Stroke after implantable cardioverter-defibrillator shocks in patients with heart failure

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INTRODUCTION

Patients with heart failure (HF) are at elevated risk of cerebrovascular events, including stroke [1]. They are often burdened with many cardiovascular risk factors, in particular, atrial fibrillation (AF), a known risk factor for both stroke and HF [2–4].

It has been demonstrated that in AF patients, the risk of stroke is markedly elevated on the first days after successful electrical cardioversion of AF [5–7]. Regardless of their appropriateness, high-voltage shock therapies delivered by implantable cardioverter-defibrillators (ICDs) often result in termination of supraventricular arrhythmias, including AF cardioversion, potentially increasing the risk of stroke in those patients. However, the association between ICD shocks and the risk of stroke in AF patients is unknown. Therefore, the present analysis aimed to define whether any association exists between ICD shocks and strokes in remotely monitored HF patients.

METHODS

Data of patients enrolled in the remote monitoring (RM) program after implantation of an ICD were obtained from the COMMIT-HF registry. The rationale and the major results of the registry were published before, and in brief, among other findings, the registry encompasses detailed demographic, clinical, echocardiographic, and angiographic data of patients with heart failure with left ventricular ejection fraction ≤35% not caused by an acute coronary syndrome at index hospitalization, who have been admitted and treated in our facility (NCT02536443) [2, 8]. During the entire follow-up, patients were treated according to the respective guidelines [9, 10]. Routinely, apart from RM based on the continuous connectivity and alert transmissions, patients with ICDs visited the outpatient clinic every 12 months for an in-person evaluation. The baseline status of AF was based on the patient's medical history records, while any newly diagnosed AF during the follow-up period, was defined as *de novo* AF. A decision regarding the introduction and/or continuation of oral anticoagulation was based on the thromboembolic risk assessment using the CHA_2DS_2-VASc score [11].

Data regarding the occurrence of the first stroke after inclusion in the registry were obtained (based on codes I63–I64 of the International Classification of Diseases) from the National Health Fund — the sole Polish healthcare provider. The RM data of all patients were obtained from the investigator-initiated and maintained registry of RM, which summarizes all major findings in remotely monitored patients in our department. The registry data are particularly focused on the occurrence of alert transmissions, especially if they are caused by arrhythmic episodes or device therapies. In the registry, each patient's data are updated annually [12]. Each patient with a stroke had their RM history evaluated for the period of the prior 30 days, with emphasis on the last 10 days preceding stroke. The period of 10 days was selected on the basis of prior, mechanistic and clinical studies, indicating that the risk of stroke after cardioversion of AF persists for 10 days [6]. The study protocol was approved by an appropriate institutional review board and ethics committee.

Statistical analysis

The categorical variables were presented as absolute numbers and percentages. After assessment for normality using the Shapiro–Wilk

test, due to non-normal distribution of numerical variables, they were presented as medians with quartiles 1 and 3. Pearson's χ^2 test was used to compare the categorical variables, and the Mann-Whitney U test was used to compare non-normally distributed numerical variables. A two-tailed *P*-value <0.05 was considered statistically significant. STATISTICA 10 (StatSoft Inc., Tulsa, OK, US) was used for all calculations.

RESULTS AND DISCUSSION

During the period between 2011 and 2020, 1299 patients with detailed clinical characteristics were enrolled in the RM program, and their clinical data are summarized in Table 1. In the studied population, 523 (40.3%) patients had cardiac resynchronization therapy defibrillator devices, 438 (33.7%) had dual-chamber ICDs, and 338 (26.0%) had single-chamber ICDs, of whom 38 had an atrial sensing dipole. There were 434 (33.4%) patients with AF at baseline, and AF *de novo* was identified during follow-up in further 182 patients (14.0%). Median (Q1–Q3) CHA_2DS_2-VASc scores in patients without and with AF at baseline were, respectively, 3 (2–4) and 3 (2–5) points (*P* <0.001). Among patients without and with AF at baseline, 267 (30.9%) and 148 (34.1%), respectively, received any (either appropriate or inappropriate) ICD shocks during follow-up (*P* = 0.24). In 25.3% of all patients, at least one appropriate shock occurred, while inappropriate shocks were reported in 11.5% of patients. In 38.2% of patients without AF at baseline, who developed *de novo* AF, at least one shock occurred.

