Cognitive Impairment: Clues Lead to Early Detection

Minimally Invasive Atrial Fibrillation: New Option for the Elderly Patient

Emphasizing Rate Control in Managing Atrial Fibrillation in Older Adults

New Alternatives to Warfarin Emerge
Dear Colleagues:

Deciding where to send your patients who need comprehensive geriatric care can be difficult. Our goal in Cleveland Clinic's Center for Geriatric Medicine is to serve as a central resource for geriatric and gerontological clinical, educational and research activity throughout the Cleveland Clinic health system. Our center coordinates programs and advises and assists clinicians throughout our system of more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), and eight hospitals. We are eager to assist and educate physicians, nurses, therapists, social workers, other clinical health providers and caregivers in improving the care of the oldest and frailest members of society.

In this issue, we add to previous Geriatric Times coverage of the subtleties and diagnosis of memory disorders in older adults. As discussed in previous issues, Cleveland Clinic Lou Ruvo Center for Brain Health — led by Jeffrey Cummings, MD, and staffed by excellent physicians such as Babak Tousi, MD; Jagan Pallai, MD; and Ryan Walsh, MD — provides important services to diagnose mild cognitive impairment (MCI). Geriatric services complement those of the Lou Ruvo Center for Brain Health. Geriatricians also may diagnose MCI, then work with the patient and primary care physician to optimize the pharmacological and nonpharmacological interventions to maintain the highest level of brain health possible. Educating the caregiver and addressing caregiver needs are crucial, since without support in the community, there is often a rapid decline in the patient and a need for nursing home placement.

We work closely with our colleagues in the Sydell and Arnold Miller Family Heart & Vascular Institute to optimize management of atrial fibrillation, the most common arrhythmia in the older population. There are new options for anti-coagulation to prevent stroke and newer drugs emerging as well. These are discussed by John Bartholomew, MD, Head of the Section of Vascular Medicine in the Department of Thoracic and Cardiovascular Medicine. Rhythm control is appropriate for some older adults, and Thomas Dresing, MD, reviews the pros and cons of current pharmacological therapies. Finally, Edward Soltesz, MD, MPH, of the Department of Thoracic and Cardiovascular Surgery, compares the totally thoracoscopic Maze procedure with catheter-based ablation in light of the needs of the oldest patients.

These articles represent a small sample of the work we do every day to help make a real difference in the quality of our patients’ lives.

Over the past few years, Cleveland Clinic has expanded its inpatient, outpatient and post-acute-care programs. With growth comes opportunity for recruiting geriatricians with an interest in patient care, education and program development. Feel free to contact me and/or to peruse our website for more information: clevelandclinic.org/geriatricmedicine.

We look forward to continuing our partnership with you. Please don’t hesitate to contact me with any questions, concerns or suggestions on how we might improve our services to you and your patients in the future, at 216.444.6801 or rapporb@ccf.org.

Kind regards,

Barbara Messinger-Rapport, MD, PhD
Director, Center for Geriatric Medicine
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Cognitive impairment describes difficulties in one or more areas of cognition, including memory, language, recognition of familiar objects, fine motor skills, complex decision-making and judgment. Mild cognitive impairment (MCI) and dementia are clinical diagnoses that require a change in baseline cognitive abilities. With MCI there is a noticeable and measurable decline in cognition, but the changes are not severe enough to affect activities of daily living. In dementia, a patient’s cognitive decline must interfere with his or her ability to function in daily life.

With the aging of the United States population and increasing prevalence of Alzheimer disease and other forms of dementia, primary care physicians will need to be vigilant for the presence of cognitive impairment in their patients. In 2003, the United States Preventive Services Task Force reported that there was insufficient evidence to recommend for or against routine screening for dementia in primary care. However, it did acknowledge the benefits of early detection and suggested that clinicians should be attentive to clues.

Medication Noncompliance
When medication noncompliance is suspected, it is helpful to ask the patient to bring all medication bottles to the visit. Reviewing dates that the prescriptions were filled and ascertaining the number of pills remaining can help provide clues to compliance. It is useful to have the patients describe how they take their medicines and to test their knowledge of the medication regimen. Family members or caregivers can often provide useful history regarding compliance. When collateral history is not available and the patient is homebound, a home health care referral for a skilled nursing assessment of medication use can help provide useful information regarding patients’ memory, compliance and ability to manage their medicines independently.

Collateral History
Patients often lack insight into changes in their cognitive and functional abilities. Being aware of potential signs of cognitive impairment and also obtaining collateral histories from family members, friends and caregivers can help physicians diagnose MCI and dementia and direct the patient to appropriate resources for assistance.

