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Review

Aggressive Rhythm Control Strategy in Atrial Fibrillation Patients Presented at the Emergency Department. The HEROMEDICUS Study Design and Initial Results

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Abstract: Atrial fibrillation has progressively become a more common reason for emergency department visits, representing 0.5% of presenting reasons. Registry data have indicated that about 60% of atrial fibrillation patients who present to the emergency department are admitted, emphasizing the need for more-efficient management of atrial fibrillation in the acute phase. Management of atrial fibrillation in the setting of emergency department varies between countries and health care systems. The most plausible reason to justify a conservative rather than aggressive strategy in the management of atrial fibrillation is the absence of specific guidelines from diverse societies. Several trials of atrial fibrillation treatment strategies, including cardioversion, have demonstrated that atrial fibrillation in emergency department can be treated safely and effectively, avoiding admission. In the present study, we review the epidemiology and characteristics of atrial fibrillation patients presenting to the emergency department will be reviewed, as well as the impact of diverse management strategies on atrial fibrillation-related hospital admissions. Lastly, the design and initial data of the HEROMEDICUS protocol, which constitutes an electrophysiology-based aggressive rhythm control strategy in patients with atrial fibrillation in the emergency department setting will be presented.

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1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the adult population globally, with an estimated prevalence between 2% and 4%[1]. Both incidence and prevalence of AF are expected to increase further, due to population aging and increasing burden of other comorbidities, such as hypertension, heart failure, obesity, diabetes mellitus, coronary artery disease, and chronic kidney disease[2-7]. AF is associated with increased morbidity[8], mortality[9] and higher healthcare costs, rendering it a major socioeconomic burden[10]. AF has progressively become a more common reason for emergency department (ED) visits, representing 0.5% of presenting reasons[11].

Registry data have indicated that about 60% of AF patients who present to the ED are admitted, leading to an increase in AF-related hospital admissions due to the aforementioned rise in ED visits, emphasizing the need for more-efficient management of AF in the acute phase[11-14]. Several trials of AF treatment strategies, including cardioversion, have demonstrated that AF in ED can be treated safely and effectively, avoiding admission[11-26].

In the present study, the epidemiology and characteristics of AF patients presenting to the ED will be reviewed, as well as the impact of diverse management strategies on AF-related hospital admissions. Lastly, the design and initial data of the HEROMEDICUS protocol, which constitutes an electrophysiology-based aggressive rhythm control strategy in patients with AF in the ED setting will be presented.

2. AF-related visits to the ED

Initial data were published by McDonald et al in 2008 drawn from the National Hospital Ambulatory Medical Care in the United States[14]. In the time period from 1993 to 2004, the absolute number of visits increased from 300.000 (1993-4) to 564.000 (2003-4). Likewise, population-adjusted visit rate increased from 0.6 to 1.2 per 1.000 US population[14]. Accordingly, data from Analysis of the Nationwide Emergency Department Sample revealed that ED visits for AF and atrial flutter (AFL) increased from 434.382 in 2006 to 568.562 in 2011, corresponding to a 30.9% increase over 6 years[13]. More specifically, ED visits per 1000 population have increased from 1.45 in 2006 to 1.82 in 2011[13]. Subsequent data from a repeated cross-sectional analysis of ED visit-level from the Nationwide Emergency Department Sample confirmed the increase by 30.7% of annual ED visits for AF from 2007 to 2014[11] (Table 1).

Table 1. Temporal trends in AF-related ED visits.

Study	ED visits	AF ED visits	AF ED visits/year	Increase of AF ED visits	Study period
McDonald AJ et al		2.700.000	300.000 (1993) 564.000 (2004)	88%	1993-2004
Lin M et al			434.382 (2006) 537.801 (2014)	30.9%	2006-2011
Rozen G et al	233.007.973	3.886.520	411.406 (2007) 537.801 (2014)	30.7%	2007-2014

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3. AF admission rates in the ED

During the 12-year study period (1993-2004) of the National Hospital Ambulatory Medical Care Registry, admission rate remained constant (64%)[14]. Concomitant congestive heart failure was associated with an increased risk for hospital admission[14]. Likewise, ED admission rates overall persisted at a high level (between 67.4% and 69.7%) in the 2006-2011 period, as derived from the Nationwide Emergency Department Sample database[13]. Hospital region and presence of comorbidities were the strongest predictors of admission in this study[13]. Subsequent data from the same database revealed stable hospital admission rates at ~70% between 2007 and 2010 after which they declined to 62% in 2014, despite an increase by 30.7% in annual ED visits[11] (Table 2).

