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Complications associated with direct-current cardioversion of atrial fibrillation and-flutter

a Danish regional quality-assurance study

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Abstract

Background

Atrial fibrillation represents a five-fold risk increase in developing systemic stroke compared to the general population. A vital treatment of atrial fibrillation consists of cardioversion to sinus rhythm, in purpose of symptom relieve and prevention of adverse events.

Cardioverting treatments represent a risk of thromboembolic events due to a possible mobilization of the formed thromboembolic material in the atrial chamber during atrial fibrillation.

Aim of the study

As a quality assurance study, we intended to evaluate the incidence of stroke, mortality and cardiac arrest as well as possible risk factors associated with short-term development of stroke following the direct-current cardioversion treatment of atrial fibrillation.

Methods

We identified all individuals from the Danish National Patient Registry, who underwent direct-current cardioversion treatment of atrial fibrillation between 1. January 2016 to 31. December 2020 at the North Denmark Regional Hospital, Hjoerring.

As primary exposure, only first-time direct-current cardioversion of atrial fibrillation to sinus rhythm were included. An additional analysis examined repeated direct-current cardioversion procedures.

Due to an extreme low incidence, this study was unable to apply inferential statistics on the dataset. Hence, this study examined the individual event as case-evaluations. To validate our study findings, we reported crude national data on stroke incidence, using data derived from a Statistics Denmark server.

Results

There was no incidence of cerebral thromboembolic events in first-time direct-current cardioversion-procedures, and one in repeated procedures (0.04%). Cardiac arrest was observed once in first time-procedures (0.10%) and no further incidences in repeated procedures (0.04%). The total of fatal incidences was 5 (0.19%) with 1 event occurring at first-time direct-current cardioversion-procedure (0.10%).

Conclusion

This study presented a low incidence of stroke, non-fatal cardiac arrest, and mortality. Hence, this study, performed as a quality-assurance study, verified the current direct-current cardioversion treatment of atrial fibrillation in the Regional Hospital of Northern Jutland Hjoerring as a high-quality clinical practice.

Abbreviations and acronyms

- Alanine-transaminase – ALT
- Anatomical Therapeutic Chemical Classification System – ATC
- Atrial Fibrillation – AF
- Automated external defibrillator – AED
- Cerebral computer tomography – CT
- Chronic Obstructive Pulmonary Disease – COPD
- C-Reactive Protein – CRP
- Danish Civil Registration System – DCRS
- Danish National Patient Registry – DNPR
- Direct Oral Anticoagulant – Same as "NOAC"
- Direct-Current Cardioversion – ECV
- European Society of Cardiology – ESC
- Implantable Cardioverter Defibrillator - ICD
- International Classification of Disease 10th Revision – ICD-10
- Novel Oral Anticoagulant – NOAC
- Magnetic resonance – MR
- Middle Cerebral artery – MCA
- Sinus Rhythm – SR
- Transient Ischemic Attack – TIA
- Transoesophageal Echocardiography – TEE
- Vitamin-K Antagonist – VKA

Introduction

The American Heart Association Council found a life-time risk of Atrial Fibrillation (AF) to be 1 in 3 among individuals of European ancestry. The European Union estimates a prevalence of AF in adults >55 years of age to be 8.8 million in 2010 and increasing to 17.9 million in 2060. (1)

While adults aged 20 years or older have a 3% lifetime risk of developing AF, it is estimated to develop among one quarter of the middle-aged population. (2)

AF represents a five-fold risk increase in developing systemic stroke compared to the general population. Anticoagulant therapy plays a vital role in stroke prevention. (3,4) The latest guidelines recommend direct oral anticoagulant (NOACs) as the preferred drug of choice, while in certain circumstances Vitamin-K antagonists (VKA) is still an option. (3,5)

A vital treatment of AF consists of cardioversion to sinus rhythm (SR), in purpose of symptom relieve and prevention of adverse events. (1,2)

