Evidence-based Guideline Update: Prevention of Stroke in Nonvalvular Atrial Fibrillation

Report of the Guideline Development Subcommittee of the American Academy of Neurology

Guideline Endorsement

This guideline was endorsed by the World Stroke Organization

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Presentation Objectives

- To present an update to the 1998 American Academy of Neurology (AAN) practice parameter on stroke prevention in nonvalvular atrial fibrillation (NVAF)
- To present evidence-based recommendations

Overview

- Background
- Gaps in care
- AAN guideline process
- Analysis of evidence, conclusions, recommendations
- Recommendations for future research

Background

- The prevalence of atrial fibrillation (AF) in the United States was estimated to be 3.03 million persons in 2005[1] and is strongly associated with increasing age.[1]
- Because AF is a major risk factor for cardioembolic stroke,[2,3] there is an urgent need to develop strategies for identification of AF and prevention of cardioembolic stroke at all ages.

Background, cont.

- The ischemic stroke rate among patients with AF averages 5% yearly[2] but varies greatly depending on individual clinical characteristics such as age, sex, race/ethnicity, and associated stroke risk factors.
- History of stroke or transient ischemic attack (TIA) identifies those patients with a high stroke risk averaging 10% yearly.[3]

Clinical Questions

- For patients with cryptogenic stroke, how often does the use of various technologies, as compared with the nonuse of these technologies, identify previously undetected NVAF?

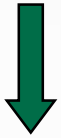
- For patients with NVAF, which therapies that include antithrombotic medication, as compared with no therapy or with another therapy, reduce stroke risk and severity with the least risk of hemorrhage?

AAN Guideline Process

- Clinical Question

- Evidence

- Conclusions



- Recommendations

AAN Guideline Process

- Systematic review of evidence available in the English-language literature from 1998 to 2012 (updated to March 2013)
- Guideline developed using a hybrid of AAN processes (2004 and 2011)[5,6]
- Literature search performed
- Articles selected and rated independently by two authors
- Evidence synthesized using a modification of the Grading of Recommendations Assessment, Development and Evaluation process[7]
- Conflicts of interest disclosed

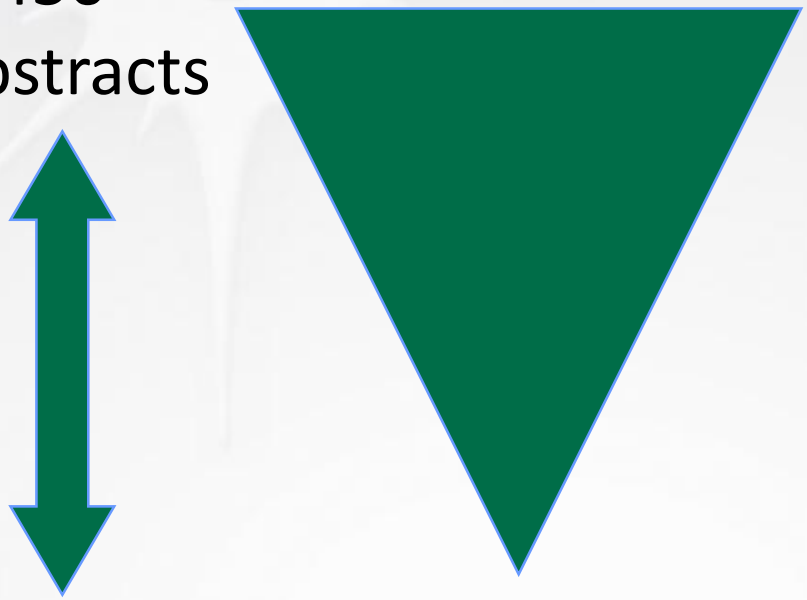
AAN Guideline Process, cont.

- Confidence in evidence anchored to the studies' risk of bias
  - "Highly likely" or "highly probable" = high confidence level
  - "Likely" or "probable" = moderate confidence level
  - "Possibly" = low confidence level
  - "Insufficient evidence" = very low confidence
- Recommendations formulated
  - Evidence systematically reviewed
  - Axiomatic principles of care applied
- Clinician level of obligation assigned (modified Delphi)
  - "Must" = "Level A," very strong
  - "Should" = "Level B," strong
  - "Might" = "Level C," weak

Literature Search/Review

- Rigorous, Comprehensive, Transparent

2,450 abstracts



83 articles

Inclusion criteria:

-Randomized, controlled trials; cohort studies; case-control studies; case series (n ≥20); review articles; meta-analyses

Exclusion criteria:

-Case reports, small case series (n <20), review articles without primary data

-Articles in languages other than English

-Animal studies

AAN Classification of Evidence for Therapeutic Intervention

- **Class I:** A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:
  - Concealed allocation
  - Primary outcome(s) clearly defined
  - Exclusion/inclusion criteria clearly defined
  - Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.

