Electrical cardioversion of atrial fibrillation and the risk of brady-arrhythmic events

Rasmussen et al: Electrical cardioversion and bradycardia

Rasmussen, Peter Vibe; Blanche, Paul; Dalgaard, Frederik; Gislason, Gunnar Hilmar; Torp-Pedersen, Christian; Tønnesen, Jacob; Ruwald, Martin H; Pallisgaard, Jannik Langtved; Hansen, Morten Lock

Published in:
American Heart Journal

DOI (link to publication from Publisher):
10.1016/j.ahj.2021.10.182

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

Electrical cardioversion of atrial fibrillation and the risk of brady-arrhythmic events

Peter Vibe Rasmussen, MD [a], Paul Blanche, PhD [a,b], Frederik Dalgaard, MD, PhD [a], Gunnar Hilmar Gislason, MD, PhD [a,c,d], Christian Torp-Pedersen, MD, DMSc [e,f], Jacob Tønnesen, MD [a], Martin H. Ruwald, MD, PhD [a], Jannik Langtved Pallisgaard, MD, PhD [a], and Morten Lock Hansen, MD, PhD [a] *Copenhagen*

Background Electrical cardioversion (ECV) is a common procedure for terminating atrial fibrillation (AF). ECV is associated with brady-arrhythmic events, however, the age-specific risks of clinically significant brady-arrhythmic events are unknown.

Methods Using Danish nationwide registers, we identified patients with AF at their first non-emergent ECV between 2005 and 2018 and estimated their 30-day risk of brady-arrhythmic events. Moreover, factors associated with increased risks of brady-arrhythmias were identified. Absolute risks were estimated using logistic regression models fitted with natural splines as well as standardization (G-formula).

Results We identified 20,725 eligible patients with a median age of 66 years (IQR 60-72) and most males (73%). The 30-day risks of brady-arrhythmic events after ECV were highly dependent on age with estimated risks ranging from 0.5% (95% CI 0.2-1.7) and 1.2% (95% CI 0.99-1.5) to 2.7% (95% CI 2.1-3.3) and 5.1% (95% CI 2.6-9.7) in patients aged 40, 65, 80, and 90 years, respectively. Factors associated with brady-arrhythmias were generally related to cardiovascular disease (eg, ischemic heart disease, heart failure, valvular AF) or a history of syncope. We found no indications that pre-treatment with anti-arrhythmic drugs conferred increased risks of brady-arrhythmic events (standardized absolute risk difference -0.25% [95% CI -0.67 to 0.17]).

Conclusions ECV conferred clinically relevant 30-day risks of brady-arrhythmic events, especially in older patients. Anti-arrhythmic drug treatment was not found to increase the risk of brady-arrhythmias. Given the widespread use of ECV, these data should provide insights regarding the potential risks of brady-arrhythmic events. (Am Heart J 2022;244:42–49.)

Electrical cardioversion (ECV) is a common procedure for restoring sinus rhythm in patients with symptomatic paroxysmal or persistent atrial fibrillation (AF).[1] ECV is generally believed to be superior to medical cardioversion for terminating AF, however, cardioversion is associated with ischemic stroke and all patients undergoing ECV are rigorously recommended appropriate anticoagulation.[2,3]

Parallel to the risk of ischemic stroke, a potential complication to ECV is arrhythmias, especially brady-arrhythmic events.[4-6] Generally, the risk of severe brady-arrhythmias associated with ECV is considered low.[7] However, studies pertaining to the subject are generally smaller observational studies with large variations in study populations as well as the reported risks of brady-arrhythmic events. Moreover, the exact relation to age has not been examined on a larger scale.

Pre-treatment with an anti-arrhythmic drug (AAD) is associated with an increased probability of restoring and maintaining sinus rhythm after ECV and is relatively common practice.[8] However, treatment with AADs carries increased risks of brady-arrhythmias.[9,10] To what extent AAD treatment prior to ECV increases the risk of brady-arrhythmic complications to the procedure has not been fully investigated.

Hence, using a large population of patients with AF undergoing non-emergent ECV, we sought to investigate the age-specific short-term risks and factors associated with brady-arrhythmic complications. Moreover, we sought to examine whether treatment with AADs increases the risk of brady-arrhythmic complications to ECV compared with patients treated exclusively with rate-lowering drugs (RLDs).

From the [a]Department of Cardiology, Herlev-Gentofte University Hospital, University of Copenhagen, Hellerup, Denmark, [b]Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark, [c]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, [d]The Danish Heart Foundation, Copenhagen, Denmark, [e]Department of Clinical Research, Nordsjaellands Hospital, Hillerød, Denmark, [f]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark

Submitted May 7, 2021; accepted October 2, 2021

Reprint requests: Peter Vibe Rasmussen, MD, Department of Cardiology, University Hospital Herlev-Gentofte, Gentofte Hospitalsvej 1, Hellerup 2900, Denmark.