The cardioversion of AF consists of direct-current cardioversion (ECV) or pharmacological cardioversion. Each treatment offers different benefits and limitations when compared. The benefits of pharmacological cardioversion consist of; no need of anesthesia, possibility of immediate repetitive- and out-hospital treatment. However, limitations consist of possible negative inotropic effect, risk of proarrhythmic events, and short- and long-term drug side-affects. (6) Benefits of ECV are immediate treatment, high efficiency, and for some patients a longer-lasting treatment effect. It is further safe to use among hemodynamic unstable patients. Limitations for ECV consist of need of general anesthesia. Both treatments options represent a risk of thromboembolic events due to a possible mobilization of the formed thromboembolic material in the atrial chamber during AF. (6)

For patients with AF lasting >48 hours, the recommendation from European Society of Cardiology (ESC) guidelines states - therapeutic anticoagulants should be used minimum 3 weeks prior, and 4 weeks following ECV. (7)
An individual assessment is performed prior to the procedure and consist of the CHA_2DS_2-VASc score, or if they are known with previous episodes of thromboembolic events, thrombophilia or if it is clinically relevant. If considered necessary or at high risk of thromboembolic events, a transesophageal echocardiogram (TEE) is performed to rule out intracardiac thrombi. As a routine procedure, 3 weeks relevant NOAC treatment prior to treatment is recommended due to a higher risk of thromboembolic events. (2)
The CHA_2DS_2-VASc score is used to predict the risk for thromboembolic episodes in AF and is presented in table 1. (8)
Patients who are not in relevant NOAC treatment, and with symptoms of AF >48 hours - are recommended a TEE prior to cardioversion. (2–4)
The TEE intends to detect presence of thromboembolic material in the left atrium. During the cardioversion, a thrombus or thrombi can be mobilized and progress to cause an embolic cardiogenic stroke. (3,4)
As a quality assurance study, we intended to evaluate the incidence of stroke, mortality and cardiac arrest as well as a series of possible risk factors associated with short-term development of stroke following the ECV treatment of AF.

Table 1 Risk stratification of stroke by CHA2DS2-VASc score (https://www.sundhed.dk/sundhedsfaglig/information-til-praksis/midtjylland/almen-praksis/patientforloeb/forloebsbeskrivelser/k-hjerte-karsystem/atrieflimren/ (table 1 on web page))

CHA2DS2-VASc	Risk factor	Score
C	Left ventricular dysfunction* and Congestive heart failure	+1p
H	Hypertension	+1p
A_2	Age ≥75 years old	+2p
D	Diabetes mellitus	+1p
S_2	Prior Thromboembolic event / Transient ischemic attack (TIA) / Stroke	+2p
V	Cardiovascular disease**	+1p
A	Age 65-74 years old	+1p
S	Female sex	+1p
Score: Max score: +9p = 12.2% stroke risk per year.		
*Left ventricular dysfunction is defines as an ejection fraction below 40% ** Cardiovascular diseases: Peripheral artery diseases, Aortic plaque and prior incidence of myocardial infarction.		

Methods

Databases

Every Danish citizen has a unique civil registration number given upon birth or immigration. Therefore, it is possible to obtain individual linkage of information throughout the Danish nationwide administrative registries. The Danish Civil Registration System (DCRS) and the Danish National Patient Registry (DNPR) has since 1978 collected information regarding age, sex, survival status, hospital admission- and discharge dates, relevant diagnoses, procedure dates and -codes. (7,8)

Since 1994 diagnoses are registered at discharge of each hospitalization according to the International Classification of Disease 10th revision (ICD-10). (9)

The Danish pharmacies register all dispensed prescriptions since 1995 into the National Registry of Medicinal Statistics. (10) The prescriptions are listed according to the Anatomical therapeutic Chemical System (ATC). (10) Therefore, dispensations of drug prescriptions contribute to a compelling and detailed registry.

