Benefits of Emergency Departments’ Contribution to Stroke Prophylaxis in Atrial Fibrillation

The EMERG-AF Study (Emergency Department Stroke Prophylaxis and Guidelines Implementation in Atrial Fibrillation)

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Background and Purpose—Long-term benefits of initiating stroke prophylaxis in the emergency department (ED) are unknown. We analyzed the long-term safety and benefits of ED prescription of anticoagulation in atrial fibrillation patients.

Methods—Prospective, multicenter, observational cohort of consecutive atrial fibrillation patients was performed in 62 Spanish EDs. Clinical variables and thromboprophylaxis prescribed at discharge were collected at inclusion. Follow-up at 1 year post-discharge included data about thromboprophylaxis and its complications, major bleeding, and death; risk was assessed with univariate and bivariate logistic regression models.

Results—We enrolled 1162 patients, 1024 (88.1%) at high risk according to CHADS2-VASc score. At ED discharge, 935 patients (80.5%) were receiving anticoagulant therapy, de novo in 237 patients (55.2% of 429 not previously treated). At 1 year, 48 (4.1%) patients presented major bleeding events, and 151 (12.9%) had died. Anticoagulation first prescribed in the ED was not related to major bleeding (hazard ratio, 0.976; 95% confidence interval, 0.294–3.236) and was associated with a decrease in mortality (hazard ratio, 0.398; 95% confidence interval, 0.231–0.686). Adjusting by the main clinical and sociodemographic characteristics, concomitant antiplatelet treatment, or destination (discharge or admission) did not affect the results.

Conclusions—Prescription of anticoagulation in the ED does not increase bleeding risk in atrial fibrillation patients at high risk of stroke and contributes to decreased mortality.  

(Stroke. 2017;48:1344-1352. DOI: 10.1161/STROKEAHA.116.014855.)

Key Words: anticoagulants ▪ atrial fibrillation ▪ hemorrhage ▪ mortality stroke

Atrial fibrillation (AF) is the most prevalent arrhythmia treated in emergency departments (EDs),1–3 and the most serious complication is stroke or systemic embolism.4 The high effectiveness of oral anticoagulants in preventing these complications5 has produced general agreement that stroke prophylaxis is the mainstay of AF management in all healthcare settings.5–8

Given the number of these patients attended in EDs who are at high risk of stroke but not receiving anticoagulants,9,10 the ED may be an underused resource for starting anticoagulation, although this remains controversial. Some authors have postulated that ED physicians should only inform patients about the need for stroke prophylaxis, and oral anticoagulation should be prescribed in other settings.11 On the other hand, as substantial underuse has been reported in them,12,13 numerous authors have called for coordinated efforts, including ED involvement, to improve treatment.14

No study to date has prospectively addressed the long-term outcomes of ED prescription and its contribution to stroke prophylaxis. Analysis of the feasibility, benefits, and

Received July 21, 2016; final revision received February 6, 2017; accepted February 9, 2017.

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The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.116.014855/-/DC1.

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Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.116.014855

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long-term safety of ED prescription of anticoagulants could contribute to categorical recommendations for stroke prophylaxis in this setting. The objectives of the EMERG-AF study (Emergency Department Stroke Prophylaxis and Guidelines Implementation in Atrial Fibrillation) were to analyze thromboprophylaxis prescription in patients with AF attended in the ED and long-term outcomes: major bleeding, stroke or systemic embolism, and death.

Methods

Study Design and Setting

The EMERG-AF was a prospective, multicenter, observational cohort study performed in 62 Spanish EDs from April 2013 to June 2014. Data were collected prospectively at the first ED visit (April 1–30, 2013) on study inclusion and at a 1-year (±4 weeks) follow-up visit. To guarantee a hospital sample representative of the Spanish healthcare system, study centers were selected from the national catalogue published by Spain’s Ministry of Health and Social Policy. Centers were categorized by size, level of services, and location; the scientific committee recruited 25% of the eligible centers, weighted by category, to participate. The study was approved by the Scientific Ethics Committee of each participating hospital.

Selection of Participants

We included consecutive patients older than 18 years attended in the ED for any reason during the study period with AF documented in clinical records or demonstrated in an ECG obtained when the treating ED physician considered it necessary during clinical evaluation. Exclusion criteria were atrial flutter and clinical trial participation. A total of 1138 patients were considered necessary for a representative sample, assuming an estimated anticoagulation ratio of 60%, 2-sided 95% confidence interval (CI), ±3% sensitivity and 10% losses to follow-up. Informed consent was obtained in all cases. To guarantee confidentiality, access to patient identity was restricted to the treating ED physician. The central database contained identification numbers for individual study participants and was password protected.