E-mail address: peter.vibe.rasmussen@gmail.com.

0002-8703

https://doi.org/10.1016/j.ahj.2021.10.182

Methods

Setting

In Denmark, it is possible to follow all citizens by linking several nationwide administrative databases and registers using a unique identifying number assigned to all Danish citizens residing in Denmark. Using these registers, any hospital diagnosis, procedure or operation, filled prescription, migration, or death can be identified on an individual level. All hospital diagnoses are registered according to the international classification of diseases 10th edition (ICD-10), and performed procedures are registered according to the Nordic Classification of Surgical Procedures. Filled prescriptions are registered according to the Anatomical Therapeutic Chemical Classification System (ATC-code), including the formulation, number of tablets per package, and the number of packages dispensed. Demographic variables, including age in years, sex, and information regarding migration and date of death, are available through the Danish civil registration system. The Danish nationwide registers have all been extensively used for epidemiological research and are continuously undergoing validation and general scrutiny of data quality.[11,12]

Study design

The study was conducted as a nationwide cohort study. Danish patients with a registered hospital diagnosis of AF or atrial flutter (both referred to as AF) prior to a procedural code for ECV of AF were eligible for inclusion. Eligible patients were included at the date of their first non-emergent hospital contact for ECV between January 1, 2005 and July 30, 2018. Patients were excluded at baseline if they were <30 years of age, not permanently residing in Denmark, had any history of an implantable device (pacemaker or implantable cardioverter-defibrillator), or a prior diagnosis of ventricular tachycardia to avoid subsequent implantation of a device due to this indication.

Outcomes

The main outcome was a composite of either a hospital discharge diagnosis of brady-arrhythmia (atrioventricular block [Mobitz type II or more advanced], sinoatrial block, or unspecified bradycardia) or a procedural code relating to pacing, whichever came first. Pacing was defined using procedural codes for temporary or permanent pacemaker implantations and implantable cardioverter-defibrillators. (Supplementary Table I) Secondary study outcomes were pacemaker implantation and all-cause mortality.

Covariates

All variables regarding comorbidity were defined as a registered diagnosis during hospital admissions or visits to outpatient clinics in a period of 5 years before or on the date of study inclusion. Operations and procedures were defined as any procedural or surgical code registered at the date or before study inclusion. Concomitant treatment with pharmacotherapy was defined as any filled prescription at any pharmacy in Denmark 180 days prior to or on the date of study inclusion. Comorbidities of interest included in the study were diabetes mellitus, prior ischemic stroke/thromboembolism, pericarditis/myocarditis, cardiomyopathy, arteriosclerosis, sleep apnea (diagnosis or code for treatment with devices for continuous positive airway pressure), heart failure, ischemic heart disease, any type of percutaneous coronary interventions, coronary artery bypass graft surgery (any coronary surgery), diagnoses associated with chronic kidney disease, thyroid disease, valvular AF (rheumatic heart disease or prosthetic heart valves), syncope, and diagnoses of first-degree atrioventricular block.

Diabetes mellitus, and thyroid disease were defined using ATC-codes for pharmacotherapy used to treat these disorders. (Supplementary Table I) Concomitant pharmacotherapy included in the study was treatment with RLDs, AADs, acetylsalicylic acid, adenosine-diphosphate receptor inhibitors, opioids, benzodiazepines, and oral anticoagulants. Included AADs and RLDs were agents available for the treatment of AF in Denmark in the study period. As such, AADs were defined as treatment with amiodarone, dronedarone, sotalol, and class 1c drugs (propafenone, flecainide). RLDs were defined as treatment with either a beta-blocker, non-dihydropyridine calcium antagonist (verapamil or diltiazem), or digoxin. Hypertension was defined as the treatment with more than one class of antihypertensive drug at the same time as previously done.[13]

Statistical methodology

The study population was characterized at baseline using descriptive statistics with continuous variables summarized by medians and inter-quartile ranges (IQR) and categories by counts and percentages. The primary measure of interest was the 30-day absolute risk of brady-arrhythmic events after ECV. The absolute risk was estimated using a logistic model with age as covariate modelling the effect of age using natural splines and depicted graphically. Factors hypothesized as potential risk factors for the primary outcome were examined using a series of logistic regression models. Each model was adjusted for age, sex, and calendar year besides the factor of interest and we reported adjusted odds ratios (OR) with corresponding 95% confidence intervals (95% CI).

