77% vs 55%, $P < .001$). Patients with atrial fibrillation on oral anticoagulation were older (53 ± 15 years vs 45 ± 18 years, $P = .005$) and had a higher CHA₂DS₂-VASc score (CHA₂DS₂-VASc score ≥2: 53% vs 32%, $P = .001$) compared with those without oral anticoagulation. In the group of patients with atrial flutter/IART no statistically significant differences in baseline characteristics were found between patients with and without oral anticoagulation.

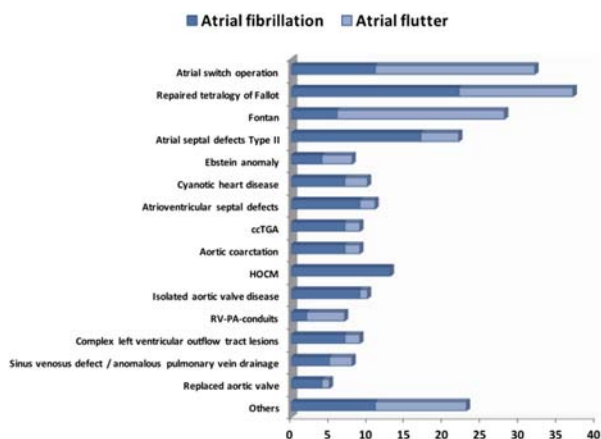


FIGURE 1 Distribution of atrial fibrillation and atrial flutter in CHD diagnoses. Abbreviations: ccTGA, congenitally corrected transition of the great arteries; HOCM, hypertrophic obstructive cardiomyopathy; RV-PA, right ventricle to pulmonary artery (Rastelli operation, Ross operation, Truncus arteriosus repair)

TABLE 2 Risk factors and mode of anticoagulation

	All AA (n = 241)	Afib (n 141)	Aflutter/IART (n = 100)	P
Age at qualifying arrhythmia, y	38 ± 17	43 ± 16	30 ± 15	<.001
Time interval first onset to inclusion, y	7.7 ± 8.5	7.7 ± 9.1	7.8 ± 7.6	.89
Body mass index, kg/m ²	24.8 ± 4.2	25.2 ± 4.6	24.2 ± 3.6	.066
SpO ₂ , %	95.5 ± 4.8	94.9 ± 5.5	96.2 ± 3.5	.064
Pulmonary hypertension, (%)	24 (10)	18 (13)	6 (6)	.084
Hypertension, (%)	59 (25)	47 (33)	12 (12)	<.001
Diabetes, (%)	9 (4)	9(6)	0	.007
Prior stroke, (%)	35 (15)	23 (16)	12 (12)	.349
Heart failure, (%)	50 (21)	32 (23)	18 (18)	.376
Vascular disease, (%)	21 (9)	15 (11)	6 (6)	.208
Renal disease, (%)	4 (2)	3 (2)	1 (1)	.500
Liver disease, (%)	4 (2)	2 (1)	2 (2)	.728
Bleeding, (%)	15 (6)	11 (8)	4 (4)	.229
Unstable INR, (%)	0	0	0	–
Age >65 years, (%)	24 (10)	22 (16)	2 (2)	.001
NSAID, (%)	35 (15)	26 (18)	9 (9)	.040
Alcohol use, (%)	7 (3)	4 (3)	3 (3)	.941
CHA ₂ DS ₂ -Vasc, (%)				<.001
0	112 (47)	50 (36)	62 (62)	
1	42 (17)	26 (18)	16 (16)	
>1	87 (36)	65 (46)	22 (22)	
HAS-BLED, (%)				.005
0	142 (59)	71 (51)	71 (71)	
1	78 (32)	54 (38)	24 (24)	
>1	21 (9)	16 (11)	5 (5)	
Oral anticoagulation, (%)	137 (57)	94 (67)	43 (43)	<.001
• Vitamin K antagonist	95 (39)	64 (45)	31 (31)	.024
• NOAC	42 (17)	30 (21)	12 (12)	.061
Platelet aggregation inhibitor, (%)				
• Aspirin	36 (15)	24 (17)	12 (12)	.281

Abbreviations: AA, atrial arrhythmia; Afib, atrial fibrillation; Aflutter, atrial flutter; IART, intraatrial reentrant tachycardia; NSAID, nonsteroidal anti-inflammatory drugs.