Initial Data Collection and Processing

Copies of the EMERG-AF study protocol (including definitions and codes) were provided to all collaborating researchers, who were trained by the lead investigator in data recording. The information was collected in a centralized electronic file after interviewing patients or their relatives and later checked and completed by chart review. The study’s scientific committee made no therapeutic recommendations and provided no specific instructions about AF and its management during the data collection.

The following information was included on the initial data collection sheet: demographic data, comorbidities, disability (according to the Katz scale), type of AF, duration of the current AF episode, risk factors for stroke (CHA2DS2-VASc score), bleeding risk (according to the HAS-BLED score [Hypertension, Abnormal Renal and Liver Function, Stroke, Bleeding, Labile INRs, Elderly, Drugs or Alcohol]), current stroke prophylaxis (anticoagulation, antiplatelet therapy, or both), symptoms that caused ED consultation and AF (yes/no), and destination. Because the prescription of anticoagulant therapy was the main variable of interest, we conducted a number of multivariate analyses, adjusting by these factors to assess its relevance as a potential independent predictor for hemorrhagic events or death. All analyses were also performed for patients without previous stroke prophylaxis treatment.

Follow-Up

Follow-up in both groups included a phone call and a review of each patient’s electronic medical record at 1 year (±4 weeks) postinclusion to address long-term outcomes. The follow-up analysis included the following variables: bleeding events, systemic embolism and stroke events, stroke prophylaxis at the time of follow-up, and mortality (date and cause of death). If bleeding or a stroke or systemic embolism had occurred, type of bleeding (minor or major) or type of complication, respectively, were recorded along with date of presentation, location, and outcome.

The study’s scientific committee independently reviewed all data-sheets to detect inconsistencies. As needed, a query was made to the principal investigator at the corresponding center to resolve any questions.

Outcome Measures

As the main objective of the present article was patient safety at 1 year post-discharge, incidence of major bleeding was the primary outcome. Mortality and stroke/systemic embolism were secondary outcomes.

Statistical Analysis

All analysis was performed with SPSS 20.0 and SAS statistical software packages, accepting a risk threshold for a 2-sided Type I error of 5%. Differences in the profiles of patients with or without anticoagulation treatment at discharge were assessed by Fisher exact test or t test for independent groups for quantitative or qualitative variables, respectively.

Univariate logistic regression models were built to assess the risk of major bleeding or death. The models estimated the hazard ratio (HR) and 95% CI using the most relevant clinical and demographic factors: age, sex, hypertension, diabetes mellitus, renal failure, acute heart failure, structural heart disease, cerebrovascular disease, previous AF, CHA2DS2-VASc, HAS-BLED, concomitant antiplatelet treatment, previous major bleeding, and relationship between the reason for ED consultation and AF (yes/no), and destination. Because the prescription of anticoagulant therapy was the main variable of interest, we conducted a number of multivariate analyses, adjusting by these factors to assess its relevance as a potential independent predictor for hemorrhagic events or death. All analyses were also performed for patients without previous stroke prophylaxis treatment.

Results

Characteristics of Study Participants

During the study period, 1162 patients were included (mean age, 74.7 years [SD 11.2], 590 [50.8%] women). In 178 patients (15.3%), de novo AF diagnosis was made during the ED inclusion visit. Comorbid conditions were common. The majority (88.1%) of the patients included were at high risk of stroke according to the CHA2DS2-VASc score. Demographic and clinical characteristics of all patients and of patients without previous anticoagulation are listed in Table 1. Two patients (0.2%) died during the ED stay. After evaluation, 512 patients (44.0%) were admitted, and 648 patients (55.8%) were discharged home.

Main Results

Anticoagulation Prescription

At the time of the ED visit, 733 patients (63.1%) were taking anticoagulants. At ED discharge, 935 patients (80.5%), including those diagnosed de novo, were receiving antithrombotic therapy with anticoagulants (146 with concomitant antiplatelets).

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Table 2 details ED anticoagulation prescription according to stroke risk. Considering both previous and de novo anticoagulant therapies, 166 high-risk patients according to the CHA₂DS₂-VASc score (14.3%) did not receive anticoagulation therapy at discharge from the ED. The main reasons given by the treating physicians for not prescribing anticoagulation in these high-risk patients were high risk of bleeding (81 patients [48.8%]) and no indication for anticoagulation (56 patients [33.7%]).

Of the 935 patients anticoagulated at ED discharge, 764 (81.7%) received vitamin K antagonists, 97 (10.4%) low-molecular-weight heparin, 73 (7.8%) direct oral anticoagulants, and 1 patient (0.1%) other anticoagulation. Prescriptions were de novo in 237 patients (55.2% of the 429 not previously anticoagulated). At discharge, all participants were referred to another healthcare facility for follow-up and long-term monitoring.