Testing the hypothesis that AAD treatment confers increased risks of brady-arrhythmic events, we compared the 30-day risk between patients treated with either an AAD orRLDs without an AAD. We computed the standardized absolute 30-day risks of brady-arrhythmic events based on a logistic model with prespecified potential confounders as covariates (age group [30-60 years, 60-80 years, >80 years], sex, ischemic heart disease, heart

failure, valvular AF, syncope, prior cardiac procedures [CABG or PCI]). Moreover, we included an interaction term between treatment (AAD vs RLDs) and age group. The absolute risks were standardized for each treatment group (G-formula estimation). We reported the standardized 30-day absolute risks for each treatment (AAD vs RLD), the standardized risk difference (average treatment effect), as well as the standardized risk ratio with 95% CIs. CIs were obtained as described by Flanders and Rhodes (1986) and implemented in the riskRegression package for R.[14]

We chose not to make a comparison with patients not receiving any RLD or AAD treatment prior to non-emergent ECV. This was done as this this small group of patients not receiving any treatment prior to non-emergent ECV (~10%) is likely not comparable as foregoing treatment could indicate increased risks of brady-arrhythmic events (eg, in patients with previous bradycardia or patients with a slow heart rate during AF not tolerating RLDs).

Supplementary analyses

The absolute risk of brady-arrhythmic events after ECV was also estimated with a 60 and 120-day time horizon. The main analysis was also conducted for the separate outcome of pacemaker implantation defined only by procedural codes.

Ethics and funding

According to Danish legislation, registry-based studies with de-identified data and no active participation by study subjects do not require approval by an ethics committee. The Danish Data Protection Agency has approved the use of registry data, and the current project is registered with the data responsible institute. (Approval No. P-2019-348). No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents

Results

A total of 20,725 patients with AF undergoing their first ECV were included in the study having a median age of 66 years (IQR 60-72) with a majority of male patients (73%). The most prevalent comorbidities were hypertension (63%), heart failure (17%), ischemic heart disease (15%), and diabetes mellitus (10%) (Table 1).

Common pharmacotherapy was treatment with oral anticoagulants (95%), beta-blockers (79%), and digoxin (30%). A total of 15,531 patients (75%) were in treatment with at least one RLD without an AAD and 2,284 patients (11%) with an AAD at study inclusion.

Patients treated with an AAD were predominantly treated with amiodarone (73%). AAD treated patients generally had a higher prevalence of heart failure, valvular AF, and ischemic heart disease (Supplementary Table II).

Table. Baseline characteristics

	N = 20,725
Male sex (%)	15,111 (73)
Age (Median [IQR])	66 (60-72)
Medication	
Beta blocker (%)	16,306 (79)
Verapamil or diltiazem (%)	1,194 (6)
Amiodarone (%)	1,659 (8)
Sotalol (%)	140 (1)
Digoxin (%)	6,216 (30)
Class 1C (%)	460 (2)
Dronedarone (%)	93 (0)
ASA (%)	5,068 (25)
ADP-Inhibitor (%)	732 (4)
Oral anticoagulants (%)	19,653 (95)
Opioids (%)	2,222 (11)
Benzodiazepines (%)	896 (4)
RLD or AAD treatment (%)	
No RLD or AAD	2,910 (14)
Only RLD	15,531 (75)
AAD	2,284 (11)
Comorbidity	
Diabetes Mellitus (%)	2,030 (10)
Ischemic stroke (%)	1,007 (5)
Arteriosclerosis* (%)	244 (1)
Heart Failure (%)	3,542 (17)
Cardiomyopathy (%)	768 (4)
Hypertension (%)	13,034 (63)
IHD (%)	3,123 (15)
Peri-/Myocarditis	70 (0)
Syncope (%)	463 (2)
First degree AVB (%)	36 (0)
Alcohol abuse (%)	378 (2)
Sleep apnea (%)	864 (4)
Kidney disease (%)	459 (2)
Thyroid disease (%)	1,139 (6)
Valvular AF (%)	883 (4)
PCI (%)	1,218 (6)
CABG (%)	809 (4)

Abbreviations: *AAD*, anti-arrhythmic drug; *ADP*, adenosine-diphosphate; *AF*, atrial fibrillation; *ASA*, acetylsalicylic acid; *AVB*, atrioventricular block; *CABG*, coronary artery surgeries; *IHD*, ischemic heart disease; *PCI*, percutaneous coronary intervention; *RLD*, rate-lowering drug.