AAN Classification of Evidence for Therapeutic Intervention, cont.

- For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
  - ✓The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.
  - ✓The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
  - ✓The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
  - ✓The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

AAN Classification of Evidence for Therapeutic Intervention, cont.

- **Class II:** A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

AAN Classification of Evidence for Therapeutic Intervention, cont.

- **Class III:** All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population and that includes a description of major confounding differences between treatment groups that could affect outcome, and where outcome assessment is masked, objective, or performed by someone who is not a member of the treatment team.**

AAN Classification of Evidence for Therapeutic Intervention, cont.

- **Class IV:** Studies that use undefined or unaccepted interventions or outcome measures and that do not include the following:
  - Patients with the disease
  - Patients receiving different interventions
  - Measures of effectiveness or statistical precision

*Note that numbers 1–3 in Class I, item 5 are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

AAN Classification of Evidence for Screening (Yield)

- **Class I:** A statistical,[a] population-based[b] sample of patients studied at a uniform point in time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective,[c] is determined in an evaluation that is masked to the patients' clinical presentations.
- **Class II:** A statistical,[b] non–referral-clinic-based[d] sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most (>80%) patients undergo the intervention of interest. The outcome, if not objective,[c] is determined in an evaluation that is masked to the patients' clinical presentations.

AAN Classification of Evidence for Screening (Yield), cont.

- **Class III:** A sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not objective,[c] is determined in an evaluation by someone other than the treating physician.
- **Class IV:** The data are derived from expert opinion, case reports, or any study not meeting criteria for Class I to III.
- **Notes:**
  - a. Statistical sample: The study uses a complete (consecutive), random, or systematic (e.g., every third patient) sample of the available population with the disease.
  - b. Population based: The available population for the study consists of all patients within a defined geographic region.
  - c. Objective: The objective consists of an outcome measure that is very unlikely to be affected by an observer's expectations (e.g., determination of death, the presence of a mass on head CT, serum B12 assays).
  - d. Non–referral-clinic based: The available population for the study consists of all patients presenting to a primary care setting with the condition. For referral-clinic-based studies, the available population consists of all patients referred to a tertiary care or specialty setting. These patients may have been selected for more severe or unusual forms of the condition and thus may be less representative.

Clinical Question 1

- **For patients with cryptogenic stroke, how often does the use of various technologies, as compared with the nonuse of these technologies, identify previously undetected NVAF?**
  - Two Class II[8,9] and 15 Class III[10–24] studies were identified that address this question. Studies were downgraded 1 level if they failed to provide data on a cryptogenic stroke cohort, because some of the patients in noncryptogenic cohorts had known NVAF.

Conclusion

- In patients with recent cryptogenic stroke, cardiac rhythm monitoring probably detects previously unidentified NVAF at a rate ranging from 0%–23% (weighted average of 10.7% [95% CI 7.9%–14.3%]).
- The detection rate is probably related to the duration of monitoring (2 Class II studies,[8,9] 15 Class III studies[10–24]).

Clinical Question 2

- **For patients with NVAF, which therapies that include antithrombotic medication, as compared with no therapy or with another therapy, reduce stroke risk and severity with the least risk of hemorrhage?**

Warfarin, Influence of Normalized Ratio Level

- Since the publication of the 1998 practice parameter 2 Class II studies[25,26] have evaluated the relationship between international normalized ratio (INR) level at the time of stroke presentation and stroke severity and mortality.
- Both studies demonstrated that an INR of less than 2 as compared with an INR greater than 2 was associated with an increased risk of disabling stroke (odds ratio 1.9 [95% CI 1.1–3.4]) or death (hazard ratio [HR] for death at 30 days 3.4 [95% CI 1.1–10.1]).[25]

Conclusion

- In patients with NVAF, anticoagulation that results in an INR of 2.0–3.0 likely reduces the frequency and severity of ischemic stroke as compared with anticoagulation resulting in lower INR levels (2 Class II studies[25,26]).