Table 2. Temporal trends in AF-related admission rates.

Study	AF ED visits	AF admissions	AF admission rate	Study period
McDonald AJ et al	2.700.000		64%	1993-2004
Lin M et al	434.382 in 2006 568.561 in 2011		69.7% in 2006 67.4% in 2011	2006-2011
Rozen G et al	3.886.520	288.225 in 2007 333.570 in 2014	70% 2007-2010 62% in 2014	2007-2014

4. AF cost of hospital stay

The annual cost of AF treatment was estimated to be $6.65 billion in 2005[10] and later estimates were even higher[22]. In 2007, inpatient charges for AF hospitalization accounted for 1.12% of $530 billion and in 2014 this further increased to 1.22% of $828 billion[11]. There is a huge difference between charges spent for hospitalized AF patients and charges spent for those discharged from the ED. In 2007, annual charges for AF hospitalization were estimated at $7.39 billion, increasing by 37% to $10.1 billion in 2014. Per patient hospitalization charges increased from $17.317 in 2007 to $22.113 in 2014[11].

A smaller European study examined the Impact on hospital resources of two different approaches to recent onset AF using a random sample of 300 patients with AF, collected from an ED electronic database from an urban community teaching hospital. Median charges for patients cardioverted and discharged from the ED were $5.460 (IQR $4.677-$6.190) whereas median charges for admitted patients with no attempt at cardioversion at the ED were at least 4 times higher ($23.202, IQR $19.663-$46.877)[16].

5. Strategies for AF management in the ED

There is no specific algorithm in ESC guidelines on management of hemodynamically stable patients presenting to the ED with primary AF, as well as guidance on when to admit or discharge them straight from the ED. There are multiple protocols that have examined the safety and efficacy of diverse strategies implemented in the ED for patients presenting with AF as the primary diagnosis. The basic goal of all different pathways was the reduction of hospital admissions.

Burton et al published in 2004 data on the feasibility of electrical cardioversion in the management of AF in the ED[18]. In this multicenter cohort study the objective was to identify the outcomes and complications associated with electrical cardioversion in AF patients[18]. Study population included 388 patients with recent-onset AF (<48hours) and electrical cardioversion was successful in 332 patients (86%). In total, the admission rate was as low as 14% since 333 patients were discharged home from the ED (301 after successful cardioversion and 32 with electrical cardioversion failure). Interestingly, 39 patients returned to the ED because of AF recurrence within 10 days[18].

A multicenter observational cross-sectional study (HERMES-AF) of patients with recent-onset AF which was carried out in 124 Spanish EDs from May 23rd to June 5th, 2011, studied the impact of a

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rhythm control strategy on admission rates and symptoms[24]. Inpatient admission rate was 14% in the rhythm control strategy. The study population was 421 patients of which 352 were allocated to the rhythm control strategy with rate control being chosen in 69 patients. In total, 60 (14.2%) patients were admitted. Control of symptoms was achieved in 95.2% of patients in the rhythm and in 88.4% of patients in the rate control group[24].

In a prospective, 2-stage study at 2 tertiary care hospitals in the Northeastern United States, utilization of a multidisciplinary AF pathway was associated with a decrease in hospital admission rates[25]. During the first stage of the study (June 27th to October 4th, 2016) AF patients who presented to the ED were treated according to the routine care. During the second stage of the study (October 5th to March 20th, 2017) patients who presented to the ED with primary AF were screened and treated according to the AF pathway[25]. Implementation of the AF treatment pathway was associated with decreased rates of hospital admission (15%) compared to the group who received routine care (55%)[25]. This was the first study that included an expert electrophysiologist besides emergency medicine doctors in decision making and AF management in ED.