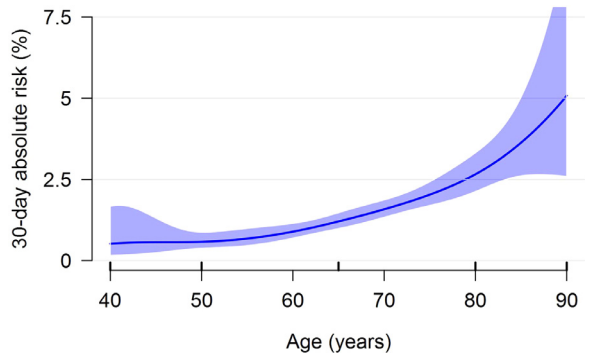
*Arteriosclerosis in aorta, kidney, retinal or peripheral arteries.

During 30 days after ECV, we identified 290 brady-arrhythmic events and 62 deaths from all causes. In patients experiencing the composite outcome of a brady-arrhythmic event, 202 (70%) underwent pacing as their first registered event.

Risk of brady-arrhythmic events

The 30-day risk of brady-arrhythmic events after ECV was generally modest in the younger and middle-aged patients increasing markedly in older patients (Figure 1). As such, in patients aged 40 years, the risk of brady-arrhythmic events was 0.5% (95% CI 0.2-1.7), increasing to 1.2% (95% CI 0.99-1.5) in patients aged 65 years. In

Figure 1



Risk of brady-arrhythmic events in relation with electrical cardioversion. Figure depicting the 30-day risk of the primary outcome of brady-arrhythmic complications after electrical cardioversion (ECV) by age. The y-axis depicts the absolute risk of brady-arrhythmic events in percentage (%) with 95% confidence intervals, and the x-axis depicts age continuously in years. Knots are marked with ticks on the x-axis, boundary knots were placed at 35 and 90 years.

older patients aged 80 years, we found a 30-day risk of 2.7% (95% CI 2.1-3.3) increasing to 5.1% (95% CI 2.6-9.7) in patients aged 90 years.

Factors associated with brady-arrhythmic events after ECV were generally related to structural heart disease, diabetes, or prior syncope (Figure 2). For example, we found notable associations with ischemic heart disease (OR 2.41, 95% CI 1.87-3.10), valvular AF (OR 3.04, 95% CI 2.13-4.34), heart failure (OR 1.58, 95% CI 1.20-2.07), cardiomyopathy (OR 2.60, 95% CI 1.65-4.10), diabetes (OR 1.75, 95% CI 1.27-2.40), and syncope (OR 2.63, 95% CI 1.61-4.29).

Anti-arrhythmic drugs and brady-arrhythmic events

The standardized absolute 30-day risks were 1.19 % (95% CI 1.01-1.36) and 0.94 % (95% CI 0.56-1.32) for RLDs and AAD treatment groups, respectively. We found no differences in the risk of brady-arrhythmic events between patients treated with an AAD or RLDs. As such, we found a standardized absolute 30-day risk difference of -0.25% (95% CI -0.67 to 0.17, $P = .244$) and a corresponding standardized 30-day risk ratio of 0.79 (95% CI 0.45-1.13, $P = .228$) (Figure 3).

Risk of mortality

The 30-day risk of mortality after ECV was generally very low with a pronounced increase for the oldest patients (Figure 4). Consequently, the risk of mortality was 0.08% (95% CI 0.01-0.5), 0.3% (95% CI 0.2-0.4), 0.6% (95% CI 0.4-0.9), and 2.7% (95% CI 0.8-9.2) in patients aged 40, 65, 80, and 90 years, respectively.

Supplemental data

Extending the horizon to 60 and 120 days of brady-arrhythmic events in the main analysis only mildly accentuated the risks compared to 30 days underlining that the majority of events occurred directly in relation to ECV (Supplementary figure S1).

Investigating an outcome consisting of pacemaker implantations mildly attenuated the absolute 30-day risks compared to the composite outcome, especially for the oldest patients, however, the estimated risks remained clinically significant (Supplementary figure S2).

During the first year from the day of index cardioversion, a total of 3,256 (16%) patients underwent catheter ablation for atrial fibrillation or atrial flutter. In a period of 180 days from the day of electrical cardioversion, an increase in the use of AADs could be observed whereas the use of RLDs remained relatively stable (Supplementary Table III).