Through the hospitals' laboratory data registries, blood test results originated from either primary-care, out-patient visits or during hospitalization were obtained for this study. NPU-codes of the blood-samples are listed in supplementary D.

Study population

We identified all individuals from the DNPR, who underwent ECV treatment of AF between 1. January 2016 to 31. December 2020 at the North Denmark Regional Hospital, Hjoerring. We included all patients with a diagnosis of AF, aged ≥18 years, who underwent an ECV procedure.

We excluded all patients without a permanent Danish civil registration number, or who migrated from Denmark in the follow-up period.

Comorbidities, procedures and medications

As acknowledged by the ESC guideline and in combination with factors of the CHA_2DS_2-VASc score, this study intended to investigate the impact of the following covariates in development of thromboembolic events following ECV (See Table 1; (2)): left ventricular dysfunction, congestive heart failure, prior thromboembolic event or TIA, peripheral artery disease, hypertension, diabetes mellitus, metabolic syndrome, kidney disease, age, and sex.

In addition, the DNPR was used to identify patients with a history of: Infectious diseases, neoplasms, hematological and immunological diseases, other cardiovascular diseases (here among arrythmia, coagulopathies, ischemic heart disease, hypertension and congenital heart diseases), respiratory and gastrointestinal illnesses, and pathologies concerning musculoskeletal system diseases. ICD-codes are listed in supplementary A and procedure-codes in supplementary B.

For the defined comorbidities, the applied diagnosis codes based on the ICD-10 and for prescription medication, the ATC-codes are listed in the supplementary C.

Internal bleeding was defined by ICD-10 codes and subcodes belong to intracranial- and gastrointestinal bleeding and bleeding-disorder due to circulating anticoagulantia.

Recent myocardial infarction is defined as a diagnosis of myocardial infarction within 90 days prior to the ECV procedure.

This study defined diabetes mellitus, hypercholesterolemia, and hypertension either through ICD-10 diagnosis codes or through at least two prescriptions in two concomitant quarters, if no available diagnosis registration during hospitalisation. A similar definition has previously been validated. (11)

Outcome

Outcomes for this study were the post-procedural ECV incidence of a cerebral thromboembolic event, death, and cardiac arrest, as well as thromboembolic events or sequelae due to thromboembolic events in the four-week follow-up period. We defined a cerebral thromboembolic event as one of the following: Ischemic stroke, TIA, arterial embolism and unspecified stroke. The applied ICD-10 diagnosis codes are also shown in the Supplementary Table.

Statistical analysis

As primary exposure, only first-time procedures were included. An additional analysis examined repeated ECV procedures in relation to outcome incidence.
This study included a sensitivity analysis by comparing the incidence of the measured outcomes presented in the local-hospital data of this study with national data from the DNPR, accessing data from a Statistics Denmark server.

This study intended to examine the data presented either as categorical or continuous data and applying to following statistical analyses; Wilcoxin Mann-Whitney-test for all non-normally distributed continuous variables, Chi^2-test for differences across categorical variables, Cox-proportional-hazards-model for individual and multivariable analysis. However, due to extreme few events, it was not possible to apply inferential statistical analyses in this study. Due to the extreme low incidence of events, this study hence examined the individual event as case-evaluations. To validate our study findings, we were given the opportunity to report crude national data on stroke incidence, using data derived from a Statistics Denmark server (see Ethics section below).

All data management of data from the registries have been programmed and designed by the study-group for this study-population using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) (12) and R Statistical Software version 3.5.0 (R Development Core Team). (13)

Ethics

This study is a quality assurance project and permission to obtain data were granted by the local hospital board in the North Denmark Regional Hospital, Hjoerring, as well as by the Data Responsible Unit in the North Denmark Region (ref. number 2021-137). We additionally obtained nationwide data on stroke risk following repeated ECV treatment of AF from a secure Statistics Denmark server. This use of this data has been approved by the Data Responsible Unit in the Capital Region of Denmark, where the server is located (approval reference P-2019-348).
Due to severely delayed delivery of data for the study, with data-access late November, and a short assignment period, with final delivery date primo January, it was not possible to apply for approval of full data access in the Danish National Registry. As mentioned above, it was not possible to apply inferential statistical analyses in this study due to extreme few events.