**Follow-Up**

After 1 year, 58 patients (4.9%) were deceased, and 52 patients (4.4%) were lost to follow-up. The reasons for losses to follow-up

| Variable                      | Total, n=1162, n (%) | Not Previously Anticoagulated | P Value |
|-------------------------------|----------------------|--------------------------------|---------|
| Age, mean (SD)                | 74.7±11.2            | 72.4±13.0                      | 0.22    |
| Sex (female)                  | 590 (50.8)           | 204 (47.6)                     | 0.47    |
| Structural heart disease      | 585 (50.3)           | 129 (30.1)                     | 0.71    |
| Acute heart failure           | 406 (34.9)           | 87 (20.3)                      | 0.18    |
| Left ventricular dysfunction  | 209 (18)             | 41 (9.6)                       | 0.65    |
| Hypertension                  | 868 (74.7)           | 286 (66.7)                     | 0.002   |
| Previous stroke               | 172 (14.8)           | 47 (11.0)                      | 1.00    |
| Previous systemic embolism    | 19 (1.6)             | 1 (0.2)                        | 0.26    |
| Diabetes mellitus             | 316 (27.2)           | 92 (21.5)                      | 0.09    |
| Renal failure                 | 191 (16.4)           | 55 (12.8)                      | 0.91    |
| CHA₂DS₂-VASc                  |                      |                                |         |
| 0                             | 49 (4.2)             | 39 (9.0)                       | <0.001  |
| 1                             | 89 (7.7)             | 55 (12.8)                      |         |
| ≥2                            | 1024 (88.1)          | 335 (78.1)                     |         |
| HAS-BLED                      |                      |                                |         |
| <3                            | 568 (48.9)           | 242 (56.5)                     | 0.08    |
| ≥3                            | 594 (51.1)           | 187 (43.6)                     |         |
| Disability                    | 126 (10.8)           | 44 (10.0)                      | 0.17    |
| Total                         | 8 (0.7)              | 3 (0.7)                        |         |
| Types of AF                   |                      |                                |         |
| First episode                 | 178 (15.3)           | 164 (38.1)                     | <0.001  |
| Paroxysmal                    | 312 (26.9)           | 154 (36.0)                     |         |
| Persistent                    | 131 (11.3)           | 44 (10.3)                      |         |
| Permanent                     | 541 (46.6)           | 67 (15.6)                      |         |
| Main complaint                |                      |                                |         |
| Related to AF*                | 681 (58.6)           | 318 (74.1)                     | <0.001  |
| Other                         | 481 (41.4)           | 111 (25.9)                     |         |
| Duration of episode           |                      |                                |         |
| <48 h                         | 210 (18.1)           | 141 (32.7)                     | 0.010   |
| >48 h                         | 539 (46.4)           | 101 (23.6)                     |         |
| Unknown                       | 413 (35.5)           | 187 (43.7)                     |         |

AF indicates atrial fibrillation.

*Related to AF or its treatment.
were change of address or other factors making contact impossible (49 patients) and decision to withdraw (3 patients). One-year follow-up was completed by 956 patients (94.6% of survivors and 82.3% of all participants). At the end of the year, 699 (73.1%) patients were taking anticoagulants; the great majority of them (670 patients, 95.8%) received de novo or continued anticoagulant treatment at ED discharge. Anticoagulation persisted in 81.2% of the patients anticoagulated de novo who survived and completed follow-up. The 29 patients prescribed an anticoagulant during follow-up constituted 12.8% of the 227 patients discharged without anticoagulation.

**Primary Outcome: Safety**

At the end of 1 year, 184 bleeding events had occurred in 150 patients (12.9%), including 55 (29.8%) major bleeding episodes that occurred in 48 patients (4.1%), with 6 fatalities. The main bleeding sites were gastrointestinal (23.9%), otorhinolaryngologic (22.7%), and urogenital (14.1%). Twelve patients had intracranial hemorrhage (6.5% of all bleeding events).

Anticoagulant treatment was not related to major bleeding (HR, 1.376; 95% CI, 0.581–3.260; Figure 1A). These results were similar when only patients who were not receiving anti-coagulation before the index visit were taken into account (HR, 0.976; 95% CI, 0.974–3.236; Figure 1B), even when adjusted for possible confounders: final outcome in the first visit (discharge versus admission), antiplatelet treatment, or other relevant clinical or sociodemographic characteristics (Table 3). A separate analysis of discharged, or not previously anticoagulated patients also found no significant relationship between starting anticoagulant treatment and major bleeding (HR, 2.597; 95% CI, 0.270–24.966).