Discussion

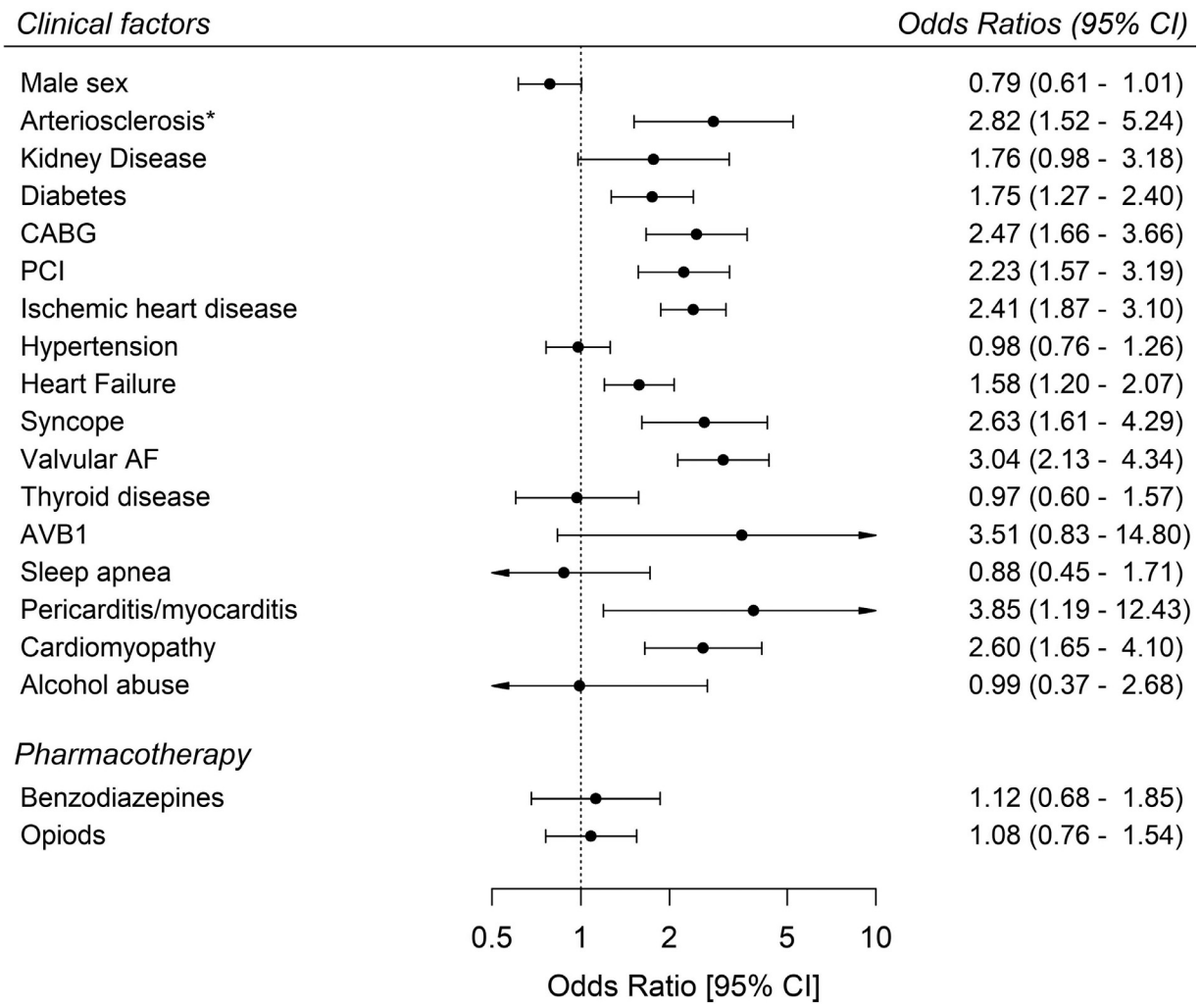
In this large nationwide cohort study of AF patients undergoing non-emergent ECV, we uncovered several important findings. (1) The absolute short-term risks of brady-arrhythmic events associated with ECV were, albeit modest, clinically relevant and higher than in previous reports, especially in older patients. (2) Factors associated with brady-arrhythmic complications were related to structural heart disease, prior syncope, or diabetes. (3) Pre-treatment with an AAD did not seem to increase the risk of brady-arrhythmic complications compared to patients treated with RLDs.

Terminating AF with a direct current shock is a procedure, which has been in clinical use since the 1960s.[1] ECV is considered a safe procedure, which can be performed during brief sedation while monitoring blood pressure and oxygen saturation. A primary safety concern is the risk of thromboembolic events directly associated with ECV and patients are recommended strict adherence to an appropriate anticoagulant regimen.[2,15]

A potential complication to ECV receiving less attention in clinical practice is the risk of brady-arrhythmias related to the procedure.[4] The mechanisms behind brady-arrhythmic events associated with ECV are likely heterogeneous, ranging from the unmasking of latent tachy-brady syndromes to the potential of impaired cardiac conduction directly induced by the electrical shock.