Family members and/or caregivers should be asked to come to office visits, or contacted by phone if this is not feasible, when cognitive impairment is suspected. Social workers can also be helpful in contacting caregivers to obtain and clarify social and functional histories. The collateral historians should be questioned about forgetfulness, repetition of stories or questions, frequent misplacement of objects, difficulty with word finding and remembering names, and difficulty with time orientation. Changes in activities of daily living should also be assessed, such as difficulty with finances, medication management, meal preparation, transportation and upkeep of household, as well as difficulty with basic hygiene.
Risk Factor Assessment

The lifestyle factors and chronic medical conditions that increase risk for heart disease and stroke (smoking, heavy alcohol use, obesity, lack of exercise, diabetes, hypertension and hyperlipidemia) also are risk factors for dementia, particularly vascular dementia and Alzheimer disease. Patients with a history of prior strokes or traumatic brain injury often later develop cognitive impairment. Impaired cognition is often seen in patients with heart failure and sleep apnea. Repeated episodes of brain hypoxia due to hypoperfusion and respiratory pauses can impair cognitive functioning and lead to deficits in executive function. This often presents as difficulty with complicated tasks, including managing finances and medicines, following lifestyle change recommendations (sodium and fluid restrictions, weight monitoring), and driving.

It is useful to consider the possibility of cognitive impairment in patients with multiple risks factors or with predisposing conditions in order to recognize problems early and to help them utilize assistance from family and community resources.

Cognitive Testing

The Patient Protection and Affordable Care Act of 2010 created the annual wellness visit (AWV) for Medicare beneficiaries. An assessment to detect cognitive impairment is a required component of the AWV. However, the Centers for Medicare & Medicaid Services did not recommend any specific assessment tool due to the absence of a universally accepted screen.

As a result, the Alzheimer’s Association recently published an algorithm for detection of cognitive impairment during the AWV (clevelandclinic.org/alzalgorithm). It recommended three screening tools (General Practitioner Assessment of Cognitive Impairment continued

When cognitive impairment is suspected, evaluation and management can include:

- History regarding cognitive changes from patient and family/caregiver
- Functional assessment
- Medication assessment
- Risk factor assessment
- Brief cognitive testing (repeated every six months to one year to monitor for decline)
- Lab work to rule out contributing factors to cognitive impairment (B12, thyroid function, CMP, CBC, screen for syphilis only if risk factors present or prior STIs)
- Head imaging if not previously available, to rule out structural causes
- Assessment for caregiver burden
- Referral to geriatric medicine for further evaluation, management, counseling, use of community resources (Alzheimer’s Association, adult day care, home care) and follow-up
- Referral to social work for additional assistance with obtaining collateral history and directing to community resources
- Referral to home health care for skilled nursing and/or behavioral nurse assessment if patient is homebound
Cognition, Mini-Cog and Memory Impairment Screen) for routine use in primary care due to their ease of administration, validation in primary care settings, and limited educational, language and/or cultural bias. These tools also can be used by clinicians without payment of fees to copyright holders.

The AD8 is another useful tool that allows caregivers to assess patients and can be completed prior to the visit. The Folstein Mini-Mental Status Exam has been validated in multiple settings, but copyright enforcement requires a fee for each use. Alternative tools such as the Montreal Cognitive Assessment and the Saint Louis University Mental Status Examination are highly sensitive for detecting cognitive impairment; however, they often require more time to administer.

Annual use of a cognitive assessment tool during the AWV can recognize cognitive decline. Abnormal screening test results signal the need for a full dementia evaluation, which can be completed in the primary care setting or through referral to geriatric medicine and/or other specialists. Benefits of geriatric medicine consultation include assistance with diagnosis, treatment and long-term follow-up; access to community resources; management of caregiver burden; and patient and family counseling.

Caregiver Burden
Caring for older adults with cognitive impairment frequently places significant strain (physical, psychological, social and financial) on the caregivers. Early recognition of cognitive impairment can allow practitioners to identify and address caregiver burden. Multiple community resources, such as the Alzheimer’s Association, adult day care, home health agencies and extended care facilities, can help lessen the burden on caregivers.

Mrs. Elinor Dunlop (see case study on page 6) exemplifies the importance of early recognition of cognitive impairment. A series of mishaps made everyone realize that she could no longer manage without straining the emotional resources of her family. With everyone’s encouragement, she moved into assisted living. Although there are ups and downs of congregate living, the overall effect has been a stabilization of her health and a relief in caregiver strain.