However, based on the above access to the Statistics Denmark server, we were permitted to report overall national data on stroke risk by year following repeated ECV treatment of AF in years 2016-2020.

Results

Among 962 individuals, who underwent a first time ECV-procedure for the treatment of AF in the Department of Cardiology, North Denmark Regional Hospital, Hjoerring, during 2016-2020, there were one outcome of cardiac arrest, zero cerebral thromboembolic events and two fatal events. Among a total of 2,649 repeated ECV procedures, one stroke event occurred within the follow-up period. There were no further cardiac arrest events and a total of five fatal events within the same time frame.

Demographics

The demographics table below presented a prominent prevalence of internal bleedings with 72 (7.48%) of the first time ECV patients and 505 (19.0%) of repeated ECV patients. There was also a prominent difference in NOAC-medicaments in the two populations.
There was a higher prevalence of antiarrhythmics type I and III among patients receiving repeated ECV compared to first-time ECV-procedures (16.5% compared to 3.6%). Among beta-blockers usage there was 19.6% among patients receiving first-time and 37.3% at repeated ECV-procedures.

*Table 2 Outcome characteristics of study population. *outcome within 30 days following procedure.*
Continuous variables presented as mean and (median), categorical variables as number=N and (mean).

	First-time ECV-procedure N=962	Repeated ECV-procedure N=2.649
Comorbidities		
Respiratory stop	0	0
Cardiac arrest	0	0
Heart Failure	94 (9.8%)	249 (9.4%)
Diabetes Mellitus	959 (99.7%)	2553 (96.4%)
Arterial hypertension	959 (99.7%)	2553 (96.4%)
Ischemic heart disease	959 (99.7%)	2553 (96.4%)
Pulmonary embolism	6 (0.62%)	14 (0.53%)
Hemorrhagic apoplexia	≤3	≤3
Internal bleeding	72 (7.5%)	505 (19.0%)
Apoplexia infarction	14 (1.5%)	39 (1.5%)
Arteriosclerosis	≤3	≤3
Arteriole with embolism or thrombotic element	4 (0.4%)	5 (0.2%)
Flebitis	≤3	6 (0.2%)
Chronic kidney disease	5 (0.5%)	8 (0.3%)
Rheumatoid mitral-valve disease	0	0
Rheumatoid aorta-valve disease	0	0
Congenital aorta-valve-stenosis	≤3	≤3
Congenital aorta-valve-insufficiency	0	0

Congenital mitral-valve-stenosis	0	0
Pharmacological medicine		
Sodiumflouride	0	13 (0.5%)
Magnesia	0	0
Proton-pump-inhibitor	4 (0.4%)	78 (2.9%)
Insulin	10 (1.0%)	47 (1.8%)
Other antidiabetics than insulin	30 (3.1%)	182 (6.9%)
Vitamin K-antagonists	36 (3.7%)	208 (7.9%)
Heparin	0	44 (1.7%)
NOAC	308 (32.0%)	994 (37.5%)
Other antithrombotic	20 (2.1%)	345 (13.0%)
Anti fibrinolytica	0	≤3
Vitamin K	0	0
Cardiac medicine excl. glycosides	0	0
Glycosides	54 (5.6%)	245 (9.3%)
Antiarrythmica type I and III	35 (3.6%)	438 (16.5%)
Antihypertensive	≤3	24 (0.9%)
Diuretics	90 (9.4%)	90 (3.4%)
Beta-blockers	189 (19.6%)	988 (37.3%)
Calcium antagonists	53 (5.5%)	433 (16.4%)
ACE-inhibitors	125 (13.0%)	719 (27.1%)
Blood-results		
s-potassium (s-K)	3.98 (3.98)	3.99 (3.99)
s-Sodium (s-Na)	140.28 (140.60)	140.27 (140.60)
INR	1.32 (1.10)	1.36 (1.10)
s-Hemoglobin	9.02 (9.10)	9.02 (9.10)
s-Albumin	36.79 (37.30)	36.81 (37.30)

The table of outcome incidence is presented below. The outcomes are defined as cerebral thromboembolic event, non-fatal cardiac arrest or fatal event.