We found the risk of brady-arrhythmic events to be highly dependent on age. As such, the risk was low and probably of minor concern in the younger patients (<1% in all patients <62 years of age). However, the risk increased notably with age and was very clinically relevant in older patients (eg, 1.3% absolute risk in patients aged 66 years, which was the median age of the study population).

Figure 2

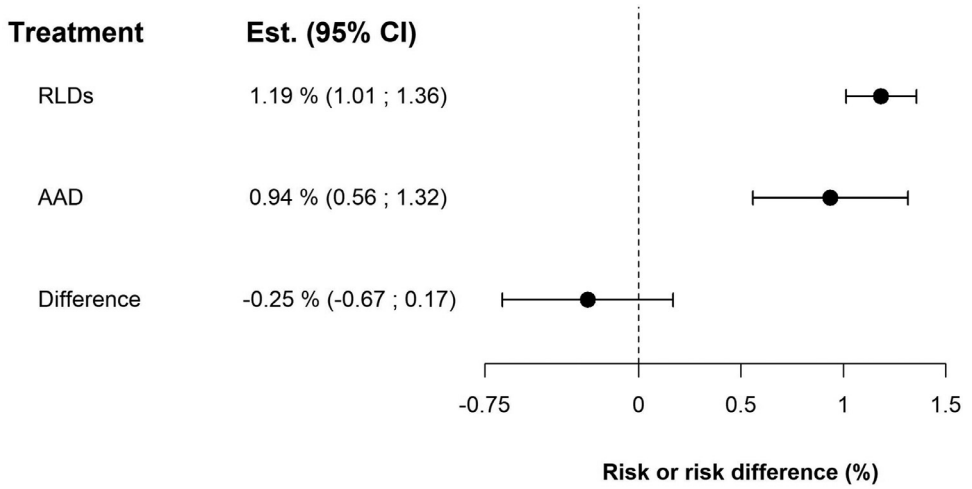


Factors associated with brady-arrhythmic events. Forest plot depicting factors associated with brady-arrhythmic complications after electrical cardioversion (ECV). Estimates are presented as adjusted odds ratios (OR) on the x-axis with corresponding 95% confidence intervals (95% CI). The factors of interest are depicted on the y-axis. Besides the factors of interest, the models were adjusted for sex, age, and calendar year. Abbreviations: *AVB1*, first degree atrioventricular block; *CABG*, coronary artery surgery; *PCI*, percutaneous coronary intervention. *Arteriosclerosis in aorta, kidney, retinal or peripheral arteries.

The largest cohort study on the subject investigated 6,906 patients undergoing ECV for acute AF and found a relatively low overall occurrence of brady-arrhythmic events (0.9%). However, the authors reported an interesting signal of a markedly increased incidence of brady-arrhythmias among the oldest and female patients (~3% in female patients >75 years of age).[5] Even so, the study sample was relatively young compared to our study population, and the authors used a definition of brady-arrhythmias based on heart rate measurements (<40 beats per minute or short asystole), which would also capture transient and clinically non-significant brady-arrhythmias, which would likely not be captured in our study.

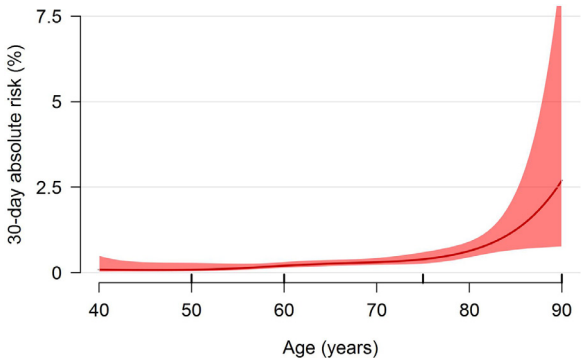
Several other smaller observational studies and case-reports have investigated brady-arrhythmic events related to ECV, generally reporting relatively moderate risks.[4,6-8,16,17] Oppositely, another study indicated a somewhat higher and clinically relevant risk of brady-arrhythmic events associated with ECV in an outpatient setting (overall risk of 1.5%).[18] However, none of these studies were designed or powered for estimating age-

Figure 3



Risk of brady-arrhythmic events between rate-lowering and anti-arrhythmic drugs. Forest plot depicting the standardized absolute 30-day risks of brady-arrhythmic events between patients treated with rate-lowering drugs (RLDs) or an anti-arrhythmic drug (AAD). The x-axis depicts the standardized 30-day risks as well as the standardized risk difference in percentage (%) with treatment groups depicted on the y-axis.