**Secondary Outcomes**

**Mortality:** During the 1-year follow-up period, 151 patients (12.8%) died, 62 (41.6%) of them because of cardiovascular causes. Anticoagulant treatment was associated with decreased mortality (HR, 0.505; 95% CI, 0.357–0.715; Figure 2A). This association also persisted when only patients who were not receiving anticoagulation before the index visit were taken into account (HR, 0.398; 95% CI, 0.231–0.686; Figure 2B), even when adjusted for the final outcome in the first visit (discharge versus admission), antiplatelet treatment, or any relevant clinical or sociodemographic characteristic (Table 4). When a separate analysis of the 257 discharged, not previously anticoagulated patients was performed, anticoagulated patients (n=137) had lower mortality than those discharged without anticoagulation (n=120) but the difference (5.8% versus 9.1% mortality, respectively) was nonsignificant (HR, 0.668; 95% CI, 0.264–1.694).

**Stroke and systemic embolism:** Thromboembolic complications were present in 31 patients (2.7%): 13 strokes, 8 transient ischemic attacks, and 13 systemic embolisms. Four of these patients died, and 15 were left with sequelae.

Anticoagulation was not associated with the presence of stroke events in the univariate analysis (HR, 0.929; 95% CI, 0.381–2.264). When only patients not previously anticoagulated were considered, those who received anticoagulants in the ED visit tended to have a lower incidence of embolic events, although this was not significant (2.1% versus 3.2%; HR, 0.614; 95% CI, 0.187–2.011), even when adjusted for final outcome, antiplatelet treatment, or any relevant clinical or sociodemographic characteristic (Table II in the online-only Data Supplement).

**Limitations**

Participation in an investigative study may have had an impact on the clinicians. To minimize this limitation, risk stratification scores were not made available in the electronic record. The large number of researchers involved could have generated variability in interpreting the questions on the data collection sheet. To avoid this bias, multiple-choice responses were specified. In addition, verbal information obtained from patients at 1-year follow-up could have been affected by recall bias. However, all serious complications would likely have been attended in a hospital and reflected in the official records reviewed to ensure accuracy of outcome information.

The EMERG-AF study was not designed to compare differences in effectiveness between stroke prophylaxis prescribed in EDs and that prescribed in other clinical settings. No such conclusions should be inferred from the study results.
Finally, our results can be generalized to the Spanish National Health System and other closely related systems. Further studies are needed to confirm the external validity of these results.

**Discussion**

The EMERG-AF is the first study to date to prospectively analyze the long-term effects of the ED physician’s contribution to stroke prophylaxis in AF patients, both in prescribing anticoagulation de novo in high-risk patients and in reinforcing the therapeutic message and encouraging long-term adherence in those patients already taking anticoagulants. In this representative sample of EDs in Spain, the clinical features and stroke risk of the patients included were comparable to those in the global AF population, especially those attended in EDs, as described in the largest studies to date.²,³,¹⁹ Therefore, the results obtained may be widely applicable to ED daily practice.

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**Figure 1.** Kaplan–Meier curves showing time to first major bleeding according to anticoagulant treatment. **A**, All patients; **B**, patients who were not receiving oral anticoagulation when they arrived to the emergency department.
This study yielded 3 main conclusions. First, prescribing anticoagulants in the ED to AF patients at a high risk of stroke is not only feasible but also beneficial in the long term, with a favorable safety profile. Anticoagulation was prescribed by the ED physicians without requiring other medical assessments, and instructions for therapy and referral to other healthcare settings were provided exclusively by ED physicians and nurses. In addition, the prescription followed current guidelines in the vast majority of cases. Nevertheless, and despite the high level of anticoagulation found in our series, almost 15% of eligible patients were not taking anticoagulants at discharge. This highlights the need for an additional effort to provide this prescription to all high-risk patients.

Second, the safety profile of anticoagulation prescribed in EDs, following the guidelines’ recommendations and providing systematic referral for follow-up at discharge, is at least as safe in the long term as are prescriptions made in other healthcare settings. After adjusting for clinical and sociodemographic variables, the major bleeding rate in patients anticoagulated de novo at the ED was similar to that in nonanticoagulated patients. Moreover, these good results reflect not only an adequate indication for anticoagulation, but also appropriate referrals to INR monitoring. Together with the finding that the majority of patients in whom anticoagulation was prescribed de novo at the ED were adhering to treatment at 1-year follow-up, these results strongly support an assertion that accurate prescription of anticoagulants is feasible in the daily ED practice and suggest that decisions made in the ED influence longitudinal care, as recently reported by Atzema et al.21