Overall, patients with nonparoxysmal arrhythmias were more likely on oral anticoagulation therapy compared with patients with paroxysmal arrhythmias (84% vs 43%, $P < .001$). This distinction was mainly made in patients with atrial fibrillation (95% vs 51%, $P < .001$) but not in patients with atrial flutter/IART (55% vs 33%, $P = .19$).

Of the 65 patients with atrial fibrillation and a CHA₂DS₂-VASC score ≥ 2 , 15 were not on oral anticoagulation therapy at the time of inclusion. Reasons were prior major bleeding in 2 patients and patient refusal in 4 patients. In 9 patients, the reason was based on the physician's decision as it was the first episode (5 patients with postoperative atrial fibrillation, 1 patient with fever and 1 patient after binge drinking) without recurrence. Of the 22 patients with atrial

flutter/IART and a CHA₂DS₂-VASC score ≥ 2 , 10 patients were not on oral anticoagulation therapy. Reasons were prior major bleeding in 2 patients and in 2 patients inclusion into the registry and occurrence of the arrhythmia was on the same date and oral anticoagulation therapy was started shortly thereafter. In 6 patients, the reason was based on physician's decision as it was the first episode (1 patient postoperative and 2 patients had subsequent ablation therapy) without recurrence.

Of 28 patients with Fontan palliation and atrial arrhythmia, 6 were not on oral anticoagulation. All of those 6 patients had prior atrial flutter/IART and a CHA₂DS₂-VASC score of 0. Three patients had a Fontan revision after the first onset and no recurrence of atrial arrhythmia

TABLE 3 Associations for oral anticoagulation therapy

Factors	All	OAC	Univariate		Multivariate				
			No OAC	OR	95%CI	P	OR	95%CI	P
Age, y	45.0 ± 16.3	48.1 ± 16.3	40.9 ± 15.5	1.03	1.01-1.06	.004	1.03	1.01-1.05	.019
Time interval AA to inclusion	7.7 ± 8.5	7.8 ± 7.7	7.7 ± 9.4	1.00	0.99-1.00	.933			
Gender, female	95	54 (57%)	41 (43%)	0.78	0.41-1.48	.453			
Prior cardiac surgery	34	21 (62%)	13 (38%)	1.65	0.59-4.62	.337			
>1 cardiac intervention	87	50 (57%)	37 (43%)	0.62	0.30-1.30	.206			
Atrial fibrillation	141	94 (67%)	47 (33%)	2.87	1.40-5.89	.004	2.57	1.30-5.08	.007
Nonparoxysmal AA	56	47 (84%)	9 (16%)			<.001	5.33	2.21-12.85	<.001
CHA ₂ DS ₂ -Vasc >1	87	62 (71%)	25 (29%)	2.82	1.82-4.38	<.001	2.94	1.87-4.62	<.001
HAS-BLED >1	21	14 (67%)	7 (33%)	0.39	0.214-0.692	.001	0.32	0.17-0.60	<.001
Atrial switch	32	16 (50%)	16 (50%)	1.83	0.67-4.99	.237			
Repaired TOF	37	18 (49%)	19 (51%)	1.07	0.42-2.69	.888			
Fontan	28	22 (79%)	6 (21%)	21.74	6.27-75.35	<.001	17.50	5.57-54.97	<.001
ASD II	22	14 (64%)	8 (36%)	1.99	0.65-6.17	.231			
AVSD	11	6 (55%)	5 (45%)	0.71	0.15-3.40	.670			
HOCM	13	11 (85%)	2 (15%)	3.850	0.666-22.272	.132			

Abbreviations: AA, atrial arrhythmia; TOF, tetralogy of Fallot; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CI, confidence interval; HOCM, hypertrophic-obstructive cardiomyopathy; OAC, on oral anticoagulation therapy.

thereafter, 1 patient had successful ablation therapy and no recurrence thereafter, and 2 patients refused to take oral anticoagulation therapy.