In summary, there was no incidence of cerebral thromboembolic in first-time ECV-procedures, and one in repeated (0.04%). Cardiac arrest was observed once in first-time ECV-procedures (0.10%) no further incidences in repeated ECV-procedures (0.04%). The total amount of fatal incidences was 5 (0.19%) with 1 event occurring at first-time ECV-procedures (0.10%).

*Table 3 Outcome incidence of study population. *outcome within 30 days following procedure.*
Continuous variables presented as mean and (median), categorical variables as number=N and (mean).

	First-time ECV-procedure N=962	**Repeated ECV-procedure N=2.649**
Cerebral thromboembolic event * N (%)	0 (0%)	1 (0.04%)
Cardiac arrest* N (%)	1 (0.10%)	1 (0.04%)
Fatal events N (%)	1 (0.10%)	5 (0.19%)

Case study

Cerebral thromboembolic case

In this case, we studied the possible factors contributing to development of cerebral thromboembolic post ECV-procedure. This case was a 72-year-old female, with a prior history of hypertension and AF. This individual had a pharmacological treatment including following agents: metoprolol succinate (100 + 50 mg daily), Xarelto (20 mg daily), Ramipril (10 mg daily) and Centyl mite med Kaliumklorid (573+1.25mg daily).

The patient was admitted in the North Denmark Regional Hospital Hjoerring, due to symptoms of AF. She underwent an ECV-procedure, with conversion to SR. On the same day she was administrated Amiodarone post ECV-procedure.
The following day she develop cerebral thromboembolic, confirmed by Magnetic resonance (MR)-scan showing sign of infarction corresponding to the left side of communis radiata and an occlusion of Middle Cerebral Artery (MCA) part M1. Subsequently, thrombectomy were performed, where total recanalization was established. During hospitalization, the blood flow through the carotis arteries were examined with DUPLEX-ultrasound showing no signs of stenosis but moderate arteriosclerotic changes with efficient flow through both arteria vertebralis.
On the day of admission, the blood examination revealed an increased Alanintransaminasis (ALT) (49 U/L). C-reactive protein (CRP) elevated (36mg/L), with a decrease in CRP (18mg/L) on the following day. During hospitalization the following were observed: p-Karamid 2,6 mmol/L, and P-Natrium at 137mmol/L with a slightly fall to 134 mmol/L.
After the given procedures were done, outcome was as following: The patient diseased due to the cerebral thromboembolic episode, however not in the follow-up period of this study. There were no further data revealing any post apoplectic sequelae.

Cardiac arrest case

A 77-year-old male known with following comorbidities: Chronic Obstructive Pulmonary Disease (COPD), AF, essential hypertension, dilated left atrium and no valvopathy.
Pharmacological treatments: NOAC (Xarelto 20mg daily), Loop diuretic (Furosemide 40mg daily), Potassium chloride 750mg daily and beta blockers (metoprolol succinate 50mg daily)
The patient had ECV-procedure performed, with a successful conversion from AF to SR. On the following day the patient developed cardiac arrest, which was defibrillated with an automated external defibrillator (AED) to pulseless electrical activity rhythm. Return of spontaneous circulation was reached after 15min under continuous cardiac arrets treatment. Coronary angiography displayed no visual stenosis, and echocardiography displayed no new pathologies. Cerebral computer tomography (CT) displayed no acute findings. CT of thorax showed a possible mural thrombus, which was disproved by a TEE.
Biochemical findings on the date of cardiac arrest were as following: CRP (1.5 mg/l), Leukocytes (12.2 * 10^9/l), Neutrophilocytes (8.66* 10^9/l), Glucose (14.5mmol/l), HbA1c (5.4 mmol/l), Urea (8.4 mmol/l), eGFR (60 ml/min), Troponin T (66 ng/l), Lactatedehydrogeanses (390 U/l), and ALT (154 U/l)
Arterial blood gas with an oxygen flow (2 L/min): pH (7.17), PCO2 (7.4 kPa), PO2 (33.7 kPa), HCO3 (16.9 mmol/l), Hemoglobin (8.1 mmol/l), Glucose (14.5 mmol/l), Potassium (3.8 mmol/l) Sodium (137 mmol/l) and Lactate (4.3 mmol/l)