The third main result of our study was that the good patient safety outcomes were not achieved at the expense of effectiveness. Although there were no significant differences in the benefits of anticoagulant prescription in the ED with respect to embolic events, likely because of the overall paucity of such events, the impact on mortality was overwhelmingly positive. Mortality decreased overall and in patients without previous anticoagulation, even after adjusting for all confounding variables. When a separate analysis was performed on discharged, not previously anticoagulated patients, although the mortality was lower in anticoagulated patients, the difference was not significant. The lack of significance in this subpopulation is likely because of the lower global mortality that would be expected in discharged patients. Although the study was not sufficiently powered for the analysis of subpopulations, this does not lessen the implications of the results because the aim was to analyze the long-term effects of the ED physician’s contribution to overall stroke prophylaxis in AF patients. Moreover, although the management of patients with AF is guided by a common protocol and is highly consistent among EDs in Spain, the management of admissions varies greatly between the participating hospitals; thus, many of the included patients were admitted to an Observation Unit or Short Stay Unit, in most cases headed by a physician from the ED staff.

It can be argued that these long-term good results could also be attributed to patient management by other healthcare specialists after ED discharge. We certainly agree with this because the objectives of the EMERG-AF study were to analyze the contribution of ED physicians to the multidisciplinary team approach to stroke prophylaxis in patients with AF; not to assess in isolation the benefits of prescribing anticoagulants.

### Table 3. Factors Associated With Major Bleeding in Patients Not Previously Anticoagulated

| Variable                                      | Nonbleeding Patients, n=418, n (%) | Bleeding Patients, n=11, n (%) | Univariate HR 95% CI | Multivariate (Anticoagulation at Discharge, Adjusted by Each Variable) HR 95% CI |
|-----------------------------------------------|-----------------------------------|-------------------------------|----------------------|----------------------------------------------------------------------------------|
| Anticoagulation at discharge                  | 231 (55.26)                      | 6 (54.55)                     | 0.976 0.294–3.236    | Nonestimable                                                                      |
| Destination (discharged home)                 | 253 (60.53)                      | 4 (36.36)                     | 0.369 0.107–1.277    | 0.868 0.261–2.882                                                                |
| Age ≥75 y                                     | 203 (48.56)                      | 8 (72.73)                     | 2.915 0.769–11.050   | 0.908 0.275–2.996                                                                |
| Sex (female)                                  | 198 (47.37)                      | 6 (54.55)                     | 1.286 0.389–4.244    | 0.997 0.298–3.339                                                                |
| Hypertension                                  | 280 (66.99)                      | 6 (54.55)                     | 0.701 0.210–2.343    | 1.013 0.305–3.368                                                                |
| Diabetes mellitus                             | 89 (21.29)                       | 3 (27.27)                     | 1.554 0.402–6.009    | 0.936 0.280–3.132                                                                |
| Renal failure                                 | 50 (11.96)                       | 5 (45.45)                     | 6.020 1.794–20.197   | 0.814 0.245–2.704                                                                |
| Acute heart failure                           | 84 (20.10)                       | 3 (27.27)                     | 1.462 0.385–5.553    | 0.913 0.270–3.082                                                                |
| Structural heart disease                      | 121 (28.95)                      | 8 (72.73)                     | 6.055 1.585–23.131   | 0.872 0.265–2.874                                                                |
| Cerebrovascular disease                       | 44 (10.53)                       | 3 (27.27)                     | 2.703 0.694–10.520   | 0.899 0.273–2.960                                                                |
| Disability                                    | 42 (10.05)                       | 2 (18.18)                     | 2.580 0.547–12.157   | 1.028 0.309–3.424                                                                |
| Consultation related to AF                   | 314 (75.15)                      | 4 (36.36)                     | 7.231 1.869–27.973   | 2.078 0.592–7.293                                                                |
| Previous AF                                   | 257 (61.48)                      | 8 (72.73)                     | 1.699 0.450–6.410    | 1.064 0.318–3.557                                                                |
| HAS-BLED score of ≥2                         | 326 (77.99)                      | 9 (81.82)                     | 1.432 0.308–6.647    | 0.903 0.264–3.086                                                                |
| Concomitant antiplatelet treatment            | 179 (42.82)                      | 8 (72.73)                     | 3.931 1.041–14.841   | 0.939 0.285–3.086                                                                |
| Previous major bleeding                      | 67 (16.03)                       | 3 (27.27)                     | 0.723 0.209–2.506    | 0.822 0.220–3.069                                                                |

