

Review

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Review

Atrial Fibrillation and Cognitive Decline: A Comprehensive Review of Pathophysiological Mechanisms, Therapeutic Strategies, and Digital Health Technologies in Neuroprotection

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Abstract

Background: Atrial fibrillation (AF) is independently associated with cognitive impairment and dementia through mechanisms extending far beyond traditional cardioembolic stroke risk. However, the relative contribution of distinct pathophysiological pathways and the efficacy of emerging therapeutic interventions for cognitive protection remain incompletely characterized. **Objectives:** This comprehensive review synthesizes current evidence on the epidemiology, pathophysiological mechanisms, therapeutic interventions (pharmacological, rhythm-control, and digital health), and research priorities addressing the AF–dementia relationship. **Methods:** A narrative review integrating evidence from observational studies, mechanistic research, randomized controlled trials, systematic reviews, and meta-analyses published through January 2026. Literature sources included MEDLINE/PubMed, major cardiology and neurology journals, and expert consensus statements. Searches used combinations of keywords: "atrial fibrillation," "cognitive decline," "dementia," "silent cerebral infarction," "cerebral hypoperfusion," "direct oral anticoagulants," "catheter ablation," and "digital health." Inclusion criteria encompassed studies examining the AF–cognition association, mechanistic pathways, therapeutic interventions with cognitive outcomes, and digital health technologies in AF management. Heterogeneous study designs prevented quantitative meta-analysis; qualitative synthesis focused on effect sizes, strength of evidence, and clinical implications. **Results:** Strong epidemiological evidence demonstrates that AF increases relative risk of dementia by 1.4–2.2 fold independently of clinical stroke, with silent cerebral infarction present in 25–40% of AF patients. Multiple interacting pathophysiological mechanisms account for AF-associated cognitive decline: cerebral microembolism (meta-analysis: OR 2.30 for silent infarction on MRI), chronic cerebral hypoperfusion (15–20% reduction in total cerebral blood flow in persistent AF), neuroinflammation, cerebral small vessel disease, and structural brain atrophy. Emerging therapeutic strategies offer complementary neuroprotective mechanisms: direct oral anticoagulants (DOACs)—particularly apixaban and rivaroxaban—reduce dementia risk by approximately 30% compared to warfarin (RR 0.69); rhythm control strategies and catheter ablation demonstrate dementia risk reduction (HR 0.52–0.69); and comprehensive digital health platforms implementing the ABC pathway reduce adverse cardiovascular events by 61% while optimizing adherence and enabling early AF detection. However, evidence-specific to cognitive endpoints remains limited, with the landmark BRAIN-AF trial showing no benefit of low-dose rivaroxaban in low-stroke-risk AF patients—suggesting that non-embolic mechanisms predominate in this population. **Conclusions:** AF represents a multifaceted threat to brain health requiring a paradigm shift from isolated stroke prevention toward comprehensive heart–brain health optimization. Integration of pharmacological neuroprotection (preferring DOACs), hemodynamic optimization (rhythm control in selected

patients), cardiovascular risk factor management, and digital health technologies provides unprecedented opportunity for cognitive preservation. However, critical knowledge gaps persist regarding AF burden thresholds, the relative contribution of competing pathophysiological mechanisms, optimal anticoagulation strategies in low-risk populations, and the long-term cognitive benefits of emerging digital technologies. Prospective randomized clinical trials with cognitive impairment as a primary endpoint, serial neuroimaging, and diverse population representation are urgently needed to validate preventive strategies and refine therapeutic decision-making.

Keywords: atrial fibrillation; cognitive impairment; dementia; silent cerebral infarction; cerebral hypoperfusion; cerebral microembolism; direct oral anticoagulants; catheter ablation; digital health; mHealth platforms; neuroprotection; heart-brain health

1. Introduction

1.1. Epidemiological Burden and Clinical Significance

Atrial fibrillation and dementia represent twin epidemics of an aging population. AF affects approximately 50–100 million individuals worldwide with prevalence projected to increase substantially in coming decades due to demographic shifts toward older populations. Similarly, dementia affects over 55 million people globally, with incidence doubling every 5 years after age 65. The intersection of these conditions presents a formidable public health challenge, yet the AF–dementia relationship remains understudied relative to well-established AF–stroke associations.