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Twelve years ago, Elinor Dunlop was an 80-year-old first-time patient at Cleveland Clinic's Center for Geriatric Medicine. Arthritic knees, insomnia and minor imbalance were her main concerns. But those issues weren’t stopping her from playing bridge, going to lunch and staying active in her Shaker Heights, Ohio, social circles. However, over the next few years, Mrs. Dunlop’s daughter, Alison Pignolet, started noticing little lapses.

“Paying bills started becoming a struggle for Mom,” says Ms. Pignolet. “She complained of feeling dizzy when she’d sit down to work on them. Or her carpal tunnel syndrome would act up. When she started missing payments altogether, I took over.”

That’s when geriatrician Barbara Messinger-Rapport, MD, PhD, ordered tests of Mrs. Dunlop’s cognition. “She was so sharp that she did well on every test we gave her,” says Dr. Messinger-Rapport. “Although screenings demonstrated no deficits, we suspected she had mild cognitive impairment and decided to continue monitoring her while encouraging her to ‘let’ her daughter help with the bills and other things.”

Mrs. Dunlop continued to manage independently with frequent help from Ms. Pignolet and her brother. They would drive her to appointments. But then planning transportation started to cause Mrs. Dunlop undue stress and confusion.

“As her skills started to go away, we’d worry about her more,” says Ms. Pignolet. “She started forgetting to hang up the phone. We’d call her, and the phone would ring and ring. I’d have to call a neighbor to check on her.”

After a series of medical mishaps, including a serious fall and an infected wound, Mrs. Dunlop’s family realized that she could no longer be without continuous care. An assisted-living apartment just minutes from her daughter was the perfect fit.

Although Mrs. Dunlop has transitioned well into assisted living, learning new names and routines in a new environment hasn’t been easy. Ms. Pignolet advises others to make the transition before cognitive impairment progresses.

“It’s a real relief to have Mom there, where they manage her medication, prepare her meals, handle housekeeping, do her laundry,” says Ms. Pignolet. “But she can still putter around in the privacy of her own apartment.”

According to Dr. Messinger-Rapport, although there are ups and downs of congregate living, the overall effect has been a stabilization of Mrs. Dunlop’s health and a relief of caregiver strain. “I agree with Ms. Pignolet; many of my patients would benefit from moving earlier rather than later, but it is hard to convince them.”

“We don’t have to worry about her so much,” says Ms. Pignolet. “Someone there is always keeping an eye on her. Now if I call and she doesn’t answer, I don’t have to bother the neighbor.”

Mrs. Dunlop, now age 92, continues to enjoy life on her terms — including season tickets to The Cleveland Orchestra and weekly music study classes. ■
Cleveland Clinic’s Connected Care program is an innovative model of care designed to improve outcomes and experience for patients transitioning from the hospital to a skilled nursing facility (SNF). Each year, Cleveland Clinic discharges more than 20,000 patients to nearly 900 SNFs. Many of these patients are older adults who are at risk for poor outcomes, rehospitalization and fragmented transitions of care. The Connected Care program offers an integrated approach in which patients can remain “connected” to the Cleveland Clinic care teams after their hospitalization.

Each Connected Care virtual unit consists of 20 to 30 beds at a community SNF that is staffed by a Cleveland Clinic physician and an advance practice nurse (APN) or physician assistant (PA). Cleveland Clinic’s Center for Post-Acute Care and Center for Geriatric Medicine have partnered to develop the program. Additional partners include palliative care for post-acute consultations when needed, and the Cleveland Clinic at Home program for skilled care and for physician visits when requested.

Key components of the Connected Care program include: medical documentation that is maintained in Cleveland Clinic’s electronic medical record and accessible to the entire care team and utilization of disease-specific care paths to guide care at the SNF.

The Connected Care program’s outcomes are measured by results rather than visit volume. Quality metrics include:

- Patient satisfaction
- Disease management targets
- Faster return to premorbid level of function
- Shorter SNF stay
- Lower readmission rates

Eight Connected Care programs, geographically distributed across Northeast Ohio, have been developed, with plans to expand to six to eight additional sites in the future.

For more information, visit clevelandclinic.org/connectedcare.
Atrial fibrillation (AF) is the most common cardiac arrhythmia and affects more than 2.3 million people in the United States. The incidence of AF increases significantly with age. AF affects 1 percent of patients younger than 60 years and 8 percent of patients older than 80 years. The Anti-coagulation and Risk Factors in Atrial Fibrillation (ATRIA) study estimated that by 2050 there would be nearly 3 million Americans over age 80 with AF, illustrating the increasing need for effective treatment that is well-tolerated in this patient group.