Canadian emergency physicians are known for publishing widely on the "AF in the ED" field and for managing these patients quickly and efficiently[20, 23, 26]. Academic centers in Canada have implemented a series of aggressive protocols of AF management in the ED setting[20, 23, 26]. An initial retrospective cohort study by Stiell et al reported the results of pharmacological cardioversion with intravenous (i.v.) procainamide in 341 patients with recent-onset AF or atrial flutter. Sinus rhythm was restored in 52% of AF patients and 28% of atrial flutter patients[20]. Admission rates were only 5.6% and adverse event rate was reported to be 10%, though without necessitating hospital admission. Return rate to the ED among those who were successfully cardioverted was 2.9% within 7 days[20]. Subsequently, electrical cardioversion was included in this procainamide-based protocol for those not successfully cardioverted with i.v. procainamide[26]. This modified protocol – called the "Ottawa aggressive protocol" – was evaluated in a retrospective cohort study. The sinus rate restoration was achieved in 92% of cases and minor adverse events rate was 7.6%[26]. Certain steps included in the Ottawa aggressive protocol need to be mentioned. Specifically, no heparin or warfarin administration was necessary if onset was clearly less than 48 hours. Importantly, procedural sedation and analgesia (i.v. propofol and fentanyl) was given by emergency physicians without the use of transesophageal echocardiography unless onset was unclear[20, 26].

Towards the same direction, ED patients at 6 urban Canadian centers with uncomplicated AF of less than 48 hours duration and $CHADS_2$ score of 0 or 1 were randomized in a 1:1 ratio to either chemical cardioversion with procainamide infusion, followed by electrical cardioversion if unsuccessful or to electrical cardioversion followed by procainamide infusion if unsuccessful[23]. The primary endpoint was the proportion of patients being discharged within 4 hours of arrival. Results of the study showed that both strategies appeared to be effective and well tolerated but the electrical-first strategy was associated with less time spent in the ED[23].

All the above led to the development of Acute AF/AFL Best Practices Checklist by the Canadian Association of Emergency Physicians (CAEP)[27]. Consequently, the RAFF-3 trial[28] sought to investigate the impact of implementing this guidance[28]. It was conducted as a stepped-wedge cluster randomized trial at 11 large community and academic hospital EDs in 5 Canadian provinces and enrolled consecutive AF/AFL patients. The study intervention was introduction of the CAEP Checklist with the use of a knowledge translation-implementation approach that included behavior change techniques and organization/system–level strategies. The RAFF-3 trial led to optimized care of AF/AFL patients with decreased ED lengths of stay by 20.9%, increased ED rhythm control by drug or electricity, and no increase in adverse events[28].

Most published AF treatment protocols have been validated in high volume-tertiary care centers. De Meester et al demonstrated that utilization of an AF treatment protocol could reduce admission rates even in a community-level hospital ED, based primarily on rate rather than rhythm control[21]. Specifically, in this retrospective cohort study, there was a pre implementation period from March 2013-February 2014 with 586 patients included and a post implementation period from March 2015-February 2016 with 522 patients included. Primary outcome was hospital admissions and

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indeed these were greatly reduced in the post-implementation group (67.4% vs 80.4% in the pre-implementation group)[21].

Study	AF duration	Intervention	Study type	Hospital type	Number of patients	SR rate (%)	Admission rate (%)	Adverse events rate (%)	ED return rate (%)
Burton[18]	<48 h	DCCV	Retrospective cohort	Tertiary	388	86	14	8	10 (10d)
Stiell[20]	Acute onset	PROC iv	Retrospective cohort	Tertiary	341	52(AF), 28(AFL)	5.6	10	2.9 (7d)
Stiell[26]	Recent onset	PROC iv +/- DCCV	Retrospective cohort	Tertiary	600 (PROC), 243(DCCV)	58 (PROC) 92 (DCCV)	3.2	7.6	8.6(7d)
Scheuermeyer[23]	<48 h	PROC iv +/- DCCV or DCCV +/- PROC	Multicenter randomized study	Tertiary care	41 PROC 43 DCCV	100 PROC 98 DCCV	0	25	12.2 (3d) 2.2 (30d)
Martin[24]	Recent onset	CC or DCCV	Multicenter observational cross sectional	Tertiary care, community	421	70	14	n/a	n/a
Ptaszek[25]	New or recurrent	CC or DCCV	Prospective 2-stage at 2 hospital study	Tertiary care, community	104 routine care 104 AF pathway	61 routine care, 76 AF pathway	55 routine care 15 AF pathway	n/a	11(in 4 months)
De Meester[21]	New or recurrent	DCCV if rate control failed	Retrospective cohort	Community	1108	n/a	67	n/a	1 (3d) 3.6 (30d)

CC: chemical cardioversion, DCCV: direct current cardioversion, PROC: procainamide

6. Long-term outcomes

While short-term (<7-day) safety and efficiency of electrical cardioversion for (ED) patients with AF have been established, 30-day outcomes with respect to stroke, thromboembolic events, or death were first investigated in a cohort of 1,233 patients during a period from 2000 to 2007. There were no deaths, strokes, or other thromboembolic events in the first 30 days following cardioversion[29].