Traditionally, AF-related cognitive impairment has been attributed predominantly to cardioembolic stroke, which accounts for 20–30% of ischemic strokes in AF patients. However, compelling epidemiological evidence over the past decade has demonstrated that AF is independently associated with cognitive decline and dementia even in the absence of clinically recognized stroke. Large population-based cohort studies and meta-analyses consistently report that AF increases the relative risk of cognitive impairment and incident dementia by 1.4–2.2 fold, with the association persisting after adjustment for shared cardiovascular risk factors (hypertension, diabetes, heart failure, smoking, advanced age) and exclusion of patients with prior clinical stroke. The population-attributable risk for dementia resulting from AF is estimated at approximately 13%, suggesting that effective AF management and prevention strategies could meaningfully reduce population burden of dementia[1].

1.2. Limitations of Traditional Paradigm

The current clinical paradigm for AF management has focused almost exclusively on: (1) stroke risk stratification using tools such as the CHA₂2-VASc score, (2) anticoagulation initiation and optimization to reduce cardioembolic stroke, and (3) rhythm or rate control strategies to improve symptoms and prevent tachycardia-mediated cardiomyopathy. This stroke-centric approach, while appropriate and evidence-based, overlooks substantial subclinical brain injury and progressive cognitive deterioration occurring in many AF patients—particularly those considered "low-risk" by traditional stroke risk scores.

Recent neuroimaging and mechanistic studies have revealed that clinically recognized stroke represents "only the tip of the iceberg" of AF-induced brain ischemia. Silent cerebral infarcts (covert brain infarcts not accompanied by acute neurological symptoms) are detected on brain MRI in 25–40% of AF patients without prior clinical stroke—a prevalence substantially higher than the 1–5% annual clinical stroke rate. These silent infarcts are associated with measurable cognitive dysfunction and increased future dementia risk. Beyond overt infarction, AF is associated with chronic cerebral hypoperfusion, neuroinflammation, accelerated cerebral small vessel disease, and structural brain atrophy—all potentially reversible through targeted intervention if identified early[2].

1.3. Rationale for Comprehensive Review Approach

This complexity of multiple interacting pathophysiological mechanisms, combined with the heterogeneity of emerging therapeutic interventions and limited primary data specifically addressing cognitive endpoints, necessitates a comprehensive narrative review synthesizing evidence across epidemiology, mechanistic pathways, therapeutic domains, and digital health technologies. This integrative approach permits identification of complementary therapeutic strategies operating through distinct mechanisms, recognition of critical knowledge gaps, and delineation of urgent research priorities to advance the field.

2. Epidemiology of Atrial Fibrillation and Cognitive Impairment

2.1. Prevalence and Incidence of Af-Associated Cognitive Decline

Large population-based cohort studies have established that AF is independently associated with cognitive impairment across diverse populations. In the Framingham Heart Study, individuals with AF demonstrated significantly lower cognitive test scores and faster rates of cognitive decline compared to those without AF, with differences persisting after adjustment for age, education, cardiovascular risk factors, and prior stroke. Meta-analyses of observational studies consistently report that AF is associated with a 1.4–2.2 fold increased relative risk of incident dementia compared to individuals without AF, depending on the population studied, follow-up duration, and adjustment for confounders[3].

2.2. Independent Association with Dementia Risk

Epidemiological studies have consistently demonstrated that the AF–dementia association is **independent of shared cardiovascular risk factors**. Adjustment for hypertension, diabetes, heart failure, smoking, obesity, and advanced age attenuates but does not eliminate the association between AF and dementia, providing evidence for AF-specific mechanisms beyond shared etiology. This independence has been demonstrated across multiple cohorts using different dementia ascertainment methods (physician diagnosis, neuropsychological testing, neuroimaging criteria), supporting the specificity of the association[4].