AF is a source of significant morbidity and mortality because it impairs cardiac function and increases the risk of stroke. AF is an independent risk factor for death and confers a 50 to 90 percent increase in mortality. Additionally, AF is a major cause of stroke and accounts for 15 percent of all strokes in the United States. Unfortunately, many elderly patients with AF are the same patients who are at a high risk for falls and bleeding, thus making anti-coagulation, the mainstay of treatment for AF, particularly challenging.

AF is a progressive disease, and patients with paroxysmal AF often progress to permanent AF. A retrospective cohort study found that 1 in 5 patients with intermittent AF progressed to permanent AF within four years. There is increasing evidence to suggest that AF produces changes in atrial structure and function that promote initiation and maintenance of AF. In fact, electrical remodeling develops within days and contributes to the stability of AF. In order to reverse the electrical remodeling and restore electrical refractoriness and normal sinus rhythm, cardioversion should be performed as early as possible after AF onset. The electrophysiological changes may become irreversible if AF continues for prolonged periods.

The main focus of AF management is symptom alleviation and stroke prevention. Rate control coupled with anti-coagulation reduces risk for stroke substantially. However, some patients require restoration of sinus rhythm to function well. Although AF is typically first treated with anti-arrhythmic medications, long-term control of AF with medicines alone is successful in only about 50 percent of patients. Additionally, drug therapy for AF is fraught with the potential for adverse reactions, ranging from the relatively minor (fatigue, malaise, nausea, etc.) to the life-threatening (ventricular arrhythmias).

Surgical and Catheter-based Options

Surgical or catheter-based ablation is typically attempted when two or more drugs have failed to control a patient's AF. Ablation has been shown to be more effective than drug therapy alone.

The benchmark for all anti-arrhythmia procedures is the Cox-Maze III operation. Originally performed through a full sternotomy on an open, arrested heart, the operation successfully relieved 96 percent of patients of anti-arrhythmia therapy. Subsequent studies have identified the central reason for the high success rate of the original Cox-Maze procedure: the isolation of the arrhythmogenic areas of the atria responsible for AF into electrically discrete compartments. The original Cox-Maze operation created these compartments through actual incisions in the atria that were subsequently sutured closed. Later procedures modeled after the Cox-Maze were designed to spare the patient the trauma of an open-chest procedure.

Catheter-based procedures using various ablation energy sources and mapping systems are being routinely performed to achieve rhythm control in patients with AF. As experience grows with these procedures, the success rates are slowly improving. The efficacy of a single radiofrequency (RF) catheter-based ablation is 60 to 80 percent for paroxysmal AF and 40 to 60 percent for persistent AF. Second catheter-based RF ablations are sometimes necessary. At Cleveland Clinic, the success rate for a single catheter-based RF ablation is 77 percent for paroxysmal AF and 92 percent after a repeat procedure; for persistent AF, success rates are 76 percent after the first procedure and 90 percent after the second. For long-standing, persistent AF (i.e., AF lasting more than a year), success was achieved in 80 percent of patients after two procedures.

Surgery for AF has changed radically over the past decade with the advent of new technology. Concomitant Maze
procedures can be performed with no increased risk to patients undergoing other open-heart surgeries such as valve replacements and repairs or coronary bypass operations. The past few years have also seen a rapid development in minimally invasive surgical techniques for those patients who have AF and do not need other heart surgery. The totally thoracoscopic Maze procedure is a closed-chest, beating-heart, truly minimally invasive procedure that replicates the original Cox-Maze procedure. Four half-inch incisions are made in each side of the chest, and a 5-mm thoracoscope guides bilateral pulmonary vein isolation and connecting lesions along with autonomic testing and ablation. This technology enhances both the safety and precision of every maneuver. No computer-enhanced imaging is necessary because all treated regions of the heart are seen in great detail with the thoracoscope.

How to Choose?

Another significant advantage of surgical ablation is the ability to gain control of the left atrial appendage (LAA), the most common site of intracardiac thrombus formation in patients with AF. The totally thoracoscopic Maze procedure makes use of the AtriClip™ Gillinov-Cosgrove LAA Exclusion System, a low-profile atraumatic device invented at Cleveland Clinic that anatomically and electrically isolates the LAA. Typically, patients undergoing the totally thoracoscopic Maze procedure are hospitalized for three days and maintained on warfarin until documentation of sinus rhythm at their four-week follow-up. If patients achieve rhythm control after a Maze with LAA occlusion, anti-coagulation can typically be stopped after six to eight weeks.