A prospective cohort study was conducted in 6 academic hospital EDs enrolling patients who had AF/AFL onset within 48 hours. Patients were followed for 30 days by health records review and telephone. Among 1.091 patients enrolled, 9% were admitted to hospital and 80.1% were converted to sinus rhythm. Although 10.5% had adverse events within 30 days, there were no related deaths and only 1 stroke (0.1%). Patients who left the ED in sinus rhythm were much less likely to experience an adverse event (P<.001)[30].

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7. Ongoing AF pathways

The U-CARE AF pathway was developed by the university of California to standardize the management of patients presenting to the ED with primary AF[31]. In addition to the management and stabilization of acute AF, the U-CARE AF pathway aims to improve the adherence to anticoagulation and reduce the unnecessary hospital admissions whenever safe with a quick outpatient follow up. The initial goal of the pathway is the control of ventricular response which is initiated pharmacologically in all patients (desired rate control <110 bpm). Although current guidelines consider safe to cardiovert patients who can definitely pinpoint the start of AF within the last 48 hours, in the U-CARE AF pathway a 12-hour cutoff is used instead. Regarding chemical cardioversion, preferred agents are oral propafenone, oral flecainide or intravenous procainamide. If a patient is not cardioverted, they may be discharged on rate control medication and anticoagulation and the decision of whether cardioversion should be again attempted is delegated to the outpatient clinic.

Contrary to the conservative U-CARE AF pathway, expert consensus in Canada limits hospital admissions only to highly symptomatic AF patients with decompensated heart failure or myocardial ischemia and to those (highly symptomatic) in whom adequate rate control cannot be achieved. ED management priorities include assessment for potential hemodynamic instability and careful assessment of the time of AF onset. For stable patients with recent-onset AF or atrial flutter there are 2 competing strategies for management, either rate- or rhythm-control[32-35]. The rate control approach consists of ventricular rate control, oral anticoagulation, no attempt to convert the patient to sinus rhythm in the ED, and delayed cardioversion after 4 weeks, if indicated. With the rhythm-control approach, attempts are made to cardiovert patients to sinus rhythm in the ED, either pharmacologically or electrically, and then discharge them home in sinus rhythm[18, 36, 37].

8. HEROMEDICUS protocol

The HEROMEDICUS protocol was developed by the National and Kapodistrian University of Athens to standardize the management of AF in ED. Our purpose is not only to reduce hospital admissions in a safe and effective environment but also to ensure the highest percentage of sinus rhythm rate through an aggressive rhythm control strategy. Most importantly the protocol is designed and executed by expert electrophysiologists in collaboration with cardiologists in the absence of emergency medicine doctors. Study protocol was approved by Ethics Committee and all included patients provide an informed consent form.

All patients who visit ED with a primary diagnosis of AF or AFL are included in the study, even if time from arrhythmia initiation cannot be specified. Patients with ischemic heart disease are randomized in the setting of FLECA-ED study and excluded from the HEROMEDICUS protocol[38, 39]. Patients with indications of acute coronary syndrome or acute heart failure are also excluded. Enrollment started in September 2023 and will end in September 2025. Retrospective data will be collected from ED archive and hospital data in the periods September 2021- September 2022 and September 2022- September 2023 in order to assess the impact of Covid pandemia on AF visits and admissions from ED.

A special application has been created by P.T for the purpose of the HEROMEDICUS protocol and installed in mobile phones of cardiologists in charge in ED. Initial baseline clinical parameters are recorded and inclusion and exclusion criteria are implemented by means of bedside echocardiogram. Furthermore, emphasis in given in prior history of AF episodes and ED visits and hospital admissions, along with use of antiarrhythmics and anticoagulant status (warfarin and time in therapeutic INR range, type, and dose of direct oral anticoagulant)

Expert electrophysiologic consultation

- Decision for rate control and subsequent (>21 days) electrical cardioversion in case of poor anticoagulant status and long (>48hrs) AF detection
  - ⇒ Use of verapamil in case of AFL or atrial tachycardia
  - ⇒ Use of β-blockers in case of AF

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- Chemical cardioversion if immediate pill in the pocket administration of propafenone or flecainide did not exceed 300mg and 200mg, respectively.
  ⇒ Use of iv flecainide (150mg IV within 10min)
- Electrical cardioversion
  ⇒ Nil by mouth for the preceding 6hrs
  ⇒ Sedation and analgesia provided by cardiologist in ED (iv use of midazolam and pethidine)
  ⇒ Use of biphasic synchronized cardioversion (registration of delevered energy)

Discharge from ED

- Modification of outpatient antiarrhythmic use based on discharge ECG.
- Outpatient follow up in AF clinic.
- Programmed electrical cardioversion in case of poor anticoagulant status and long (>48hrs) AF detection (use of transesophageal echocardiogram only in cases of suspected severe valvulopathy).