3. Pathophysiological Mechanisms Linking Atrial Fibrillation to Cognitive Decline

3.1. Cerebral Microembolism and Silent Brain Infarcts

Epidemiology of Silent Infarction:

Subclinical embolic brain ischemia (covert brain infarcts, cerebral microinfarcts) is likely the predominant mechanism accounting for cognitive deterioration associated with AF. A meta-analysis of 11 studies including 5,317 AF patients and control subjects demonstrated that AF is associated with:

- **2.30-fold increased odds** of silent cerebral infarction on MRI (95% CI 1.44–3.68)
- **3.45-fold increased odds** of silent cerebral infarction on CT (95% CI 2.03–5.87)

The **prevalence of silent cerebral infarction** in AF patients is substantial:

- 40% on MRI
- 22% on CT

(The higher MRI detection rate reflects superior sensitivity for small infarcts compared to CT.)[5]

3.2. Chronic Cerebral Hypoperfusion

Hemodynamic Consequences of AF:

AF is associated with reduced cardiac output and cerebral blood flow. The irregular rate and loss of atrial contribution to ventricular filling compromise cardiac output, which may reduce cerebral perfusion—particularly in elderly patients with limited cerebrovascular autoregulation or concurrent cerebrovascular disease.

Quantitative Hemodynamic Evidence:

A landmark study using phase-contrast magnetic resonance imaging to measure blood flow velocity in the cervical arteries found striking differences between AF phenotypes / see Table 1:

Table 1. Differences between AF phenotypes.

Measurement	Persistent AF	Paroxysmal AF	No AF
Total cerebral blood flow (mL/min)	472.1	512.3	541.0
Brain tissue perfusion (mL/100 g/min)	46.4	50.9	52.8

These findings demonstrate that persistent AF results in **15–20% reduction in total cerebral blood flow** compared to sinus rhythm, with the greatest deficit in continuous arrhythmia [6].

3.3. Neuroinflammation and Systemic Inflammation

Inflammatory Profiles in AF and Dementia:

AF and Alzheimer's disease share strikingly similar inflammatory profiles, both characterized by elevated systemic markers of inflammation:

Proinflammatory mediators elevated in both conditions:

- Interleukin-1 (IL-1)
- Interleukin-8 (IL-8)
- Tumor necrosis factor-alpha (TNF-α)
- High-sensitivity C-reactive protein (hsCRP)
- Growth differentiation factor 15 (GDF-15)

The convergence of inflammatory profiles in AF and neurodegenerative disease suggests shared pathophysiological pathways linking cardiac arrhythmia to brain injury [7].

3.4. Brain Structural Changes and Atrophy

Comprehensive Neuroimaging Findings:

Multimodal neuroimaging studies have revealed that AF is associated with widespread structural brain alterations extending beyond focal vascular lesions. Analysis of 1,335 stroke-free individuals with AF and 2,683 matched controls using multimodal neuroimaging (structural MRI, diffusion tensor imaging, and free water imaging) revealed that AF patients exhibited:

1. **Reduced cortical thickness** in multiple brain regions
2. **Decreased gray matter volume** in cortical and subcortical structures
3. **Elevated extracellular free-water content** indicating neuroinflammation and neurodegeneration
4. **Widespread white matter abnormalities** consistent with small vessel pathology [8]

4. Therapeutic Strategies for Cognitive Protection in Atrial Fibrillation

4.1. Anticoagulation and Neuroprotection

4.1.1. Doacs Versus Warfarin: Evidence for Cognitive Benefit

Observational Evidence for Cognitive Benefit:

Multiple observational cohort studies and meta-analyses have found that oral anticoagulation is associated with **40–60% reduction in dementia risk** compared to no anticoagulation in AF patients. More specifically, **direct oral anticoagulants (DOACs)** appear to confer greater cognitive benefit than warfarin.

A meta-analysis synthesizing data from multiple observational studies found that DOACs (particularly apixaban and rivaroxaban) were associated with approximately **30% additional dementia risk reduction** compared to warfarin (RR 0.69) [9].

4.1.2. The Brain-Af Trial: Limitations of Anticoagulation in Low-Risk Af

The BRAIN-AF (Blinded Randomized Trial of Anticoagulation to Prevent Ischemic Stroke and Neurocognitive Impairment in Atrial Fibrillation) trial was a landmark study designed to address a critical clinical question: Does oral anticoagulation prevent cognitive decline in AF patients at low thromboembolic risk?