Deciding between surgical and catheter-based ablation can be challenging. Patients with refractory AF should be evaluated by both a cardiothoracic surgeon and an electrophysiologist. Patients with severe chronic lung disease and patients who had previous heart surgery are not good candidates for the totally thoracoscopic Maze procedure. On the other hand, patients who are at a high risk of stroke from AF and a high risk of bleeding from anti-coagulation are excellent candidates for minimally invasive Maze procedure with LAA occlusion. The duration of AF should also guide the ablation strategy because patients with long-standing persistent AF have better success rates with surgical ablation than with catheter-based ablation.

Our understanding of the management of AF is evolving. Newer minimally invasive surgical techniques with excellent success rates are available for patients who have failed medical therapy. These new techniques are also able to exclude the LAA and thereby reduce the risk of thromboembolism and stroke, obviating the need for lifelong anti-coagulation. These new treatment modalities may improve quality of life and reduce the risk of bleeding and stroke, particularly in the elderly population.

For references, please contact the author.

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Two such clinical trials are the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) and the Rate Control Versus Elective Cardioversion (RACE) for atrial fibrillation. Clinical outcomes, including death, stroke and heart failure, were not significantly different between the two strategies, and there were fewer hospitalizations in the rate-control group.

These studies suggest that for most older patients, control of the ventricular response rate together with anticoagulation, compared with aggressive attempts to maintain sinus rhythm, is an acceptable strategy, reducing the risk of stroke without compromising safety or quality of life.

Reaching the Rate Control Goal — Potential Therapies and Risks to Consider

The goal of rate control is a physiologic heart rate not higher than 80 bpm at rest and not higher than 110 bpm during light activity. The most commonly used drugs to achieve rate control are those that block the atrioventricular (AV) node (i.e., beta blockers, calcium channel blockers and digoxin).

Physicians have shied away from beta blockade, even cardioselective beta blockers, in older adults due to medical or cognitive concerns. However, used at doses currently recommended by the U.S. Food and Drug Administration (FDA), there is no evidence that beta blockers adversely affect cognition. For older adults with chronic obstructive lung disease, retrospective cohort analyses suggest that beta blockade is associated with decreased mortality in a magnitude comparable to that of statins.

Calcium channel blockers may be more effective in lowering blood pressure than are beta blockers in older adults, so if that is also a goal, this class of drug may be more useful.

Digoxin is considered a potentially inappropriate medication in older adults. Even at lower doses, frail elders may experience weight loss, confusion, delusions and hallucinations, which resolve when the drug is discontinued. Cardioselective beta blockers in doses approved by the FDA have the fewest adverse effects in older adults and are the agents most likely to achieve the target heart rate.

Amiodarone, a Class III anti-arrhythmic that may be prescribed either for rhythm control or as a third- or fourth-line agent for rate control, has a constellation of potential adverse effects. Amiodarone in all doses is listed as a potentially inappropriate drug for older adults. Its newer cousin, dronedarone, may have less end-organ toxicity than amiodarone, although there is a concern for liver toxicity, and it may be less effective in maintaining sinus rhythm.

Another Class III anti-arrhythmic, dofetilide, is available only to prescribers, hospitals and retail pharmacies that have participated in a required educational program regarding effects and drug interactions.

The Class IC drugs, which include flecainide, encainide and propafenone, may be safer drugs to use in older adults without structural heart disease for whom rhythm control is desired. Sotalol has Class II, Class III and nonselective beta blocker anti-arrhythmic properties. Because sotalol has significant beta-blocker activity, initiation of this drug calls for assessment of the patient’s other medications, particularly the AV nodal blocking agents and anti-hypertensives, as these may need to be reduced or eliminated.
In summary, most older adults with AF can be managed with an anti-thrombotic drug such as warfarin to reduce the risk of stroke and a low-dose cardioselective beta blocker for rate control. Those requiring additional drugs for rate control may need a calcium channel blocker and/or digoxin in addition to the beta blocker. Select individuals may need an anti-arrhythmic for functional and/or quality-of-life reasons. Sotalol may have the best profile for the older adult with structural heart disease who requires an anti-arrhythmic drug. For the older adult without structural heart disease, sotalol or a Class I agent such as extended release propafenone or flecainide can be used. Select individuals may need an anti-arrhythmic for functional and/or quality-of-life reasons. Sotalol may have the best profile for the older adult with structural heart disease who requires an anti-arrhythmic drug. For the older adult without structural heart disease, sotalol or a Class I agent such as extended release propafenone or flecainide can be used.