Preference of iv flecainide was based on the largest published so far network meta-analysis that indirectly compared and ranked antiarrhythmic agents focusing exclusively on adults with paroxysmal AF[40]. Forty-one randomized controlled trials (6013 patients) were included with i.v. vernakalant and i.v. flecainide found to have the highest conversion rate within 4hr, possibly allowing discharge from the ED and reducing hospital admissions[40]. Vernakalant was not selected due to its prohibitive cost in the setting of ED.

8. Initial results

During the first 100 days of the study period, 63 patients visited ED with a primary diagnosis of AF (n=55) or AFL (n=8) and included in the study. It is notable that in half of them this was the first episode of AF (n=32). Among the 31 patients with a known history of AF, 5 had undergone a previous AF ablation. Electrical cardioversion was performed in 18 patients and restoration of SR was achieved in 17 of them. Finally, only 2 patients were admitted to the hospital (3.2%) and both of them were discharged within 48 hours.

9. Conclusion

Management of AF in the setting of ED varies between countries and health care systems. It is noteworthy that rate control rather than rhythm control is historically a preferred strategy in the United States while in other western countries such as Canada, Australia, and the United Kingdom rhythm control is attempted in patients with AF who visit the ED[26, 30, 41]. The most plausible reason to justify a conservative rather than aggressive strategy in the management of AF is the absence of specific guidelines from diverse societies. Towards this direction, in the RACE 7 ACWAS, a multicenter, randomized, open-label, noninferiority trial, a wait-and-see approach was noninferior to early cardioversion in achieving a return to sinus rhythm at 4 weeks in patients presenting to the ED with recent-onset, symptomatic AF[42]. It should also be taken into account that in certain hospitals there is a lack of ED resources to perform electrical cardioversion, as well as a lack of payer scrutiny of short hospitalizations or readmissions due to AF, in contrast to other conditions such as angina, syncope, and decompensated heart failure[42]. On the other hand, the very encouraging results yielded by aggressive AF management protocols, resulting in significantly fewer hospitalizations without evidence of worse outcomes, along with data suggesting patient preference for sinus rhythm restoration, constitute the fundamental reasons for pursuing an early cardioversion strategy[43-48].