Study Population and Intervention:

- Participants: 1,235 of intended 1,424 individuals with AF but without prior stroke/TIA and low thromboembolic risk (CHADS₂-VASc score 0–1, excluding female sex)
- Intervention: Rivaroxaban 15 mg daily versus placebo
- Follow-up: Median 3.7 years (trial halted early for futility)

Primary Outcome Results:

The trial demonstrated a **negative primary outcome**:

- **Primary outcome:** Composite of cognitive decline (≥ 2 -point drop in Montreal Cognitive Assessment), stroke, or transient ischemic attack
 - Rivaroxaban: 7.0% annual event rate
 - Placebo: 6.4% annual event rate
 - Hazard ratio: 1.10 (95% CI 0.86–1.40, P = 0.46)[10]

4.2. *Rhythm Control and Hemodynamic Optimization*

Theoretical Advantages:

Restoration and maintenance of sinus rhythm offer potential cognitive benefits through multiple mechanisms:

1. **Improved cardiac output and cerebral perfusion:** Restoration of atrial contribution to ventricular filling and elimination of the irregular ventricular response improves cardiac output and cerebral blood flow
2. **Reduced microemboli:** Elimination or suppression of AF episodes reduces formation of atrial thrombi and microemboli
3. **Reduced neuroinflammation:** Restoration of sinus rhythm and resolution of atrial remodeling reduce systemic and brain inflammatory markers [11]

Catheter Ablation Evidence:

Multiple observational studies have examined the relationship between catheter ablation and cognitive outcomes. Population-based cohort studies from Korean and European registries found that AF patients who underwent successful catheter ablation had **52–69% reduction in incident dementia** compared to medically managed controls (HR 0.52–0.69) [12].

4.3. *Comprehensive Cardiovascular Risk Factor Management*

Multi-Domain Risk Factor Control:

Beyond anticoagulation and arrhythmia management, comprehensive control of modifiable cardiovascular risk factors contributes to cognitive protection, see Table 2.:

Table 2. Control of modifiable cardiovascular risk factors and cognitive protection.

Risk Factor	Target	Rationale
Blood pressure	<130/80 mmHg	Reduces stroke and cognitive decline risk
LDL cholesterol	<70 mg/dL (high-risk)	Neuroprotective effects
HbA1c	7–8% (individualized)	Intensive control associated with cognitive benefit
Smoking	Complete cessation	Critical for preventing vascular injury
Physical activity	≥ 150 min/week moderate aerobic	Promotes cerebral blood flow
Sleep apnea	Screen and treat (CPAP)	Bidirectionally associated with AF and cognitive decline

5. Digital Health Technologies in Atrial Fibrillation Management

5.1. *Remote Monitoring and Early Af Detection*

5.1.1. Wearable Technologies and Smartwatch Algorithms

Evolution of Wearable Technology:

Consumer-grade wearable devices (smartwatches, fitness trackers) with integrated photoplethysmography (PPG) or electrocardiographic (ECG) sensors have revolutionized AF detection capability. These devices enable:

- Continuous or frequent rhythm monitoring
- Detection of asymptomatic (silent) AF episodes
- Early intervention before symptom development or extensive silent infarct accumulation

Diagnostic Accuracy Data: (See Table 3)

Table 3. Diagnostic accuracy of wearable devices for AF detection.

Detection Method	Sensitivity	Specificity	PPV
PPG-based irregular rhythm	97–100%	—	84–98%
ECG-based smartwatch	90–95%	96–98%	—

Apple Heart Study (2019):

- Enrolled 419,297 participants
- Detected 2,161 (0.52%) participants with irregular pulse notification
- Among those who provided recordings, AF confirmed in 34%
- Demonstrated feasibility of population-scale AF screening via consumer wearables[13]

5.2. Mobile Health Platforms and the Abc Pathway

5.2.1. Abc Pathway Implementation

The "ABC pathway" (Anticoagulation, Better symptom management, Cardiovascular risk factor management) provides an evidence-based, multifactorial framework for comprehensive AF management. Digital mHealth platforms operationalize this pathway through:

A. Anticoagulation optimization:

- Medication reminders and adherence tracking
- INR monitoring in warfarin users
- Bleeding risk assessment and monitoring

B. Better symptom and AF management:

- Symptom tracking and severity assessment
- Rhythm monitoring data integration

C. Cardiovascular risk factor management:

- Blood pressure tracking with smart home devices
- Weight and physical activity monitoring
- Medication reminders[14]

5.2.2. Evidence for Effectiveness: Mafa-Ii Trial

The **mAFA-II randomized clinical trial** tested the ABC pathway implemented via a smartphone application in China.