Antithrombotics Compared with Warfarin or Its Derivatives

- Search strategy identified 6 randomized studies[27–32] (5 Class I studies,[27–31] 1 Class II study[32]) comparing various antithrombotic regimens with warfarin or its derivatives in patients with NVAF.
- All studies employed masked or adjudicated outcome assessment. Antithrombotic regimens studied were dabigatran,[27] rivaroxaban,[28] apixaban,[29] fluindione plus aspirin,[32] clopidogrel plus aspirin,[30] and triflusal plus acenocoumarol.[31]

Antithrombotics Compared with Warfarin or Its Derivatives, cont.

- Dabigatran is a direct thrombin inhibitor. Rivaroxaban and apixaban are factor Xa inhibitors. Dabigatran, rivaroxaban, and apixaban are administered in fixed doses and do not require regular blood coagulation monitoring. Antithrombotic reversal agents for these drugs are unavailable.
- Triflusal is an antiplatelet drug structurally related to aspirin that is used in Europe, Latin America, and Southeast Asia (see appendix e-9 of the complete guideline for the relevant countries).[33,34] Acenocoumarol, a coumarin derivative, is used mostly in European countries. Fluindione is a vitamin K antagonist used in France.

Conclusions

- In patients with NVAF, dabigatran administration is probably more effective for reducing the risk of stroke or systemic embolism (150 mg twice daily, relative risk [RR] 0.66; RRR 34%) than is warfarin administration.
- Hemorrhage risks were similar overall between dabigatran 150 mg administration twice daily and warfarin administration (INR 2.0–3.0), but intracranial hemorrhage was less frequent with administration of dabigatran 150 mg twice daily (dabigatran vs warfarin, RR 0.40 [95% CI 0.27%–0.60%]) (1 Class I study[27]).

Conclusions, cont.

- In patients with NVAF at high risk of cerebral or systemic embolism, rivaroxaban is probably as effective as warfarin for the prevention of cerebral and systemic embolism, without difference in the risks of major bleeding episodes overall except GI bleeding.
- However, rivaroxaban is associated with a lesser frequency of intracranial hemorrhage and fatal bleeding as compared with warfarin (RRR 22% [95% CI 5.5%–35.3%]) (single Class I study[28]).

Conclusions, cont.

- Apixaban 5 mg twice daily is likely more effective than warfarin in patients with NVAF at moderate risk of embolism (RRR 20.3% [95% CI 4.8%–33.3%]).
- The superiority of apixaban is related to decreased risk of bleeding (including intracranial bleeding) and reduced mortality (1 Class I study[29]), whereas its effect on reduction of risk of cerebral and systemic embolism is not superior to that of warfarin.[29]

Conclusions, cont.

- In patients who have NVAF and are at risk of stroke, oral anticoagulation therapy is likely more effective than clopidogrel plus aspirin for stroke prevention (RR 1.44).
- Intracranial bleeding is more common with oral anticoagulation therapy than with clopidogrel plus aspirin (single Class I study[30]).
- In patients who have NVAF and are at moderate stroke risk, treatment with triflusal plus acenocoumarol and moderate-intensity anticoagulation (INR target 1.25–2.0) is likely more effective than treatment with acenocoumarol alone and conventional-intensity anticoagulation (INR target 2.0–3.0) for reducing stroke risk (RRR 61%, vascular death, TIA, nonfatal stroke, systemic embolism plus severe bleeding) (single Class I study,[31] smaller than recent studies with new oral anticoagulants).

Conclusions, cont.

- In patients with NVAF, the combination of low-dose aspirin and dose-adjusted vitamin K antagonist therapy probably increases the risk of hemorrhagic complications (1 Class II study[32]).
- There is insufficient evidence to determine whether the combination of aspirin and vitamin K antagonist therapy decreases the risk of ischemic stroke or other thromboembolic events.

Antithrombotics Compared with Aspirin

- Search strategy identified 2 randomized Class I studies[35,36] comparing different antithrombotic regimens with aspirin in patients with NVAF. Antithrombotic regimens studied were apixaban and clopidogrel plus aspirin.