Figure 4



Risk of mortality in relation with electrical cardioversion. Figure depicting the 30-day risk of death from all causes after electrical cardioversion (ECV) by age. The y-axis depicts the absolute risk of mortality in percentage (%) with 95% confidence intervals, and the x-axis depicts age continuously in years. Knots are marked with ticks on the x-axis, boundary knots were placed at 35 and 90 years.

specific risks of brady-arrhythmic events and often only captured arrhythmias occurring directly in relation to the electrical shock.

Factors associated with an increased risk of brady-arrhythmic events after ECV were generally related to cardiovascular and structural heart disease. As such, ischemic heart disease, heart failure and cardiomyopathies, certain valvular heart diseases, prior cardiac procedures, diabetes, peri- or myocarditis, and a history of syncope conferred elevated risks of brady-arrhythmic events. Interestingly, having a registered diagnosis of first-degree atrioventricular block was also associated with a tendency toward an increased risk of brady-arrhythmia albeit with a lack of statistical power. This is in line with reports that first-degree atrioventricular block is associated with an increased risk of pacemaker implantation in the general population.[19] As such, electrocardiographic markers relating to the conduction system (eg, bundle branch blocks, QRS Duration, slow heart rate during AF) could serve as relevant clinical markers of an elevated risk when performing ECV.[20] Female sex has been described as a risk factor for developing brady-arrhythmia both in patients undergoing ECV as well as in AF patients in general.[5,21] Interestingly, we were also able to observe a tendency toward a lower risk among male patients than females, albeit not meeting statistical significance.

In patients with AF, the use of AADs is associated with increased risks of brady-arrhythmias primarily driven by the class III drug amiodarone, which was also by far the most frequently used AAD in our study population (73% of all AAD treated).[9,10] Pre-treatment with an AAD increases the likelihood of restoring and maintaining sinus rhythm after ECV and is a widespread practice.[7,8] As such, it could be hypothesized that AAD treatment prior to ECV would also confer increased risks of brady-arrhythmic events directly related to the procedure. However, reassuringly, using modern statistical

techniques designed for causal inference, we did not find any evidence to suggest that AAD treatment was associated with increased risks of brady-arrhythmic events compared to patients treated with RLDs.

The risk of mortality associated with ECV was generally very low, except for the very old patients, where the short-term mortality increased rapidly. However, whether this was due to a general short life-expectancy in older comorbid patients with AF and not associated with the procedure itself is probable.

Conclusively, non-emergent ECV in patients with AF was associated with low short-term risks of brady-arrhythmic events in the young and the middle-aged but relatively high risks in older patients. Given the widespread use of ECV, these data are very relevant for physicians treating AF and informing patients when considering ECV as a treatment option.

Limitations

The current study has several limitations, which should be acknowledged. Most of these are related to the study design and the available data in the used registers. This study is observational and, as such, causal conclusions regarding treatment effects cannot be directly inferred.

When interpreting results based on diagnostic coding, the risk of misclassification bias is present and should be acknowledged as the positive predictive values of many of the codes employed in this study are not known. However, most of the codes used for defining important study variables (eg, AF, cardioversion, bradycardia, and pacemaker implantation) have all been manually evaluated with high positive predictive values.[11,12]

Granular data regarding certain factors potentially influencing the study results were not available such as AF subtype (ie, paroxysmal or persistent), AF duration, electrocardiographic recordings, medication administered during the procedure, administered shock energy, symptoms, or heart rate measurements. Unfortunately, anthropometric measurements such as body mass index or blood pressure were also not available. Moreover, our study population was defined using only hospital contacts registered as non-emergent. In terms of ECV, this definition has not been validated, however, we have no reason to suspect it should not be fairly accurate. This is underlined by the very high proportion of patients having a recently claimed prescription for oral anticoagulants (95%). It should also be mentioned that in the case of tachy-brady syndromes, pacemaker implantation is often a part of the overall treatment strategy and, as such, should not necessarily be seen as a direct effect of cardioversion.

Conclusions

Using a nationwide study population of AF patients undergoing ECV, we uncovered that the risk of brady-arrhythmic complications was low in the young and middle-aged but relatively high in older patients. Factors associated with an increased risk of brady-arrhythmias were generally related to cardiovascular diseases. Pre-treatment with AADs did not confer increased risks of brady-arrhythmic events. These data should raise awareness regarding the risks of brady-arrhythmic events, especially in older patients undergoing ECV.

Data availability

The data used in this work cannot be shared relating to Danish legislation protecting patient privacy. The used data can only be made available through a government institution, Statistics Denmark.