Trial Design:

- Participants: Approximately 2,000 AF patients
- Intervention: Mobile app with ABC pathway components vs. standard care
- Primary outcome: Composite adverse events

Major Results:

- **61% reduction in composite adverse cardiovascular events**
- **Hazard ratio: 0.37** (95% CI approximately 0.27–0.50)
- Benefits driven by improved anticoagulation adherence, blood pressure control, and symptom management [15]

5.3. Medication Adherence Optimization

5.3.1. Adherence Challenges and Digital Interventions

Prevalence of non-adherence:

Despite evidence that oral anticoagulants reduce stroke and mortality in AF patients, medication adherence remains suboptimal:

- **Proportion of days covered (PDC) $\geq 80\%$ ("good adherence"):** Only 60–70% of AF patients on DOACs in routine practice
- **Mean adherence:** Approximately 77% across multiple real-world cohorts
- **Non-adherence consequences:** Associated with 39% increased hazard of ischemic stroke (HR 1.39, 95% CI 1.06–1.81) [16]

Strategies with Evidence:

1. **Prescription fill optimization:**
 - 90-day prescription fills vs. 30-day fills: 75% increased odds of good adherence at 12 months (OR 1.75, 95% CI 1.54–1.97)
2. **Smartphone app-based medication reminders:**
 - Structured reminders at medication times improve adherence
 - Integration with wearables enhances engagement
3. **Combined digital + human interventions:**
 - Blended electronic app reminders + phone-based counseling for nonadherence
 - Face-to-face digital literacy education superior to app-based approaches [17]

5.4. Artificial Intelligence and Machine Learning in Af

5.4.1. Ai-Enhanced Ecg Analysis

Deep Learning for ECG Interpretation:

Artificial intelligence algorithms trained on large ECG databases have achieved diagnostic accuracy exceeding individual cardiologists:

- **AF detection from sinus rhythm ECG:** AI algorithms can identify patients likely to develop future AF before any arrhythmia is manifest [18]
- **Interpretability challenges:** "Black box" nature of deep neural networks limits clinical understanding of decision factors

5.4.2. Virtual Assistants and Chatbot Technology

LOLATAO and Conversational AI for AF Management:

LOLATAO (a virtual assistant for non-valvular AF anticoagulation follow-up) demonstrates feasibility of chatbot-based patient engagement:

Capabilities:

- 24/7 patient support and education
- Medication reminders and adherence tracking
- Symptom assessment and triage
- Escalation to human healthcare provider when necessary

Outcomes:

- High adherence rates to follow-up recommendations
- Reduced clinical workload (decreased phone calls and routine emails)
- Feasible for implementation in resource-limited settings [19]

6. Clinical Practice Recommendations

6.1. Anticoagulation Strategy

1. **DOAC preferability:** In AF patients meeting anticoagulation criteria (CHA_{22} -VASc ≥ 2 men, ≥ 3 women), prefer DOACs (particularly apixaban, rivaroxaban) over warfarin when no contraindications exist, considering both stroke reduction and potential neuroprotection benefits.
2. **Low-risk population management:** In patients with very low stroke risk (CHA_{22} -VASc 0–1, excluding female sex), anticoagulation decision should incorporate:
 - Individual cognitive decline risk factors
 - Baseline cognitive status assessment
 - AF burden (if quantifiable via monitoring)
 - Bleeding risk
 - Patient preferences

3. **Adherence optimization:** Implement adherence-enhancing strategies:
 - 90-day prescription fills vs. 30-day
 - Smartphone app reminders
 - Face-to-face digital literacy education (most effective in elderly)

6.2. Arrhythmia Management Strategy

1. **Rate control as minimum standard:** All AF patients should achieve adequate rate control at rest (60–80 bpm) and with exertion, as poor rate control impairs cardiac output and cerebral perfusion.
2. **Rhythm control consideration:** In selected patients, rhythm control via antiarrhythmic drugs or catheter ablation should be considered not solely for symptom relief but for hemodynamic benefit and cognitive preservation:
 - Candidates: AF patients ≥65 years with significant cognitive impairment risk
 - Early rhythm control (within 3 months of AF diagnosis) preferred
3. **Shared decision-making:** Discuss with informed patients the potential cognitive benefits of rhythm control alongside symptomatic and hemodynamic benefits.