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References

1. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Jordan LC, Khan SS, Kissela BM, Knutson KL, Kwan TW, Lackland DT, Lewis TT, Lichtman JH, Longenecker CT, Loop MS, Lutsey PL, Martin SS, Matsushita K, Moran AE, Mussolino ME, O'Flaherty M, Pandey A, Perak AM, Rosamond WD, Roth GA, Sampson UKA, Satou GM, Schroeder EB, Shah SH, Spartano NL, Stokes A, Tirschwell DL, Tsao CW, Turakhia MP, VanWagner LB, Wilkins JT, Wong SS, Virani SS. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. Circulation. 2019;139(10):e56-e528.
2. Aune D, Feng T, Schlesinger S, Janszky I, Norat T, Riboli E. Diabetes mellitus, blood glucose and the risk of atrial fibrillation: A systematic review and meta-analysis of cohort studies. Journal of diabetes and its complications. 2018;32(5):501-11.
3. Boriani G, Savelieva I, Dan GA, Deharo JC, Ferro C, Israel CW, Lane DA, La Manna G, Morton J, Mitjans AM, Vos MA, Turakhia MP, Lip GY. Chronic kidney disease in patients with cardiac rhythm disturbances or implantable electrical devices: clinical significance and implications for decision making-a position paper of the European Heart Rhythm Association endorsed by the Heart Rhythm Society and the Asia Pacific Heart Rhythm Society. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2015;17(8):1169-96.
4. Cadby G, McArdle N, Briffa T, Hillman DR, Simpson L, Knuiman M, Hung J. Severity of OSA is an independent predictor of incident atrial fibrillation hospitalization in a large sleep-clinic cohort. Chest. 2015;148(4):945-52.
5. Di Carlo A, Bellino L, Consoli D, Mori F, Zaninelli A, Baldereschi M, Cattarinussi A, D'Alfonso MG, Gradia C, Sgherzi B, Pracucci G, Piccardi B, Polizzi B, Inzitari D. Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAI Project. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2019;21(10):1468-75.
6. Hobbelt AH, Siland JE, Geelhoed B, Van Der Harst P, Hillege HL, Van Gelder IC, Rienstra M. Clinical, biomarker, and genetic predictors of specific types of atrial fibrillation in a community-based cohort: data of the PREVEND study. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2017;19(2):226-32.
7. Staerk L, Wang B, Preis SR, Larson MG, Lubitz SA, Ellinor PT, McManus DD, Ko D, Weng LC, Lunetta KL, Frost L, Benjamin EJ, Trinquart L. Lifetime risk of atrial fibrillation according to optimal, borderline, or elevated levels of risk factors: cohort study based on longitudinal data from the Framingham Heart Study. BMJ (Clinical research ed). 2018;361:k1453.
8. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. The American journal of medicine. 2002;113(5):359-64.
9. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation. 1998;98(10):946-52.
10. Coyne KS, Paramore C, Grandy S, Mercader M, Reynolds M, Zimetbaum P. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2006;9(5):348-56.
11. Rozen G, Hosseini SM, Kaadan MI, Biton Y, Heist EK, Vangel M, Mansour MC, Ruskin JN. Emergency Department Visits for Atrial Fibrillation in the United States: Trends in Admission Rates and Economic Burden From 2007 to 2014. Journal of the American Heart Association. 2018;7(15).
12. Jackson SL, Tong X, Yin X, George MG, Ritchey MD. Emergency Department, Hospital Inpatient, and Mortality Burden of Atrial Fibrillation in the United States, 2006 to 2014. The American journal of cardiology. 2017;120(11):1966-73.
13. Lin MP, Ma J, Weissman JS, Bernard KR, Schuur JD. Hospital-level variation and predictors of admission after ED visits for atrial fibrillation: 2006 to 2011. The American journal of emergency medicine. 2016;34(11):2094-100.
14. McDonald AJ, Pelletier AJ, Ellinor PT, Camargo CA, Jr. Increasing US emergency department visit rates and subsequent hospital admissions for atrial fibrillation from 1993 to 2004. Annals of emergency medicine. 2008;51(1):58-65.
15. Gulizia MM, Cemin R, Colivicchi F, De Luca L, Di Lenarda A, Boriani G, Di Pasquale G, Nardi F, Scherillo M, Lucci D, Fabbri G, Maggioni AP. Management of atrial fibrillation in the emergency room and in the cardiology ward: the BLITZ AF study. Europace : European pacing, arrhythmias, and cardiac