Long-term amiodarone and dronedarone should be used only cautiously for rhythm or rate control, at the lowest possible dose, with close monitoring for adverse effects, particularly central nervous system effects. Dofetilide may be reserved for older patients who require rhythm control but are refractory to other anti-arrhythmics, and for older patients who are otherwise healthy whose disease management needs do not place them at risk for drug interactions or QT prolongation. Careful explanation of the pro-arrhythmic risks and regular reassessment to monitor for heart failure or other structural changes are suggested.

**Preventing Thromboembolic Events**

Because thromboembolism is the most serious consequence of AF, the most important component of either strategy appears to be therapeutic anti-coagulation. When warfarin anti-coagulation is selected, the target international normalized ratio (INR) is 2.0 to 3.0. An INR less than 2.0 is ineffective at reducing thrombotic risk while an excessive INR exposes the patient to a significantly increased risk of bleeding, which may be fatal. Fixed-dose alternatives to warfarin — factor Xa inhibitors and direct thrombin inhibitors — that do not require monitoring have recently become available. Unlike warfarin, these agents have few known drug-drug interactions and no known interactions with food. The ease of use of these agents may therefore enhance compliance with anticoagulation, although the clinical trial experience with them in the older population is less than it is in their younger counterparts.

Ablation of the AV node to interrupt the normal AV conduction system along with implantation of a ventricular pacemaker is another option for rate control, with the attendant risks of an invasive procedure. The success rate of AV nodal ablation is very high, whereas the success rate for ablation of AF declines with age. Ideal candidates for AF ablation are patients younger than 70 years with paroxysmal AF and no other cardiac abnormalities.

**The Role of Pacing**

Pacing does not act on the AF itself; rather, a pacemaker sends electrical impulses to the heart to enable maintenance of a regular heartbeat. In patients who undergo an ablation procedure or are taking medicines to slow the heart rate, a pacemaker can respond to an abnormally slow heart rate by stimulating the heart to increase the rate. With either a rate control or a rhythm control strategy, pacing may be required eventually. In the AFFIRM trial, patients randomized to the rhythm control strategy were more likely to require pacing over a mean follow-up of 3.5 years.

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New Alternatives to Warfarin Emerge

By John R. Bartholomew, MD, and Barbara Messinger-Rapport, MD, PhD

Anti-coagulation is an important component of the management of atrial fibrillation (AF) for both rate and rhythm control strategies. For more than 50 years, vitamin K antagonists were the only available oral anti-coagulants in the United States that were indicated for the prevention of thromboembolic complications associated with AF. When well managed, warfarin, the most commonly prescribed vitamin K antagonist, is an effective anti-coagulant.

However, warfarin is challenging to administer: it has a slow onset of action, large dosing differences, a narrow therapeutic index, and extensive drug-drug and drug-food interactions. Warfarin users outside of trials remain in therapeutic range only 50 to 60 percent of the time. In addition, warfarin is the drug most often responsible for emergency room visits. Skin necrosis is a rare but serious complication of warfarin.

The recent approval of oral direct thrombin inhibitors and factor Xa inhibitors heralds a new era in anti-coagulation. Thus far, one direct thrombin inhibitor, dabigatran etexilate, and two factor Xa inhibitors, rivaroxaban and apixaban, have been approved by the Food and Drug Administration (FDA).

The new anti-coagulants offer the potential to improve outcomes and quality of life for patients who require anti-coagulant therapy. Their advantages include a fixed dose with a predictable response, a short half-life, a wide therapeutic window, no clear interactions with food, few drug interactions, no requirement for monitoring and no need for bridging with invasive procedures. The availability of the new agents may allow for greater use of anti-coagulants, an important consideration given that data suggest that many patients with AF are undertreated.

Dabigatran

Dabigatran is a direct thrombin inhibitor that reaches peak plasma levels one and one-half to three hours after administration. Its half-life is 12 to 17 hours, and 80 percent of absorbed dabigatran is cleared renally. It is administered at doses of 150 mg twice daily. Use of rifampin should be avoided with dabigatran. When converting from warfarin to dabigatran, start dabigatran when the international normalized ratio (INR) is < 2 to avoid periods of inadequate anti-coagulation.

Many older adults have impaired renal function. The FDA recommends that if creatinine clearance (CrCl) is 15-30 mL/min, the dabigatran dose should be reduced to 75 mg twice daily. If the patient is receiving dronedarone or oral ketoconazole and CrCl is 30-50 mL/min, the dose may be reduced to 75 mg twice daily.