The median (Q1–Q3) follow-up was 4.4 (2.1–5.9) years, and the incidence of stroke was 45 (3.5%) in the studied population, with a rate of stroke of 25 (2.8%) in patients without AF at baseline and 20 (4.6%) in patients with AF (*P* = 0.11), as presented in Supplementary material, *Figure S1*. The median (Q1–Q3) time from ICD implantation to stroke was 1.5 (0.8–2.5) years.

In one patient without AF and one patient with AF, stroke occurred in less than 24 hours from ICD shock. In the first case, in a patient on acetylsalicylic acid monotherapy, the device appropriately terminated ventricular tachycardia which degenerated to ventricular fibrillation after anti-tachycardia pacing, and in the second case, shock therapy was delivered due to ventricular fibrillation in a 59-year-old male with HF and concomitant paroxysmal AF, who was on chronic treatment with warfarin.

Previous studies have identified AF cardioversion as a clinical event significantly elevating the risk of stroke. Successful cardioversion results in the return of rhythmic function of the atria, and thus potentially increases the risk of mobilization of the already-formed thrombus from the left atrial appendage, with increased risk of stroke persisting for approximately 10 days [5, 6]. To date, no study assessed the temporal association between ICD shocks and stroke.

In the studied population, the overall risk of stroke (3.5% during the median follow-up of 4.4 years) was comparable with other European populations of HF patients [13]. However, a temporal association between high-voltage ICD therapies and stroke was noted in only two patients. The first patient with AF had oral anticoagulation administered, and the second with VT had an appropriate shock. The post-shock stroke in the overall cohort was observed in approximately 0.5% of patients with any shock therapy.

A few limitations of our study are worth noting, as no exact information on the anticoagulation status of the studied patients was available — despite administration of oral anticoagulants in AF patients, according to individual assessment of thrombo-embolic risk, lack of adherence to therapy or being outside the therapeutic range cannot be excluded. Second, based on the International Classification of Diseases, no differentiation between types of stroke (e.g., hemorrhagic, ischemic, etc.) could be made for this analysis. Finally, although the study has been conducted on a meticulously remotely monitored cohort, the present analysis could be considered numerically too small to draw straightforward conclusions, and its retrospective nature

Table 1. Baseline characteristics and pharmacotherapy of the studied population on discharge based on the COMMIT-HF registry

Demographics at baseline	Overall population (n = 1299)
Female, n (%)	230 (17.7)
Age at implantation, years, median (Q1–Q3)	62 (55–70)
Indication for implantation	**Overall population (n = 1299)**
Ischemic cardiomyopathy, n (%)	788 (60.7)
Non-ischemic cardiomyopathy, n (%)	511 (39.3)
Arterial hypertension, n (%)	695 (53.5)
Atrial fibrillation, n (%)	434 (33.4)
Diabetes, n (%)	475 (36.6)
NYHA classification	
II, n (%)	554 (42.6)
III, n (%)	532 (41.0)
IV, n (%)	91 (7.0)
GFR ≤60 ml/min/1.73 m^2, n (%)	324 (24.9)
NT-proBNP, pg/ml, median (Q1–Q3) [n/n]	1885 (770–4195) [340/1299]
LVEF, %, median (Q1–Q3)	25 (20–30)
Pharmacotherapy on discharge from baseline hospitalization	**Overall population (n = 1299)**
ACE-I/ARB, n (%)	926/129 (71.3/9.9)
Beta-blocker, n (%)	1248 (96.1)
Diuretics, n (%)	1126 (86.7)
Amiodarone, n (%)	185 (14.2)
Aldosterone antagonist, n (%)	1107 (85.2)
Ivabradine, n (%)	70 (5.4)
Digitalis, n (%)	266 (20.5)
Any oral anticoagulants, n (%)	464 (35.7)
Vitamin K antagonists, n (%)	421 (32.4)
Direct oral anticoagulants, n (%)	45 (3.5)
Low molecular-weight heparin, n (%)	19 (1.5)
Single antiplatelet therapy, n (%)	508 (39.1)
Dual antiplatelet therapy, n (%)	331 (25.5)