6.3. Comprehensive Cardiovascular Risk Factor Management

Implement multifactorial risk factor control targeting blood pressure (<130/80 mmHg), lipid management (LDL <70 mg/dL in high-risk patients), glycemic control, smoking cessation, sleep apnea treatment, weight management, and regular physical activity (≥150 minutes/week moderate aerobic activity).

6.4. Digital Health Technology Integration

1. **Wearable devices for AF detection:**
 - Offer wearable-based AF screening to at-risk populations
 - Never use wearable detection as sole diagnostic modality; positive findings require ECG/rhythm confirmation
 - Educate patients on algorithm limitations and need for clinical follow-up
2. **Mobile health ABC pathway implementation:**
 - Implement mHealth platforms incorporating anticoagulation, symptom management, and cardiovascular risk factor control
 - Choose user-friendly platforms with demonstrated adherence benefits
 - Provide technical support and digital literacy education, especially for elderly users
3. **Telemedicine for chronic AF follow-up:**
 - Implement remote anticoagulation management for suitable patients (especially DOAC users)
 - Video-based follow-up annually or biannually appropriate for stable AF patients

6.5. Cognitive Assessment and Monitoring

1. **Baseline cognitive screening:**
 - Consider brief cognitive screening (Montreal Cognitive Assessment, Mini-Cog, or equivalent) in AF patients, particularly those ≥75 years
2. **Serial cognitive evaluation:**
 - Integrate cognitive assessment into routine AF follow-up, with repeat evaluation annually or biannually in high-risk patients
3. **Neuroimaging consideration:**
 - Consider baseline brain MRI in AF patients with cognitive decline to identify silent infarction burden and small vessel disease markers

7. Critical Research Gaps and Priorities

7.1. Cognitive Endpoints in Af Trials

Gap: Most AF therapeutic trials lack cognitive assessment as formal endpoint.

Solution: Future AF trials should incorporate:

- Objective cognitive testing (neuropsychological battery)
- Serial testing to measure cognitive trajectory
- Neuroimaging biomarkers (MRI for silent infarction, white matter disease, atrophy)
- Long follow-up (5+ years) for dementia diagnosis
- Diverse population representation

7.2. *Af Burden and Cognitive Outcome Relationship*

Gap: The relationship between quantified AF burden and cognitive outcomes remains nearly entirely unexplored prospectively.

Research needed:

- Enrollment of AF patients with device-based AF burden quantification
- Baseline neuropsychological assessment and neuroimaging
- Prospective follow-up assessing whether AF burden predicts cognitive change
- Determination of potential threshold of AF burden at which cognitive decline risk increases substantially

7.3. *Mechanistic Clarification Studies*

Critical questions requiring dedicated research:

1. **Microembolism vs. hypoperfusion:** Design prospective studies measuring microembolic signal on transcranial Doppler during AF episodes and cerebral blood flow via advanced MRI sequences
2. **Inflammatory pathway specificity:** Mechanistic studies clarifying which inflammatory mediators drive brain injury in AF and development of selective inhibitors
3. **Blood-brain barrier dysfunction:** Imaging studies quantifying BBB integrity in AF patients (advanced MRI, PET) and correlation with cognitive impairment

7.4. *Biomarker-Driven Risk Stratification*

Gap: Clinical tools to identify AF patients at highest cognitive decline risk are lacking.

Solutions:

- Development and validation of cognitive decline risk prediction models
- Incorporation of clinical features, biomarkers (hsCRP, GDF-15, NfL, GFAP, phosphorylated tau), neuroimaging markers, and genetic factors
- Prospective validation in independent cohorts
- Development of stratified treatment strategies

7.5. *Digital Health Long-Term Effectiveness*

Gap: Limited long-term randomized trial data on digital health interventions specifically assessing cognitive outcomes.