Conclusions

- Based on 1 Class I study,[35] apixaban 5 mg twice daily is likely more effective than aspirin for decreasing risk of stroke or systemic embolism in patients with NVAF who have a moderate risk of embolism and are not candidates for warfarin treatment (RRR 55.1% [95% CI 37.8%–67.6%]). Bleeding risks are similar for both treatment forms.
- In patients with NVAF for whom vitamin K antagonist therapy is unsuitable, the combination of clopidogrel and aspirin (as compared with aspirin alone) reduces the risk of major vascular events, especially stroke (RR 0.72 relative to aspirin) but increases the risk of major hemorrhage (RR 1.57 relative to aspirin), including intracranial bleeding (RR 1.87 [95% CI 1.19–2.94]) (1 Class I study[36]).

Anticoagulants in Special Populations

- One Class I study[37] randomized patients aged ≥75 years with NVAF to warfarin (INR 2.0–3.0) or aspirin 75 mg/day. The RRR for disabling stroke (including intracranial hemorrhage) or systemic embolism favoring warfarin was 52% (95% CI 20%–72%). Extracranial hemorrhage rates were similar in the 2 treatment groups.
- In a Class II study[38] patients aged ≥75 years with NVAF were randomized to a target INR of 1.8 (range 1.5–2.0) or 2.5 (range 2.0–3.0). The composite outcome of thromboembolism and major hemorrhage occurred nonsignificantly less often in the lesser-intensity INR group (HR 0.7 [95% CI 0.4–1.1]).

Anticoagulants in Special Populations, cont.

- Among patients with chronic kidney disease (CKD) participating in the Stroke Prevention in Atrial Fibrillation III (Class I) trials,[39] adjusted-dose warfarin (INR target 2.0–3.0) reduced ischemic stroke/systemic embolism in patients with CKD and a high risk of stroke (RRR 76% [95% CI 42%–90%]) as compared with aspirin or low-dose warfarin, with no difference in major hemorrhage rates.
- For patients with stage 3 CKD[40] apixaban as compared with aspirin significantly reduced stroke and systemic embolism event rates (HR 0.32 [95% CI 0.18–0.55], $p < 0.001$) without an increase in major bleeding (absolute rate apixaban 2.5% vs aspirin 2.2%) (1 Class I study).

Conclusion

- The benefit of anticoagulation likely extends to elderly patients (1 Class I study[37]) and patients with CKD (2 Class I studies[39,40]). Bleeding risk increases in all patients with CKD taking warfarin.

A. Recommendations

A. Identification of Patients with Occult NVAF.

Clinical Context. In patients with recent cryptogenic stroke, outpatient cardiac rhythm monitoring performed with nonimplanted devices probably detects unsuspected NVAF at a rate that ranges from 0%–23% (weighted average 10.7% [95% CI 7.9%–14.3%]), with longer monitoring periods probably associated with a greater yield.

Many of the NVAF episodes that are detected are clinically asymptomatic, and thus monitoring devices with continuous recording or automatic detection algorithms, rather than patient-triggered recording, are preferred.

A. Recommendations, cont.

A. Identification of Patients with Occult NVAF.

Clinical Context, cont. The risk of recurrent stroke is uncertain in patients with very brief (e.g., <30 seconds) or very infrequent episodes of NVAF; however, previous studies have demonstrated that NVAF tends to occur for progressively longer periods, and the stroke risk in patients with paroxysmal NVAF is similar to that in patients with persistent NVAF.[e1–e4]

A. Practice Recommendations

A1. Clinicians might obtain outpatient cardiac rhythm studies in patients with cryptogenic stroke without known NVAF, to identify patients with occult NVAF (Level C).

A2. Clinicians might obtain cardiac rhythm studies for prolonged periods (e.g., for 1 or more weeks) instead of shorter periods (e.g., 24 hours) in patients with cryptogenic stroke without known NVAF, to increase the yield of identification of patients with occult NVAF (Level C).

B. Recommendations

B. Selection of Patients for Antithrombotic Therapy.

- ***Clinical Context.*** Within the NVAF population the absolute risk of ischemic stroke varies widely on the basis of the presence of other stroke risk factors.[4] The absolute stroke risk is highest among patients with NVAF and a history of stroke and TIA (aggregated absolute risk about 10%/year).[4]
- Although multiple risk stratification tools are available for estimating the absolute stroke risk of patients with NVAF, the absolute stroke risks estimated by these tools vary widely.[e5]

B. Recommendations, cont.

B. Selection of Patients for Antithrombotic Therapy.

- ***Clinical Context, cont.*** Because it is difficult to determine with precision the absolute stroke risk in patients with NVAF, determining when the benefit from reduced stroke risk outweighs the harm of increased bleeding is likewise difficult. In these circumstances patient preferences and physician judgment become especially important.