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electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2019;21(2):230-8.
16. Sacchetti A, Williams J, Levi S, Akula D. Impact of emergency department management of atrial fibrillation on hospital charges. The western journal of emergency medicine. 2013;14(1):55-7.
17. von Besser K, Mills AM. Is discharge to home after emergency department cardioversion safe for the treatment of recent-onset atrial fibrillation? Annals of emergency medicine. 2011;58(6):517-20.
18. Burton JH, Vinson DR, Drummond K, Strout TD, Thode HC, McInturff JJ. Electrical cardioversion of emergency department patients with atrial fibrillation. Annals of emergency medicine. 2004;44(1):20-30.
19. Santini M, De Ferrari GM, Pandozi C, Alboni P, Capucci A, Disertori M, Gaita F, Lombardi F, Maggioni AP, Mugelli A, Salerno-Uriarte JA, Sermasi S, Schwartz PJ. Atrial fibrillation requiring urgent medical care. Approach and outcome in the various departments of admission. Data from the atrial Fibrillation/flutter Italian REgistry (FIRE). Italian heart journal : official journal of the Italian Federation of Cardiology. 2004;5(3):205-13.
20. Stiell IG, Clement CM, Symington C, Perry JJ, Vaillancourt C, Wells GA. Emergency department use of intravenous procainamide for patients with acute atrial fibrillation or flutter. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2007;14(12):1158-64.
21. DeMeester S, Hess RA, Hubbard B, LeClerc K, Ferraro J, Albright JJ. Implementation of a Novel Algorithm to Decrease Unnecessary Hospitalizations in Patients Presenting to a Community Emergency Department With Atrial Fibrillation. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2018;25(6):641-9.
22. Lee WC, Lamas GA, Balu S, Spalding J, Wang Q, Pashos CL. Direct treatment cost of atrial fibrillation in the elderly American population: a Medicare perspective. Journal of medical economics. 2008;11(2):281-98.
23. Scheuermeyer FX, Andolfatto G, Christenson J, Villa-Roel C, Rowe B. A Multicenter Randomized Trial to Evaluate a Chemical-first or Electrical-first Cardioversion Strategy for Patients With Uncomplicated Acute Atrial Fibrillation. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2019;26(9):969-81.
24. Martín A, Coll-Vinent B, Suero C, Fernández-Simón A, Sánchez J, Varona M, Cancio M, Sánchez S, Carbajosa J, Malagón F, Montull E, Del Arco C. Benefits of Rhythm Control and Rate Control in Recent-onset Atrial Fibrillation: The HERMES-AF Study. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2019;26(9):1034-43.
25. Ptaszek LM, Baugh CW, Lubitz SA, Ruskin JN, Ha G, Forsch M, DeOliveira SA, Baig S, Heist EK, Wasfy JH, Brown DF, Biddinger PD, Raja AS, Scirica B, White BA, Mansour M. Impact of a Multidisciplinary Treatment Pathway for Atrial Fibrillation in the Emergency Department on Hospital Admissions and Length of Stay: Results of a Multi-Center Study. Journal of the American Heart Association. 2019;8(18):e012656.
26. Stiell IG, Clement CM, Perry JJ, Vaillancourt C, Symington C, Dickinson G, Birnie D, Green MS. Association of the Ottawa Aggressive Protocol with rapid discharge of emergency department patients with recent-onset atrial fibrillation or flutter. Cjem. 2010;12(3):181-91.
27. Stiell IG, de Wit K, Scheuermeyer FX, Vadeboncoeur A, Angaran P, Eagles D, Graham ID, Atzema CL, Archambault PM, Tebbenham T, McRae AD, Cheung WJ, Parkash R, Deyell MW, Baril G, Mann R, Sahsi R, Upadhye S, Brown E, Brinkhurst J, Chabot C, Skanes A. 2021 CAEP Acute Atrial Fibrillation/Flutter Best Practices Checklist. Cjem. 2021;23(5):604-10.
28. Stiell IG, Archambault PM, Morris J, Mercier E, Eagles D, Perry JJ, Scheuermeyer F, Clark G, Gosselin S, Vadeboncoeur A, Parkash R, de Wit K, Patey AM, Thiruganasambandamoorthy V, Taljaard M. RAFF-3 Trial: A Stepped-Wedge Cluster Randomised Trial to Improve Care of Acute Atrial Fibrillation and Flutter in the Emergency Department. The Canadian journal of cardiology. 2021;37(10):1569-77.
29. Scheuermeyer FX, Grafstein E, Stenstrom R, Innes G, Poureslami I, Sighary M. Thirty-day outcomes of emergency department patients undergoing electrical cardioversion for atrial fibrillation or flutter. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2010;17(4):408-15.
30. Stiell IG, Clement CM, Rowe BH, Brison RJ, Wyse DG, Birnie D, Dorian P, Lang E, Perry JJ, Borgundvaag B, Eagles D, Redfearn D, Brinkhurst J, Wells GA. Outcomes for Emergency Department Patients With Recent-Onset Atrial Fibrillation and Flutter Treated in Canadian Hospitals. Annals of emergency medicine. 2017;69(5):562-71.e2.
31. Do DH, Bernardes-Souza B, Merjanian M, Lombardo B, Donaldson DM, McCullough LB, Boyle NG, Cooper RJ. Development of a Care Pathway for Atrial Fibrillation Patients in the Emergency Department. Critical pathways in cardiology. 2022;21(3):105-13.
32. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC, Jr., Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 9 January 2024 doi:10.20944/preprints202401.0712.v1

M, Morais J, Osterspey A, Tamargo JL, Zamorano JL. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation. 2006;114(7):e257-354.