Definitions detailed in the Statistical Analysis. AF indicates atrial fibrillation; CI, confidence interval; and HR, hazard ratio.
in the acute setting. Indeed, as a general rule and as one of the pillars of starting anticoagulation, all AF patients discharged from EDs in our setting are referred to another level of health care (internal medicine, cardiology, neurology, geriatrics, and primary care) for follow-up and to specialized clinics or primary care to monitor anticoagulation and reinforce patient education. Thus, our results are an accurate reflection of the potential benefits of a coordinated and multidisciplinary strategy of stroke prophylaxis involving ED physicians and nurses, and specifically highlight the potential ED contribution to maximize appropriate prophylaxis in these patients.\textsuperscript{22–24}

**Conclusions**

Prescription in the ED of anticoagulation in AF patients at a high risk of stroke is not only feasible but also beneficial in the long term to decrease mortality. Therefore, the active

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**Figure 2.** Kaplan–Meier curves showing mortality according to anticoagulant treatment. **A**, All patients; **B**, patients who were not receiving oral anticoagulation when they arrived to the emergency department.
involvement of ED physicians could help to improve the global results of stroke prophylaxis in AF and thus help to improve the prognosis and quality of life of this increasing population of patients attended in the acute setting.

Appendix

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Acknowledgments

We thank Elaine Lilly, PhD, for her careful English language revision of the article.

Sources of Funding

The study was supported by a grant from Bayer Hispania, which had no influence on the content of the article.

Disclosures

Dr Ràfols is an employee of Bayer Hispania SL. Dr Suero has received modest honoraria from Bayer, Boehringer-Ingelheim, and Bristol Myers-Squibb for specific speech and advisory board. The other authors report no conflicts.

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Benefits of Emergency Departments' Contribution to Stroke Prophylaxis in Atrial Fibrillation: The EMERG-AF Study (Emergency Department Stroke Prophylaxis and Guidelines Implementation in Atrial Fibrillation)

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*Stroke*. 2017;48:1344-1352; originally published online April 7, 2017;
doi: 10.1161/STROKEAHA.116.014855

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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SUPPLEMENTAL MATERIAL
| Table I. Multiple-choice set of reasons for not prescribing anticoagulation |
|---------------------------------------------------------------|
| o Patient’s advanced age                                    |
| o Disability                                                 |
| o Allergy                                                    |
| o Drug abuse                                                 |
| o Poor adherence to therapy                                 |
| o Frequent falls                                             |
| o Previous haemorrhage related to oral anticoagulants        |
| o Potential risk of haemorrhage:                            |
|   o Active peptic disease                                   |
|   o Neoplasm                                                 |
|   o Recent bleeding unrelated to anticoagulants              |
|   o Recent stroke                                            |
|   o Haemostasis disorder                                    |
|   o Vascular or genitourinary diseases with a high risk of bleeding |
|   o Recent surgery                                           |
|   o Severe trauma                                            |
| o Patient’s rejection                                       |
| o Decision transferred to other specialist                   |
| o Not considered indicated                                   |
| Variable                        | Non embolic patients n=418 n(%) | Embolic patients n=11 n(%) | Univariate | Multivariate (Anticoagulation at discharge, adjusted by each variable) |
|--------------------------------|--------------------------------|---------------------------|------------|-------------------------------------------------------------|
|                                | OR    | 95% CI       | p          | OR    | 95% CI       | p          |
| Anticoagulation at discharge   | 232(55.50) | 5(45.45) | 0.668 0.201-2.223 | 0.5108 |
| Destination (discharged home)  | 252(60.29) | 5(45.45) | 0.546 0.164-1.817 | 0.3236 |
| Age ≥ 75 years                 | 204(48.80) | 7(63.64) | 1.836 0.529-6.365 | 0.3383 |
| Sex (female)                   | 198(47.37) | 6(54.55) | 0.907 0.444-1.851 | 0.7876 |
| Hypertension                   | 278(66.51) | 8(72.73) | 1.343 0.351-5.140 | 0.6670 |
| Diabetes mellitus              | 90(21.53) | 2(18.18) | 0.810 0.172-3.815 | 0.7898 |
| Renal failure                  | 53(12.68) | 2(18.18) | 1.530 0.322-7.276 | 0.5927 |
| Acute heart failure            | 84(20.10) | 3(27.27) | 1.491 0.387-5.742 | 0.5614 |
| Structural heart disease       | 129(30.86) | 0(0.00) | - - | 0.9557 0.681 0.203-2.283 0.5340 |
| Cerebrovascular disease        | 41(9.81) | 6(54.55) | 11.0.322-37.749 | 0.0001 |
| Disability                     | 41(9.81) | 3(27.27) | 3.448 0.880-13.509 | 0.0756 |
| Consultation related to AF     | 308(73.68) | 10(90.91) | 0.280 0.035-2.213 | 0.2274 |
| Previous AF                    | 256(61.24) | 9(81.82) | 2.847 0.608-13.342 | 0.1843 |
| CHA₂DS₂-VASc ≥ 2              | 324(77.51) | 11(100) | - - | 0.9625 0.537 0.161-1.797 0.3132 |
| HAS-BLED ≥ 3                   | 178(42.58) | 9(81.82) | 6.067 1.295-13.342 | 0.0221 |
|                                | Count | Ratio   | OR    | CI          | P     | CI          | P     |
|--------------------------------|-------|---------|-------|-------------|-------|-------------|-------|
| Concomitant antiplatelet       | 176   | 42.11%  | 2.406 | 0.694-8.346 | 0.1664| 0.249-3.268 | 0.8757|
| treatment                      | 7     | 63.64%  |       |             |       |             |       |
| Previous major bleeding        | 66    | 15.79%  | 3.048 | 0.868-10.704| 0.0821| 0.233-2.754 | 0.7239|
|                                | 4     | 36.36%  |       |             |       |             |       |