B. Practice Recommendations

B1. Clinicians should inform patients with NVAF that these patients have an increased stroke risk and that this risk can potentially be reduced by antithrombotic use. Patients should also be informed that antithrombotic use increases their risk of major bleeding (Level B).

B2. Clinicians should counsel all patients with NVAF that the decision to use antithrombotics must be made only after the potential benefit from the stroke risk reduction has been weighed against the potential harm from the increased risk of major bleeding. Clinicians should also emphasize the important role of judgment and preferences in this decision (Level B).

B. Practice Recommendations, cont.

B3. Clinicians should routinely offer anticoagulation to patients with NVAF and a history of TIA or stroke, to reduce these patients' subsequent risk of ischemic stroke (Level B).

B4. Clinicians might not offer anticoagulation to patients with NVAF who lack additional risk factors ("lone" NVAF patients). Clinicians might reasonably offer antithrombotic therapy with aspirin to such patients or might not offer antithrombotic therapy at all (Level C).

B5. To inform their judgments as to which patients with NVAF might benefit more from anticoagulation, clinicians should use a risk stratification scheme to help identify patients with NVAF who are at higher risk for stroke or at no clinically significant risk. However, clinicians should not rigidly interpret anticoagulation thresholds suggested by these tools as being definitive indicators of which patients require anticoagulation (Level B).

C. Recommendations

C. Selection of Specific Oral Anticoagulant

- ***Clinical Context.*** Our review indicates that several anticoagulant medications decrease the risk of ischemic stroke in patients with NVAF. In clinical trials the new oral anticoagulants are noninferior or superior to warfarin for reducing stroke, and in most patients the reduction in ischemic stroke risk outweighs the risk of bleeding complications.[e6]

C. Practice Recommendations

C1. To reduce the risk of stroke or subsequent stroke in patients with NVAF judged to require oral anticoagulants, clinicians should choose 1 of the following options (Level B):

- Warfarin, target INR 2.0–3.0
- Dabigatran 150 mg twice daily (if creatinine clearance [CrCl] > 30 mL/min)
- Rivaroxaban 15 mg/day (if CrCl 30–49 mL/min) or 20 mg/day
- Apixaban 5 mg twice daily (if serum creatinine <1.5 mg/dL) or 2.5 mg twice daily (if serum creatinine >1.5 and <2.5 mg/dL, and body weight <60 kg or age at least 80 years [or both])
- Triflusal 600 mg plus acenocoumarol, target INR 1.25–2.0 (patients at moderate stroke risk, mostly in developing countries)

C. Practice Recommendations, cont.

Patients Already Taking Warfarin. Duration of warfarin treatment and time in optimal INR therapeutic range (2.0–3.0) are predictors of favorable efficacy and safety.[25]

Practice Recommendation.

C2. Clinicians might recommend that patients taking warfarin whose condition is well controlled continue warfarin treatment rather than switch to treatment with a new oral anticoagulant (Level C).

C. Practice Recommendations, cont.

Intracranial Bleeding Risk. The new oral anticoagulants have a more favorable intracranial-bleeding profile than warfarin (dabigatran 150 mg bid vs warfarin, 0.3%/year vs 0.74%/year, RR 0.40 [95% CI 0.27–0.60], $p<0.001$; rivaroxaban 20 mg daily, 0.5%/year vs 0.7%/year, HR 0.67 [95% CI 0.47–0.93], $p=0.02$; apixaban 5 mg bid, 0.33%/year vs 0.80%/year, HR 0.42 [95% CI 0.30–0.58], $p<0.001$).

Practice Recommendation.

C3. Clinicians should administer dabigatran, rivaroxaban, or apixaban to patients who have NVAF requiring anticoagulant medication and are at higher risk of intracranial bleeding (Level B).