33. Wyse DG, Simpson CS. Rate control versus rhythm control--decision making. The Canadian journal of cardiology. 2005;21 Suppl B:15b-8b.
34. Hiatt WR, Lincoff AM, Harrington RA. Acute pharmacological conversion of atrial fibrillation to sinus rhythm: is short-term symptomatic therapy worth it? A report from the December 2007 Meeting of the Cardiovascular and Renal Drugs Advisory Committee of the Food and Drug Administration. Circulation. 2008;117(22):2956-7.
35. Page RL. Clinical practice. Newly diagnosed atrial fibrillation. The New England journal of medicine. 2004;351(23):2408-16.
36. Raghavan AV, Decker WW, Meloy TD. Management of atrial fibrillation in the emergency department. Emergency medicine clinics of North America. 2005;23(4):1127-39.
37. Taylor DM, Aggarwal A, Carter M, Garewal D, Hunt D. Management of new onset atrial fibrillation in previously well patients less than 60 years of age. Emergency medicine Australasia : EMA. 2005;17(1):4-10.
38. Tsiachris D, Doundoulakis I, Tsioufis P, Pagkalidou E, Antoniou CK, Zafeiropoulos SM, Gatzoulis KA, Tsioufis K, Stefanadis C. Reappraising the role of class Ic antiarrhythmics in atrial fibrillation. European journal of clinical pharmacology. 2022;78(6):1039-45.
39. Tsioufis P, Tsiachris D, Doundoulakis I, Kordalis A, Antoniou CK, Vlachakis PK, Theofilis P, Manta E, Gatzoulis KA, Parissis J, Tsioufis K. Rationale and Design of a Randomized Controlled Clinical Trial on the Safety and Efficacy of Flecainide versus Amiodarone in the Cardioversion of Atrial Fibrillation at the Emergency Department in Patients with Coronary Artery Disease (FLECA-ED). Journal of clinical medicine. 2023;12(12).
40. Tsiachris D, Doundoulakis I, Pagkalidou E, Kordalis A, Deftereos S, Gatzoulis KA, Tsioufis K, Stefanadis C. Pharmacologic Cardioversion in Patients with Paroxysmal Atrial Fibrillation: A Network Meta-Analysis. Cardiovascular drugs and therapy. 2021;35(2):293-308.
41. Rogenstein C, Kelly AM, Mason S, Schneider S, Lang E, Clement CM, Stiell IG. An international view of how recent-onset atrial fibrillation is treated in the emergency department. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2012;19(11):1255-60.
42. Pluymaekers N, Dudink E, Luermans J, Meeder JG, Lenderink T, Widdershoven J, Bucx JJJ, Rienstra M, Kamp O, Van Opstal JM, Alings M, Oomen A, Kirchhof CJ, Van Dijk VF, Ramanna H, Liem A, Dekker LR, Essers BAB, Tijssen JGP, Van Gelder IC, Crijns H. Early or Delayed Cardioversion in Recent-Onset Atrial Fibrillation. The New England journal of medicine. 2019;380(16):1499-508.
43. Atzema CL. Atrial Fibrillation: Would You Prefer a Pill or 150 Joules? Annals of emergency medicine. 2015;66(6):655-7.
44. Atzema CL, Austin PC, Chong AS, Dorian P. Factors associated with 90-day death after emergency department discharge for atrial fibrillation. Annals of emergency medicine. 2013;61(5):539-48.e1.
45. Ballard DW, Reed ME, Singh N, Rauchwerger AS, Hamity CA, Warton EM, Chettipally UK, Mark DG, Vinson DR. Emergency Department Management of Atrial Fibrillation and Flutter and Patient Quality of Life at One Month Postvisit. Annals of emergency medicine. 2015;66(6):646-54.e2.
46. Kriz R, Freynhofer MK, Weiss TW, Egger F, Gruber SC, Eisenburger P, Wojta J, Huber K, Koch J. Safety and efficacy of pharmacological cardioversion of recent-onset atrial fibrillation: a single-center experience. The American journal of emergency medicine. 2016;34(8):1486-90.
47. Seaburg L, Hess EP, Coylewright M, Ting HH, McLeod CJ, Montori VM. Shared decision making in atrial fibrillation: where we are and where we should be going. Circulation. 2014;129(6):704-10.
48. Fuster V, Rydén LE, Asinger RW, Cannom DS, Crijns HJ, Frye RL, Halperin JL, Kay GN, Klein WW, Lévy S, McNamara RL, Prystowsky EN, Wann LS, Wyse DG, Gibbons RJ, Antman EM, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Hiratzka LF, Jacobs AK, Russell RO, Smith SC, Klein WW, Alonso-Garcia A, Blomström-Lundqvist C, De Backer G, Flather M, Hradec J, Oto A, Parkhomenko A, Silber S, Torbicki A. ACC/AHA/ESC guidelines 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 European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation): developed in Collaboration With the North American Society of Pacing and Electrophysiology. Journal of the American College of Cardiology. 2001;38(4):1231-66.

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