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association

does not allow causality determination. Nonetheless, our findings indicate an overall low risk of stroke associated with ICD shocks, both in patients with and without AF.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

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REFERENCES

1. Alberts VP, Bos MJ, Koudstaal PJ, et al. Heart failure and the risk of stroke: the Rotterdam Study. Eur J Epidemiol. 2010; 25(11): 807–812, doi: 10.1007/s10654-010-9520-y, indexed in Pubmed: 21061046.
2. Gąsior M, Pyka Ł, Gorol J, et al. COnteMporary Modalities In Treatment of Heart Failure: a report from the COMMIT-HF registry. Kardiol Pol. 2016; 74(6): 523–528, doi: 10.5603/KP.a2015.0224, indexed in Pubmed: 26596896.
3. Aktan A, Güzel T, Aslan B, et al. Comparison of the real-life clinical outcomes of warfarin with effective time in therapeutic range and non-vitamin K antagonist oral anticoagulants: Insight from the AFTER-2 trial. Kardiol Pol. 2023; 81(2): 132–140, doi: 10.33963/KP.a2022.0287, indexed in Pubmed: 36594528.
4. Myrda K, Streb W, Wojakowski W, et al. Long-term outcomes in patients after left atrial appendage occlusion: The results from the LAAO SILESIA registry. Kardiol Pol. 2022; 80(3): 332–338, doi: 10.33963/KP.a2022.0047, indexed in Pubmed: 35167113.
5. Manning WJ, Leeman DE, Gotch PJ, et al. Pulsed Doppler evaluation of atrial mechanical function after electrical cardioversion of atrial fibrillation. J Am Coll Cardiol. 1989; 13(3): 617–623, doi: 10.1016/0735-1097(89)90602-5, indexed in Pubmed: 2918167.
6. Berger M, Schweitzer P. Timing of thromboembolic events after electrical cardioversion of atrial fibrillation or flutter: a retrospective analysis. Am J Cardiol. 1998; 82(12): 1545–15477, A8, doi: 10.1016/s0002-9149(98)00704-8, indexed in Pubmed: 9874066.
7. Hellman T, Kiviniemi T, Nuotio I, et al. Intensity of anticoagulation and risk of thromboembolism after elective cardioversion of atrial fibrillation. Thromb Res. 2017; 156: 163–167, doi: 10.1016/j.thromres.2017.06.026, indexed in Pubmed: 28662483.
8. Kurek A, Tajstra M, Gadula-Gacek E, et al. Impact of remote monitoring on long-term prognosis in heart failure patients in a real-world cohort: results from all-comers COMMIT-HF trial. J Cardiovasc Electrophysiol. 2017; 28(4): 425–431, doi: 10.1111/jce.13174, indexed in Pubmed: 28176442.
9. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation. Eur Heart J. 2021; 42(5): 373–498, doi: 10.1093/eurheartj/ehaa612, indexed in Pubmed: 32860505.
10. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021; 42(36): 3599–726, doi: 10.1093/eurheartj/ehab368, indexed in Pubmed: 34447992.
11. Lip GYH, Nieuwlaat R, Pisters R, et al. 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, doi: 10.1378/chest.09-1584, indexed in Pubmed: 19762550.
12. Dyrbuś M, Pyka Ł, Kurek A, et al. Alert transmissions from remote monitoring of patients with cardiac implantable devices. JACC Clin Electrophysiol. 2023; 9(10): 2163–2165, doi: 10.1016/j.jacep.2023.07.005, indexed in Pubmed: 37565950.
13. Adelborg K, Szépligeti S, Sundbøll J, et al. Risk of stroke in patients with heart failure: A population-based 30-year cohort study. Stroke. 2017; 48(5): 1161–1168, doi: 10.1161/STROKEAHA.116.016022, indexed in Pubmed: 28377383.