The reason for the patient's cardiac arrest is suspected to be due to malign cardiac arrhythmia and therefore an Implantable Cardioverter Defibrillator (ICD)-unit were implanted.

Patients with fatal events as outcome

Five patients presented with a fatal event, where one received ECV treatment for the first time.

The patient receiving first-time ECV treatment were hospitalized due to dyspnoea and diagnosed with AF and prescribed NOAC. After a TEE without signs of thromboembolic materials ECV-treatment were performed. The patient was dismissed from hospital the following day. Two days later the patient was found death at home. The patient was known with prostate gland hypertrophy , hypertension and severe COPD. The patient had a previous coronary angiography with minor atherosclerotic findings. There was no known cause of death.

Three of four patients receiving any recurrent ECV treatment were known with a cancer diagnosis.

One patient was known with Morbus Waldenstrøm and received ECV treatment due to AF. The patient was prescribed amiodarone at hospital-release due to recurrent AF. Two weeks later, the patient was hospitalized for two days for another ECV treatment. One week following, the patient was admitted at hospital with COPD in exacerbation for four days. 13 days following the latest hospitalization, 22 days following the ECV treatment, the patient was found deceased at home with an expected cause of hypoxic cardiac arrest.

Patient with known kidney insufficiency and cardiomyopathy. Earlier lobectomy was performed due to C. Pulmonalis. Due to an episode of AF, ECV treatment was performed. Later admitted due to the need of hemodialysis.

The cardiac arrest was suspected to be caused by hyperkalemia. Nine days after cardiac arrest - readmitted with AF, where recurrent ECV was performed. The following day, the patient was found with an asystole.

Terminal ill patient with disseminated mammae cancer. Presumably inevitable, expecting fatal due to terminal cancer status. Earlier diagnosed with paroxysmal AF and atrial flutter treated with ablation.

Eight days prior to the presumably terminal cancer course, the patient was admitted with recurrent AF. ECV was performed and SR later established. Two days following the ECV event, the patient was admitted with dyspnea and fatigue and was deceased 11 days following hospital-admission. A specific cause of death was not described. It was not possible to conclude the cause of death to be either complications of ECV or disseminated cancer.

The last patient was previously known with a thromboembolic event of an artery belonging to the crus, hypertension and hypercholesterolemia. The patient was admitted with AF and received ECV the following day before being dismissed. Two days post-procedure, the patient was readmitted and was prescribed amiodarone before receiving ECV treatment the day after. Two days later, the patient was found deceased at home. The emergency rescuers found excessive frothy expectorate from the airways when trying to intubate. The cause of death was assumed hypoxic cardiac arrest.

Additional analysis

As a sensitivity analysis, we compared incidences of stroke after all ECV procedures by years 2016-2020 in the North Denmark Regional Hospital, Hjoerring with corresponding incidences in the national data of the DNPR.
The following numbers are applicable for the DNPR:

Table 4 DNPR-national data: Stroke within 30 days/total number of ECV-procedures.