3.4 | Mode of oral anticoagulation therapy

Of those patients with oral anticoagulation therapy, 42 (31%) were on NOACs. Patients on NOACs had on average less complex congenital heart defects, characterized by lower rate of prior palliative interventions (16% vs 39%, $P = .007$), lower rate of subsequent interventions after intracardiac repair (24% vs 42%, $P = .029$), and a lower rate of previous stroke (12% vs 35%, $P = .018$). Less patients on NOACs had a CHA₂DS₂-VASC score ≥ 2 (33% vs 51%, $P = .027$) compared with patients on vitamin K antagonists. Patients with Fontan palliation were less likely on NOACs compared with patients with other congenital heart defects (9% vs 35%, $P = .017$).

3.5 | Associations with oral anticoagulation therapy

In the multivariate analysis the following factors were independently positively associated with oral anticoagulation in patients with atrial arrhythmias (Table 3): age [odds ratio (OR) 1.03 per year, 95%CI (1.01–1.05), $P = .019$], atrial fibrillation [OR 2.75, 95%CI (1.30–5.08), $P = .007$], nonparoxysmal atrial arrhythmia [OR 5.33, 95%CI (2.21–12.85)], CHA₂DS₂-VASC-Score >1 [OR 2.93, 95%CI (1.87–4.61), $P < .001$], and Fontan palliation [OR 17.5, 95%CI (5.57–54.97), $P < .001$]. On the other hand, HAS-BLED scores >1 were negatively associated with the use of oral anticoagulation therapy [OR 0.32, 95%CI (0.17–0.60), $P < .001$].

4 | DISCUSSION

The main finding of this study is that in daily clinical practice, even among expert centers, oral anticoagulation strategies differ between CHD patients with atrial fibrillation vs atrial flutter/IART. As in current guidelines of thromboprophylaxis in patients with acquired heart disease with atrial fibrillation,^{5,6,12} the CHA₂DS₂-VASC score as well as the HAS-BLED score had an important impact on the treating cardiologists' decision making whether or not an adult CHD patient with atrial fibrillation should be on anticoagulation therapy. In contrast, in patients with atrial flutter/IART the decision about anticoagulation was influenced by other factors. Neither CHA₂DS₂-VASC score nor age were associated with thromboprophylaxis management in our cohort, and the overall rate of anticoagulation therapy was significantly lower compared with patients in the atrial fibrillation group.

4.1 | Extrapolation from studies in the general population—and its limits

In studies from the general population thromboembolic risks seem to be similar in patients with atrial fibrillation and patients with atrial flutter.¹³ In the TACTIC study, a North American retrospective multicenter study (12 centers) with 482 adult CHD patients, similar thromboembolic risk was reported regardless of the underlying atrial arrhythmia.^{14,15} However, in patients with CHD, stroke is not always related to atrial arrhythmias, as also shown in this study. Of 35 patients with a previous stroke, 37% were related to previous operations or

interventions or paradoxical embolism and only in 49% stroke was related to atrial arrhythmias. Thus, the use of the CHA₂DS₂-VASc for (younger) patients with CHD may be of limited use and may even be misleading, as one of its major components—previous stroke—may not reliably predict future risk of cardio-embolic stroke due to the atrial arrhythmia. If the distinction between atrial fibrillation and atrial flutter/IART on the risk of cardio-embolic stroke is justified, requires further prospective studies with larger study populations and long follow-up duration.

In the absence of such studies, recommendations on thromboprophylaxis therapy in CHD patients with atrial arrhythmias are based on expert consensus.^{7,8} Jensen et al. suggested that in all patients with atrial fibrillation, atrial flutter or IART (paroxysmal or persistent) with prior intracardiac repair, with cyanosis, with a Fontan palliation or with a systemic right ventricle, oral anticoagulation therapy is recommended, regardless of the CHA₂DS₂-VASc score. All other CHD patients should be treated according the CHA₂DS₂-VASc score in line with current guidelines for the general population. In our study, Fontan palliation was associated with the use of oral anticoagulation whereas prior intracardiac repair was not.