OR, Odds ratio; CI, confidence interval; AF, atrial fibrillation
Table III. Factors associated with major bleeding in patients not previously anticoagulated (logistic regression)

| Variable*                              | Non-bleeding patients n=418 n (%) | Bleeding patients n=11 n (%) | Univariate                                      | Multivariate (Anticoagulation at discharge, adjusted by each variable) |
|----------------------------------------|-----------------------------------|-----------------------------|-----------------------------------------------|---------------------------------------------------------------------|
|                                        | OR                                | 95% CI                      | p                                             | OR                                | 95% CI                      | p                                           |
| Anticoagulation at discharge           | 231 (55.26)                       | 6 (54.55)                   | 0.9671                                        | 0.292-3.233                  | 0.9623                                      | -                                           |
| Destination (discharged home)          | 253 (60.53)                       | 4 (36.36)                   | 0.370                                         | 0.107-1.285                  | 0.1177                                      | 0.274-3.070                                 | 0.8888                                     |
| Age ≥ 75 years                         | 203 (48.56)                       | 8 (72.73)                   | 2.824                                         | 0.739-10.793                 | 0.1291                                      | 0.287-3.202                                 | 0.9452                                     |
| Sex (female)                           | 198 (47.37)                       | 6 (54.55)                   | 1.333                                         | 0.401-4.437                  | 0.6391                                      | 0.295-3.269                                 | 0.9753                                     |
| Hypertension                           | 280 (66.99)                       | 6 (54.55)                   | 0.591                                         | 0.177-1.972                  | 0.3926                                      | 0.311-3.560                                 | 0.9343                                     |
| Diabetes mellitus                      | 89 (21.29)                        | 3 (27.27)                   | 1.386                                         | 0.360-5.333                  | 0.6347                                      | 0.283-3.171                                 | 0.9308                                     |
| Renal failure                          | 50 (11.96)                        | 5 (45.45)                   | 6.135                                         | 1.806-20.842                 | 0.0036                                      | 0.290-3.317                                 | 0.9761                                     |
| Acute heart failure                    | 84 (20.10)                        | 3 (27.27)                   | 1.491                                         | 0.387-5.742                  | 0.5614                                      | 0.283-3.165                                 | 0.9298                                     |
| Structural heart disease               | 121 (28.95)                       | 8 (72.73)                   | 6.546                                         | 1.708-25.089                 | 0.0061                                      | 0.278-3.165                                 | 0.9171                                     |
| Cerebrovascular disease                | 44 (10.53)                        | 3 (27.27)                   | 3.188                                         | 0.816-12.459                 | 0.0956                                      | 0.290-3.244                                 | 0.9614                                     |
| Disability                             | 42 (10.05)                        | 2 (18.18)                   | 1.990                                         | 0.416-9.515                  | 0.3889                                      | 0.301-3.369                                 | 0.9911                                     |
| Consultation related to AF             | 314 (75.15)                       | 4 (36.36)                   | 5.284                                         | 1.516-18.411                 | 0.0090                                      | 0.528-7.284                                 | 0.3143                                     |
| Previous AF                            | 257 (61.48)                       | 8 (72.73)                   | 1.671                                         | 0.437-6.3889                 | 0.4534                                      | 0.317-3.727                                 | 0.8936                                     |
| CHA$_2$DS$_2$-VASc ≥ 2                 | 326 (77.99)                       | 9 (81.82)                   | 1.270                                         | 0.2710-5.979                 | 0.7626                                      | 0.276-3.175                                 | 0.9145                                     |
|                                | Value 1 | Value 2 | OR    | 95% CI  | p    | 95% CI  | 95% CI  |
|--------------------------------|---------|---------|-------|---------|------|---------|---------|
| **HAS-BLED ≥ 3**               | 179 (42.82) | 8 (72.73) | 3.560 | 0.931-13.608 | 0.0634 | 1.082 | 0.322-3.633 | 0.8990 |
| **Concomitant antiplatelet**    | 179 (42.82) | 4 (36.36) | 0.763 | 0.220-2.646 | 0.6699 | 0.867 | 0.240-3.136 | 0.8284 |
| **treatment**                   |         |         |       |         |       |         |         |
| **Previous major bleeding**    | 67 (16.03) | 3 (27.27) | 1.965 | 0.508-7.596 | 0.3277 | 1.084 | 0.316-3.711 | 0.8982 |