Year	2016 N/total (%)	2017 N/total (%)	2018 N/total (%)	2019 N/total (%)	2020 N/total (%)
Cerebral thromboembolism within 30days	36/9813 (0.4)	34/11110 (0.3)	36/13302 (0.3)	34/11600 (0.3)	37/7320 (0.4)

In accordance with the DNPR-national data table 4 we observe a range from 0.3% to 0.4% for stroke within 30days/total number of ECV-procedures from the year 2016 to 2020.
Compared with North Denmark Regional Hospital, Hjoerring we determined that 0.04% repeated ECV procedure developed cerebral thromboembolic within 30 days.

Discussion

In this study of 962 first-time and 2,649 repeated ECV treatments of AF in the Department of Cardiology, North Denmark Regional Hospital, Hjoerring, between 2016-2020, we found the incidence of non-fatal cardiac arrest for first time ECV-procedures was 0.1%, and there was one fatal event (0.1%), with no event of cerebral thromboembolic.
Among repeated ECV-procedures, the cerebral thromboembolic event incidence was 0.04%, and cardiac arrest events rate at 0.04% and a total of five fatal events (0.19%).

To verify the results, this study compared to the incidence found in the DNPR. As presented in results, table 3 and -4, the national incidence is thus higher than the local incidence of North Denmark Regional Hospital, Hjoerring. This study examined five fatal events. There was no specified cause of death among three of the events. The two known events were assumed to be related to hypoxic conditions.
Several Danish National Registry studies have examined the risk assessment of stroke among patients with AF. One study describing a population from 1991-1998 found an incidence thromboembolic events of respectively 0.30% and 0.31% among men and women with AF.(14) Another study found a rate of 1.59 thromboembolism per 100 person-years in patients with a $ChADS_2$-Score = 0. (15)
In comparison to this study, the incidence is thus reported lower following ECV-procedures than in the general population of patients with AF. However, the follow-up period differs from this study, which is procedural related and thus limited to 30 days following an ECV-procedure. Additionally, thus compared studies present Danish National registry data, while this study is limited to a Danish Regional population.

As this study is unable to apply inferential statistics on the different variables included, due to limited events, it is not possible to verify the individual and correlating risk factors for such events.
However, in Denmark, regional Hospitals, such North Denmark Regional Hospital, Hjoerring, does not perform the same variety of procedures as the University Hospitals. As an example, among university hospitals, it is possible to perform ablation therapy against arrhythmia in conjunction with ECV treatment.
The study by Noseworthy, P. A. et al., found ablation therapy to pose a risk of 0.5% in development of post-procedural cerebral thromboembolic, compared to 0.3% of the ECV procedures.(16)
As ablation therapy hence poses a single standing risk of cerebral thromboembolic, it could be thought as a possible risk factor increasing the incidence among the DNPR. However, it is not clarified whether ablation therapy with simultaneously ECV treatment poses an additive- or multiplicative risk factor, if a significant risk-increase at all.
The most consistent factor for the patients who developed cardiac arrest post ECV is hypertension, hyperglycemia with a P-glucose of 14,5 mmol/L on procedure date, COPD, Left ventricular ejection fraction 45%, and a dilated left atrium with no visual valvopathy. CHA_2DS_2-VASc-score of 3points, which are in accordance with a yearly stroke risk of 3,2%. Regarding the cerebral thromboembolic outcomes, we observed the most consistent factor being AF prior to event and hypertension. CHA_2DS_2-VASc-score of 4 points, which are in accordance with a yearly stroke risk of 4,8%. Common for both outcomes were a history of hypertension, use of NOAC, diuretics and beta-blockers. Both outcomes had a long-term history of AF. However, no definite conclusion is possible from the two compared cases.

While studies suggest cardioembolic material can be variable in size, they usually are large in size and often cause large vessel occlusions such as MCA and basilar artery occlusions.(17) Another suggest that large-vessel cardioembolic strokes when affecting larger cerebral vessels, usually are possible to differentiate from small-vessel occlusions, such as lacunar strokes, by cortical symptoms such as focal neurological symptoms. (18)
In this addition, this study presented a cerebral thromboembolic event. The event presented with an occlusion in the M1 part of MCA, hence a large vessel occlusion, and a minor occlusion of communis radiata. This study therefore finds it likely that the thromboembolic event of this study could be related to a cardioembolic ethology and hence related to the recent ECV-procedure.