Dabigatran is not recommended in the U.S. for patients with severe renal impairment (CrCl < 30 mL/min). For adults over 80 years of age, the FDA recommends “extreme caution” due to post-marketing reports of hemorrhage, including hemorrhagic stroke. This drug is also contraindicated in patients of all ages with mechanical prosthetic heart valves due to an increased risk of stroke, myocardial infarction and mechanical valve thrombosis compared with patients taking warfarin. Dabigatran use with bioprosthetic valves has not been evaluated. There is no specific antidote to reverse anti-coagulation, and this drug is only partially dialyzable. If serious bleeding develops, the manufacturer suggests that recombinant factor VIIa may be considered.

Rivaroxaban

Rivaroxaban is a synthetic direct factor Xa inhibitor with once-daily dosing that reaches peak plasma levels within three hours. In the elderly, its half-life is prolonged to 11 to 13 hours. Rivaroxaban is cleared by the kidneys and the liver.

For patients taking rivaroxaban for the treatment of AF, the recommended dosage is 20 mg once daily with an evening meal if CrCl is > 50 mL/min, and 15 mg once daily with an evening meal if CrCl is 15 to 50 mL/min. It is not to be used if the CrCl is < 15 mL/min or in the presence of moderate to severe hepatic impairment. When transitioning from warfarin to rivaroxaban, start rivaroxaban as soon as the INR is < 3. There is no specific antidote to reverse anti-coagulation, and this drug is not dialyzable.
There is limited evidence that prothrombin complex concentrates may be helpful if there is serious bleeding.

**Apixaban**

Apixaban, like rivaroxaban, is a direct factor Xa inhibitor. Peak plasma levels with apixaban are achieved after three hours following administration; the half-life is nine to 14 hours. Primary excretion appears to be fecal; only about 25 percent is cleared by the kidneys.

The usual dose in AF is 5 mg twice daily unless the patient has any two of the following: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL; in that case reduce the dose to 2.5 mg twice daily. Use in severe hepatic impairment is not recommended. There is no need to dose with meals. The drug is not dialyzable.

**Candidates for the New Anti-coagulants**

The new anti-coagulants are attractive alternatives to warfarin for patients whose INRs are not well-controlled or who are having complications or other difficulties with warfarin, including those who seek convenience, as no monitoring is required with the new agents. However, all the new anti-coagulants lack specific reversal agents or antidotes in cases of overdose, bleeding or need for emergency surgery. Studies evaluating these drugs have excluded patients with renal impairment or hepatic insufficiency. Although dabigatran is the only drug among these new anti-coagulants with a warning for patients with mechanical heart valves, it is also the only one that has been compared with warfarin in a clinical trial. Also, although dabigatran is the only drug among the newer anti-coagulants with a labeling of “extreme caution” for patients over 80 years of age, none of these drugs have had extensive post-marketing experience in patients 80 years and over. Cost is also a major issue in prescribing the new anti-coagulants because they are more expensive than warfarin.

Selecting older candidates for anti-coagulation therapy to reduce the risk of stroke in AF is difficult. Approximately 30 percent of adults 65 years and over fall annually, as do about half of older adults living in nursing facilities. Although any anti-thrombotic or anti-coagulant drug can result in life-threatening bleeding if the patient sustains an injury, the inability to reverse the agent makes bleeds particularly more difficult to manage. On the other hand, strokes caused by AF may cause severe functional impairment and even death, and it is difficult for many to attain a therapeutic INR. The use of the new anti-coagulants will go far toward the reduction of strokes in this population.

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The availability of the new agents may allow for greater use of anti-coagulants, an important consideration given that data suggest that many patients with AF are undertreated.

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- Geriatric Psychiatry
  - John Sanitato, MD

**Independence Family Health Center**
- Ronan Factora, MD

**Lakewood Hospital/Utheran Hospital**
- Geriatrics
  - Babak Tousi, MD
  - Christine Nelson, MSN, CNP
- Geriatric Psychiatry
  - Mark Frankel, MD
  - John Sanitato, MD

**Lorain Institute**
- Lynn “Chris” Chismer, MD
- Itri Eren, MD
- Rebecca Haney, CNP
- Kashif Khan, MD
- Ali Mirza, MD
- Sathya Reddy, MD
- Pragati Singh, MD
- Renee Smith, CNP
- Alisha Steward, CNP
- Wanda Williams, CNP