Ongoing/needed trials:

- Long-term follow-up (≥5 years) studies assessing whether sustained digital health engagement prevents cognitive decline
- Health equity substudies ensuring technology benefits reach underrepresented populations
- Cost-effectiveness analyses

8. Conclusions and Future Directions

8.1. *Paradigm Shift: From Stroke Prevention to Heart–Brain Health*

This comprehensive review demonstrates that **atrial fibrillation is not merely a cardiac arrhythmia requiring stroke prevention, but a systemic condition with profound implications for brain health and cognitive function.** The evidence supports a fundamental **paradigm shift** in AF management from a stroke-centric focus to comprehensive **heart–brain health optimization.**

Key evidence supporting this paradigm shift:

1. **AF independently affects cognitive health** through multiple mechanisms beyond traditional cardioembolic stroke
2. **Therapeutic interventions** (anticoagulation, rhythm control, risk factor management) address distinct cognitive neuroprotection pathways
3. **Digital technologies** enable integrated monitoring of cardiac and cognitive health simultaneously
4. **Prevention strategies must begin early**, before extensive irreversible brain injury accumulates

8.2. *Clinical Synthesis and Therapeutic Integration*

The convergence of evidence across multiple therapeutic domains creates unprecedented opportunity for comprehensive patient management:

Pharmacological neuroprotection: DOACs, particularly apixaban and rivaroxaban, reduce dementia risk by ~30% through microembolism prevention, anti-inflammatory effects, and cerebral perfusion preservation (RR 0.69).

Hemodynamic optimization: Rhythm control strategies and catheter ablation demonstrate robust observational evidence for dementia risk reduction (HR 0.52–0.69) through restoration of cardiac output and cerebral perfusion.

Cardiovascular risk factor management: Comprehensive ABC pathway implementation addressing anticoagulation optimization, symptom management, and vascular risk factor control reduces adverse cardiovascular events by 61% (mAFA-II trial).

Digital health transformation: Telemedicine, mHealth platforms, wearable technologies, and artificial intelligence-enhanced analytics enable early AF detection, therapeutic adherence optimization, and comprehensive risk factor monitoring, extending access to care while reducing healthcare burden.

8.3. *Future Integrated Heart–brain Health Platforms*

The future of AF care lies in integrated platforms that simultaneously address cardiac and cognitive health:

Comprehensive system components:

- Continuous AF monitoring via wearable devices or implanted sensors
- Automated anticoagulation management with adherence tracking and INR/renal function monitoring
- Cardiovascular risk factor optimization (blood pressure, glucose, lipids, weight) via home monitoring devices
- Regular cognitive screening (validated brief instruments, voice-based AI analysis)
- Serial neuroimaging when appropriate (baseline and interval MRI assessing silent infarction burden, small vessel disease, brain atrophy)
- Coordinated care between cardiology and neurology specialists
- Early intervention protocols for detected cognitive decline

Such platforms could enable seamless prospective studies of cognitive trajectories and interventions, with remote data collection reducing participant burden and increasing long-term adherence.

8.4. *Conclusion*

Atrial fibrillation represents a multifaceted challenge to brain health requiring a comprehensive, integrated approach far more sophisticated than traditional stroke-focused management. The convergence of emerging pharmacological therapies (DOACs with neuroprotective properties), hemodynamic optimization strategies (rhythm and rate control), and transformative digital technologies (enabling early detection, therapeutic monitoring, and comprehensive risk factor management) creates unprecedented opportunity to preserve both cardiac and cognitive function.

However, realizing this potential requires:

- **Rigorous prospective research** to validate preventive strategies and establish causality

- **Mechanistic elucidation** of pathways linking AF to brain injury, enabling targeted therapies
- **Development of predictive biomarkers** to identify highest-risk patients
- **Intentional equity-focused strategies** ensuring benefits reach all populations
- **Clinician education** emphasizing cognitive health as core therapeutic goal alongside stroke prevention
- **Patient engagement** in shared decision-making regarding comprehensive heart–brain health strategies

By embracing comprehensive heart–brain health management, leveraging digital innovations, committing to rigorous scientific investigation, and prioritizing health equity, the medical community can meaningfully reduce the burden of AF-associated cognitive decline and dementia in the decades ahead.

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