As for our cases with apoplexia cerebri and cardiac arrest with a successful resuscitation, they presented with increased biomarkers for infection. The patient who developed cardiac arrest with a successful resuscitation presented with increased neutrophilic leukocytosis and increased CRP on the date of cardiac arrest. This study is thus unable to verify the specific cause or characteristics leading to cardiac arrest.
According to European Heart Journal, Guidelines for patients with concurrent AF during infections are unclear.(3) The study found the 1-year absolute risk of AF and thromboembolic events were equal to 36,4% for patients with infection related AF.(3) Additionally, infection-related AF possess 26 times increased risk of a new hospital contact with AF.(3)
Whether a possible infectious condition has contributed to the development of complication post-ECV in terms of cerebral thromboembolic and cardiac arrest, remains indefinite.

However, based on the above-mentioned study, it could be a possible risk factor influencing the outcome. (19)
Some studies report a relationship between acute infections and malignant ventricular arrhythmias. (19) A study done by Lazerinni et al, states that systemic inflammation induce significant QTc prolongation, which increase the risk of life-threatening ventricular arrhythmia. (20)
Concerning the fatal events, several cases were known with terminal disseminated cancer, and could be a concurrent cause leading to death. The two events of expected cause of death were described as hypoxic derived. However, as this study lacked sufficient events, it was not possible to verify different variates through interferential statistics. In addition, as a registral study, it was not possible to verify any specific cause of death precisely since an autopsy examination would be needed.

Strengths and limitations

As a Danish cohort study of the Patient Registry of the North Denmark Regional Hospital, Hjoerring, with quality assurance, a closer evaluation of the individual event was possible. This study was bound for a detailed description of cerebral thromboembolic events and correlating risk factors related to ECV treatment of AF.
However, this study was limited in time with data available, and was followed by many resources advocated for data management by the study-group. In addition to a low number of events, this study was nonetheless unable to apply inferential statistics to the results.
Through limited access to the DNPR, it was possible to compare the incidence of cerebral thromboembolic among the entire population of Denmark. This was helpful as a sensitivity analysis to verify that the very low number of events in the Northern Denmark cohort in this study were plausible.

Conclusion

At the Department of Cardiology, North Denmark Regional Hospital, Hjoerring, 962 patients received first-time ECV treatment of AF between 2016-2020. Among these, one experienced cardiac arrest with a successful resuscitation (0.10%), while one had a fatal event within the 30-day follow-up period (0.10%). Further analyses of repeated ECV treatment, consisting of 2,649 ECV treatments, we additionally found one event of cerebral thromboembolic event (0.04%), and a total of five fatal events (0.19%).

Compared to national data on stroke risk following ECV treatment of AF, the incidence was 0.04% in the Northern Denmark Regional Hospital in Hjoerring versus 0.34% of the Danish National population in a similar time period. Hence, this study, performed as a quality-assurance study, verified the current guidelines and practice of the North Denmark Regional Hospital, Hjoerring as consistent and of high quality with a low risk of severe outcomes of stroke, mortality, and cardiac arrest.

Clinical implication and future research

This study presented with a very low incidence of the measured outcomes including stroke, mortality and cardiac arrest. Hence, this study, performed as a quality-assurance study, verified the current ECV treatment of AF in the Regional Hospital of Northern Jutland as a high-quality clinical practice.

While this study presented with limited data results, we found ground for further discussion in form of: Differences in anticoagulant therapy prior to procedure, and multivariate risk evaluation of simultaneous procedures, comorbidities, medicaments, and blood-results. Future studies should strive to collect wider and more data regarding simultaneous procedures, differences in medicaments prior to ECV-procedures and a larger nationwide-based population.

Table- and figure list

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