Author Contributions

Study concept and design were determined by: PVR, FD, MLH, PB. Acquisition of data was performed by: PVR, GG, CTP. Drafting of the manuscript was carried out by: PVR, FD, MLH. Critical revision of the manuscript for important intellectual content was carried out by: FD, GG, JT, CTP, MR, PB, JLP, MLH. Statistical analysis and data interpretation were performed by: PVR, FD, PB, MLH.

Conflict of interest

None declared.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2021.10.182.

References

1. Lown B, Perlroth MG, Kaidbey S, et al. Cardioversion" of atrial fibrillation. A report on the treatment of 65 episodes in 50 patients. N Engl J Med 1963;269:325–31.
2 Hindricks G, Potpara T, Dagres N, Arbelo E, J Bax J, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). Eur Heart J 2021;42(5):373–498. doi:10.1093/eurheartj/ehaa612.
3. Van Gelder IC, Tuinenburg AE, Schoonderwoerd BS, et al. Pharmacologic versus direct-current electrical cardioversion of atrial flutter and fibrillation. Am J Cardiol 1999;84(9A):147R–151R.
4. Mehta PM, Reddy BR, Lesser J, Carson BE. Severe bradycardia following electrical cardioversion for atrial tachyarrhythmias in patients with acute myocardial infarction. Chest 1990;97:241–2.
5. Grönberg T, Nuotio I, Nikkinen M, et al. Arrhythmic complications after electrical cardioversion of acute atrial fibrillation: the FinCV study. EP Eur 2013;15:1432–5.
6. Gallagher MM, Yap YG, Padula M, et al. Arrhythmic complications of electrical cardioversion: relationship to shock energy. Int J Cardiol 2008;123:307–12.

7. Pisters R, Nieuwlaat R, Prins MH, et al. Clinical correlates of immediate success and outcome at 1-year follow-up of real-world cardioversion of atrial fibrillation: the Euro Heart Survey. Europace 2012;14:666–74.
8. Crijns HJGM, Weijs B, Fairley A-M, et al. Contemporary real life cardioversion of atrial fibrillation: results from the multinational RHYTHM-AF study. Int J Cardiol 2014;172:588–94.
9. Vorperian VR, Havighurst TC, Miller S, January CT. Adverse effects of low dose amiodarone: a meta-analysis. J Am Coll Cardiol 1997;30:791–8.
10. Essebag V, Hadjis T, Platt RW, Pilote L. Amiodarone and the risk of bradyarrhythmia requiring permanent pacemaker in elderly patients with atrial fibrillation and prior myocardial infarction. J Am Coll Cardiol 2003;41:249–54.
11. Sundbøll J, Adelborg K, Munch T, et al. Positive predictive value of cardiovascular diagnoses in the Danish National Patient Registry: a validation study. BMJ Open 2016;6.
12. Adelborg K, Sundbøll J, Munch T, et al. Positive predictive value of cardiac examination, procedure and surgery codes in the Danish National Patient Registry: a population-based validation study. BMJ Open 2016;6.
13. Olesen JB, Lip GYH, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:d124.
14. Flanders WD, Rhodes PH. Large sample confidence intervals for regression standardized risks, risk ratios, and risk differences. J Chronic Dis 1987;40:697–704.
15. Hansen ML, Jepsen RMHG, Olesen JB, et al. Thromboembolic risk in 16 274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy. EP Eur 2015;17:18–23.
16. Berry C, Stewart S, Payne EM, et al. Electrical cardioversion for atrial fibrillation: outcomes in 'real-life' clinical practice. Int J Cardiol 2001;81:29–35.
17. Botkin SB, Dhanekula LS, Olshansky B. Outpatient cardioversion of atrial arrhythmias: efficacy, safety, and costs. Am Heart J 2003;145:233–8.
18. Morani G, Cicoira M, Pozzani L, et al. Outpatient electrical cardioversion of atrial fibrillation: 8 years' experience. Analysis of shock-related arrhythmias. Pacing Clin Electrophysiol 2009;32:1152–8.
19. Rasmussen PV, Nielsen JB, Skov MW, et al. Electrocardiographic PR interval duration and cardiovascular risk: results from the Copenhagen ECG study. Can J Cardiol 2017;33:674–81.
20. Rasmussen PV, Skov MW, Ghouse J, et al. Clinical implications of electrocardiographic bundle branch block in primary care. Heart Br Card Soc 2019;105:1160–7.
21. Barrett TW, Abraham RL, Jenkins CA, et al. Risk factors for bradycardia requiring pacemaker implantation in patients with atrial fibrillation. Am J Cardiol 2012;110:1315–21.