OR, Odds ratio; CI, confidence interval; AF, atrial fibrillation
| Variable                                           | Alive at one year n=371 | Deceased at one year n=58 | Univariate | Multivariate (Anticoagulation at discharge adjusted by each variable) |
|----------------------------------------------------|--------------------------|---------------------------|------------|---------------------------------------------------------------------|
|                                                    | n (%)                    | n (%)                     | OR 95% CI  | p                      | OR 95% CI  | p                      |
| Anticoagulation at discharge                      | 217 (58.49)              | 20 (34.48)                | 0.374 0.209-0.667 | 0.0009        | -          | -                      |
| Destination (discharged home)                     | 238 (64.15)              | 19 (32.76)                | 0.279 0.155-0.504 | <.0001       | 0.338 0.185-0.667 | 0.0004     |
| Age ≥ 75 years                                    | 164 (44.20)              | 47 (81.03)                | 5.393 2.711-10.727 | <.0001       | 0.341 0.187-0.621 | 0.0004     |
| Sex (female)                                      | 169 (45.55)              | 35 (60.34)                | 1.819 1.034-3.198 | 0.0378       | 0.378 0.211-0.617 | 0.0010     |
| Hypertension                                      | 241 (64.96)              | 45 (77.59)                | 1.867 0.972-3.587 | 0.0609       | 0.332 0.184-0.600 | 0.0003     |
| Diabetes mellitus                                 | 75 (20.22)               | 17 (29.31)                | 1.636 0.881-3.041 | 0.1192       | 0.353 0.196-0.635 | 0.0005     |
| Renal failure                                     | 37 (9.97)                | 18 (31.03)                | 4.063 2.117-7.796 | <.0001       | 0.358 0.197-0.649 | 0.0007     |
| Acute heart failure                               | 66 (17.79)               | 21 (36.21)                | 2.623 1.442-4.769 | 0.0016       | 0.335 0.185-0.608 | 0.0003     |
| Structural heart disease                          | 100 (26.95)              | 29 (50.00)                | 2.710 1.543-4.761 | 0.0005       | 0.354 0.196-0.640 | 0.0006     |
| Cerebrovascular disease                           | 34 (9.16)                | 13 (22.41)                | 2.864 1.407-5.829 | 0.0037       | 0.365 0.203-0.656 | 0.0008     |
| Disability                                         | 26 (7.01)                | 18 (31.03)                | 5.972 3.012-11.839 | <.0001       | 0.388 0.213-0.706 | 0.0020     |
| Consultation related to AF                        | 287 (77.36)              | 31 (53.45)                | 2.976 1.682-5.264 | 0.0002       | 0.486 0.262-0.901 | 0.0029     |
| Previous AF                                        | 221 (59.57)              | 44 (75.86)                | 2.133 1.129-4.030 | 0.0196       | 0.418 0.231-0.757 | 0.0040     |
| CHA₂DS₂-VASc ≥ 2                                  | 282 (76.01)              | 53 (91.38)                | 3.345 1.297-8.628 | 0.0125       | 0.308 0.170-0.557 | <.0001     |
| HAS-BLED ≥ 3                                       | 142 (38.27)              | 45 (77.59)                | 5.582 2.909-<.0001 | 0.402        | 0.221-0.0009          |            |
Concomitant antiplatelet treatment & 217 (58.49) & 20 (34.48) & 1.409 & 0.809-2.454 & 0.2255 & 0.373 & 0.201-0.692 & 0.0018
Previous major bleeding & 48 (12.94) & 22 (37.93) & 4.113 & 2.233-7.576 & <.0001 & 0.444 & 0.245-0.807 & 0.0077

OR, Odds ratio; CI, confidence interval; AF, atrial fibrillation
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**Journal** Stroke  
**Manuscript Number** STROKE/2016/014855  
**First Author** Blanca Coll-Vinent  
**Title of Work** BENEFITS OF EMERGENCY DEPARTMENTS' CONTRIBUTION TO STROKE PROPHYLAXIS IN ATRIAL FIBRILLATION. THE EMERG-AF STUDY

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