In the expert consensus statement on the recognition and management of arrhythmias in adult CHD patients⁸ recommendations are based on the complexity of the underlying CHD. It is suggested as a class I indication that all adults with complex CHD and sustained or recurrent atrial flutter/IART or atrial fibrillation should receive long-term anticoagulation regardless of the CHA₂DS₂-VASc score. In accordance with these recommendations, our cohort was more likely on oral anticoagulation therapy if nonparoxysmal atrial arrhythmias were present. Again, these recommendations are based solely on expert opinion and not on solid prospective scientific data. Important individual disease characteristics such as ventricular and valvar function, size of heart chambers and other factors, such as patient compliance and individual bleeding risk are not reflected in these expert recommendations.

In our cohort from expert centers in Switzerland decisions on anticoagulation strategy differed from the expert opinion documented in the aforementioned expert consensus recommendations. While there seems agreement about the high risk of thromboembolic complications in patients with prior Fontan palliation and thus high rate of long-term anticoagulation in the case of atrial arrhythmias, in other patient groups with complex lesions, expert opinion on the utility of long-term anticoagulation in other CHD patient groups with complex lesions (eg, patients after atrial switch operation for transposition of the great arteries) differed substantially from published expert recommendations. From our study, it is obvious that the expert centers in SACHER used an individual approach in complex lesions. For example, despite the higher risk of thrombo-embolic complications in cyanotic patients, there is also a higher risk for life-threatening bleeding complications due to altered hemostasis and abnormal pulmonary vascular architecture. These aspects need to be taken into account and require careful weighing of risks and benefits in the individual patient. Patients with Fontan palliation may have different thromboembolic risks due to different surgical circumstances. Therefore, as suggested by the North

American guidelines,¹⁶ patients with an atriopulmonary Fontan palliation with dilated right atrium, fenestrated tunnel or veno-venous collaterals may benefit from long-term oral anticoagulation whereas Fontan patients with an extracardiac conduit, no fenestration, and no arrhythmia may be less likely to have a benefit.

In our cohort, almost one third of anticoagulated patients were on NOACs. It has been suggested that NOAC should only be used in a selected group of CHD patients, without cyanosis, Fontan palliation, systemic right ventricle or intracardiac repair as there is lack of research in pharmacokinetics and—dynamics in these patients.⁸ A recent report from the NOTE registry implies that the use of NOAC even in complex CHD seems to be safe.¹⁷ In SACHER, patients with a Fontan palliation are less likely on NOAC. This is in accordance to current international recommendations.⁸ If this strategy is justified is under current investigation (NOACs for thromboembolic prevention in patients with a Fontan circulation, unpublished data (NCT02928133—ClinicalTrial.gov)). Antiplatelet therapy has no important role in thromboprophylaxis in our cohort, in contrast to the TACTIC study, where 38% of patients with atrial fibrillation, atrial flutter or IART tachycardia were on aspirin.¹⁴

5 | LIMITATIONS

This is an observational study of patients followed at specialized centers for adults with CHD and therefore, the number of simple lesions was under-represented. We have no information on the anticoagulation regimen of patients followed by local cardiologists. A successful ablation may have an influence on long-term anticoagulation and therefore, the rate of anticoagulation may be underestimated, particularly in the group of patients with atrial flutter/IART. Although the type of arrhythmia was determined by experienced cardiologists, no cross checking occurred to verify the underlying rhythm. The study was not designed to predict thromboembolic risks of CHD patients with atrial arrhythmias and to analyze risk reduction with long-term oral anticoagulation. Larger studies with prospective constructs are needed to evaluate which CHD patients with atrial arrhythmia need long-term oral anticoagulation. In this regard, SACHER will allow multicenter data-collection in adults with CHD and its structure enables prospective data analysis to assess detailed, lesion-specific outcomes.