C. Practice Recommendations, cont.

GI Bleeding Risk. In patients with NVAF, GI bleeding was greater with dabigatran 150 mg twice daily as compared with warfarin (1.51%/year vs warfarin 1.02%/year). Bleeding from GI sites occurred more frequently in the rivaroxaban group than in the warfarin group, as did bleeding that led to a drop in the hemoglobin level or required transfusion (decrease in hemoglobin ≥2 g/dl, 2.8%/year in rivaroxaban group vs 2.3%/year in warfarin group). GI bleeding was nonsignificantly lesser with apixaban (0.76%/year) relative to that with warfarin (0.86%/year).

Practice Recommendation.

C4. Clinicians might offer apixaban to patients with NVAF and GI bleeding risk who require anticoagulant medication (Level C).

C. Practice Recommendations, cont.

Other Factors Affecting Administration of New Oral Anticoagulants. INR monitoring is not required for dabigatran, rivaroxaban, and apixaban for maintaining anticoagulation within the therapeutic window. Liberation from frequent periodic INR testing may be attractive to patients unwilling or unable to submit to frequent periodic testing.

Practice Recommendations.

C5. Clinicians should offer dabigatran, rivaroxaban, or apixaban to patients unwilling or unable to submit to frequent periodic testing of INR levels (Level B).

C6. Clinicians should offer apixaban to patients unsuitable for being treated, or unwilling to be treated, with warfarin (Level B).

C7. Where apixaban is unavailable, clinicians might offer dabigatran or rivaroxaban (Level C).

C. Practice Recommendations, cont.

Other Factors Affecting Administration of New Oral Anticoagulants.

Practice Recommendations, cont.

C8. Where oral anticoagulants are unavailable, clinicians might offer a-combination of aspirin and clopidogrel (Level C).

C9. Where triflusal is available and patients are unable or unwilling to take new oral anticoagulants (mostly in developing countries), clinicians should offer acenocoumarol (target INR 1.25–2.0) and triflusal to patients with NVAF who are at moderate stroke risk and higher bleeding risk (Level B).

D. Recommendations

D. Special Populations

- ***Clinical Context.*** Some clinicians are reluctant to use anticoagulants to treat elderly patients with NVAF because of perceived high risk of bleeding.[e8] However, anticoagulation with warfarin is superior to that with aspirin for reducing the risk of ischemic stroke in patients ≥75 years with NVAF, whereas rates of major bleeding are comparable.[37]
- In one important subgroup, elderly patients who have frequent falls or advanced dementia, data are insufficient to determine whether anticoagulants are safe or effective. One study that used a decision analysis model estimated that an elderly patient would need to fall 295 times in 1 year to offset the stroke reduction benefits with warfarin.[e9]

D. Recommendations, cont.

D. Special Populations

- ***Clinical Context, cont.*** Another important subgroup is patients with renal failure. For dabigatran, one of the newer anticoagulants, a lower dose of 75 mg bid is recommended by the FDA when the CrCl reaches 15–30 ml/min. Apixaban is recommended at 5 mg twice daily, if serum creatinine <1.5 mg/dL, or at 2.5 mg twice daily, if serum creatinine >1.5 and <2.5 mg/dL. Rivaroxaban was tested in patients at 15 mg daily, if CrCl 30–49 mL/min, or at 20 mg daily, if CrCl >50 mL/min, and recommendations are limited to these patient groups.
- With regard to warfarin, data have shown that warfarin treatment is associated with a decreased risk of stroke or systemic thromboembolism among patients with non–end-stage CKD but that warfarin treatment may be associated with an increased bleeding risk.[e1]

D. Practice Recommendations

D1. Clinicians should routinely offer oral anticoagulants to elderly patients (aged >75 years) with NVAF if there is no history of recent unprovoked bleeding or intracranial hemorrhage (Level B).

D2. Clinicians might offer oral anticoagulation to patients with NVAF who have dementia or occasional falls. However, clinicians should counsel patients or their families that the risk–benefit ratio of oral anticoagulants is uncertain in patients with NVAF who have moderate to severe dementia or very frequent falls (Level B).

D3. Because the risk–benefit ratio of oral anticoagulants in patients with NVAF and end-stage renal disease is unknown, there is insufficient evidence for making practice recommendations (Level U).

References

References cited here can be found in either the summary publication (appearing in print) or the e-references (online data supplement to the print publication). To locate references, please access the full guideline at:

AAN.com/guidelines

Question-and-Answer Period

- Questions/comments?

Closing

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- Thank you for your participation!