6 | CONCLUSION

In this multicenter study, age, type, and duration of atrial arrhythmias, CHA₂DS₂-VASc and HAS-BLED scores as well as a Fontan palliation had an impact on the use of thromboprophylaxis in adult CHD patients with atrial arrhythmias. In daily practice, anticoagulation strategies differ between patients with Afib and those with Aflut/IART. Prospective observational studies are necessary to clarify whether this attitude is justified. NOAC is a frequently used mode of anticoagulation therapy among SACHER patients.

CONFLICT OF INTEREST

None.

ORCID

Daniel Tobler MD  <http://orcid.org/0000-0002-0821-3196>

REFERENCES

- Bouchardy J, Therrien J, Pilote L, et al. Atrial arrhythmias in adults with congenital heart disease. *Circulation*. 2009;120(17):1679–1686.
- Engelfriet P, Boersma E, Oechslin E, et al. The spectrum of adult congenital heart disease in Europe: morbidity and mortality in a 5 year follow-up period. The Euro Heart Survey on adult congenital heart disease. *Eur Heart J*. 2005;26(21):2325–2333.
- Kirsh JA, Walsh EP, Triedman JK. Prevalence of and risk factors for atrial fibrillation and intra-atrial reentrant tachycardia among patients with congenital heart disease. *Am J Cardiol*. 2002;90(3):338–340.
- Hoffmann A, Chockalingam P, Balint OH, et al. Cerebrovascular accidents in adult patients with congenital heart disease. *Heart*. 2010;96(15):1223–1226.
- Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37(38):2893–2962.
- January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation*. 2014;130(23):2071–2104.
- Jensen AS, Idorn L, Norager B, Vejstrup N, Sondergaard L. Anticoagulation in adults with congenital heart disease: the who, the when and the how? *Heart*. 2015;101(6):424–429.
- Khairy P, Van Hare GF, Balaji S, et al. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology (ACC), the American Heart Association (AHA), the European Heart Rhythm Association (EHRA), the Canadian Heart Rhythm Society (CHRS), and the International Society for Adult Congenital Heart Disease (ISACHD). *Can J Cardiol*. 2014;30(10):e1–e63.
- Tobler D, Schwerzmann M, Bouchardy J, et al. Swiss Adult Congenital HEart disease Registry (SACHER) - Rationale, design and first results. *Swiss Med Wkly*. 2017;147:w14519.
- Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest*. 2010;137(2):263–272.
- Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010;138(5):1093–1100.
- Lip GY, Andreotti F, Fauchier L, et al. Bleeding risk assessment and management in atrial fibrillation patients. Executive Summary of a Position Document from the European Heart Rhythm Association [EHRA], endorsed by the European Society of Cardiology [ESC] Working Group on Thrombosis. *Thromb Haemost*. 2011;106(6):997–1011.
- Sparks PB, Kalman JM. Is atrial flutter a risk factor for stroke?. *J Am Coll Cardiol*. 2001;38(3):785–788.
- Khairy P, Aboulhosn J, Broberg CS, et al. Thromboprophylaxis for atrial arrhythmias in congenital heart disease: a multicenter study. *Int J Cardiol*. 2016;223:729–735.
- Feltes TF, Friedman RA. Transesophageal echocardiographic detection of atrial thrombi in patients with nonfibrillation atrial tachyarrhythmias and congenital heart disease. *J Am Coll Cardiol*. 1994;24(5):1365–1370.
- Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2008;52(23):e143–e263.
- Yang H, Bouma BJ, Mulder BJM. Non vitamin K antagonist Oral anticoagulants for ThromboEmbolic prevention in adult congenital heart disease (NOTE) investigators. Is initiating NOACs for atrial arrhythmias safe in adults with congenital heart disease? *Cardiovasc Drugs Ther*. 2017;31(4):413–417.

How to cite this article: Arslani K, Notz L, Zurek M, et al. Anti-coagulation practices in adults with congenital heart disease and atrial arrhythmias in Switzerland. *Congenital Heart Disease*. 2018;13:678–684. <https://doi.org/10.1111/chd.12627>