**Willoughby Hills Family Health Center**
- Ami Hall, DO

**Joint Appointment with the Center for Geriatric Medicine**
- TAUSIG Cancer Institute
  - Mellar Davis, MD
  - Mona Gupta, MD
  - Terence Gutgsell, MD
  - Abdou Haddad, MD
  - Susan LeGrand, MD
  - Armida Parala-Metz, MD
  - Dale Shepard, MD, PhD

**Digestive Disease Institute**
- Brooke Gurland, MD
- Tracy Hull, MD
- Matthew Kalady, MD
- Jamilee Wakim-Fleming, MD

**Emergency Services Institute**
- Fredric Hustey, MD

**Endocrinology & Metabolism Institute**
- Angelo Licata, MD, PhD

**Head & Neck Institute**
- Catherine Henry, MD

**Sydell and Arnold Miller Family Heart & Vascular Institute**
- Karen James, MD
- Michael Maier, DPM

**Neurological Institute**
- Charles Bae, MD
- Karen Broer, PhD
- Neil Cherven, MD
- Kathy Cofman, MD
- Kathy Franco, MD
- Richard Lederman, MD, PhD
- Mark Luciano, MD, PhD
- Richard Naugle, PhD
- Leo Pozuelo, MD
- Babak Tousi, MD

**Brain Tumor and Neuro-Oncology**
- Gene Barnett, MD
- Glen Stevens, DO, PhD

**Physical Medicine and Rehabilitation**
- Frederick Frost, MD
- Vernon Lin, MD, PhD

**Center for Connected Care**
- Michael Felver, MD
- Carol Hall, CNP
- Ethel Smith, MD
- Renato Ramon Samala, MD
- Maidana Vaccia, MD
- William Zafirau, MD

**OB/GYN & Women's Health Institute**
- Matthew Barber, MD
- Marie Fidela Paraiso, MD
- Beri Ridgeway, MD

**Orthopaedic & Rheumatologic Institute**
- Abby Abelson, MD
- Wael Barsoum, MD
- Chad Deal, MD
- Elaine Husni, MD
- Bruce Long, MD

**Glickman Urological & Kidney Institute**
- Raymond Rackley, MD
- Sandip Vasavada, MD

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*All physicians with appointments in Regional Geriatrics have a joint appointment in the Center for Geriatric Medicine.*
Resources for Physicians

Referring Physician Center and Hotline
Cleveland Clinic’s Referring Physician Center has established a 24/7 hotline — 855.REFER.123 (855.733.3712) — to streamline access to our array of medical services. Contact the Referring Physician Hotline for information on our clinical specialties and services, to schedule and confirm patient appointments, for assistance in resolving service-related issues, and to connect with Cleveland Clinic specialists.

Track Your Patient’s Care Online
DrConnect is a secure online service providing our physician colleagues with real-time information about the treatment their patients receive at Cleveland Clinic. To receive your next patient report electronically, establish a DrConnect account at clevelandclinic.org/drconnect.

Physician Directory
View all Cleveland Clinic staff online at clevelandclinic.org/staff.

Critical Care Transport Worldwide
Cleveland Clinic’s critical care transport teams and fleet of vehicles are available to serve patients across the globe.
- To arrange for a critical care transfer, please call 216.448.7000 or toll-free 866.547.1467 (see also clevelandclinic.org/criticalcaretransport).
- For STEMI (ST elevated myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subarachnoid hemorrhage) or aortic syndrome transfers, call toll-free 877.379.CODE (2633).

Outcomes Data
View clinical Outcomes books from all Cleveland Clinic institutes at clevelandclinic.org/outcomes.

Clinical Trials
At any given time, we offer thousands of clinical trials for qualifying patients. For more information, visit clevelandclinic.org/clinicaltrials.

CME Opportunities: Live and Online
The Cleveland Clinic Center for Continuing Education’s website offers convenient, complimentary learning opportunities. Visit ccfcmce.org to learn more and use Cleveland Clinic’s myCME portal (available from the site) to manage your CME credits. Web portal available 24/7.

Executive Education
Cleveland Clinic has two education programs for healthcare executive leaders — the Executive Visitors’ Program and the two-week Samson Global Leadership Academy immersion program. Visit clevelandclinic.org/executiveeducation.

Executive Health
Available in three locations (Cleveland, Florida and Toronto), our Executive Health Program provides active individuals and leaders with a fully integrated, head-to-toe health evaluation by some of the top medical staff in the world. For more information, go to clevelandclinic.org/executivehealth or call toll-free 866.320.1385.

About Cleveland Clinic
Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a nonprofit academic medical center with a main campus, eight community hospitals, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2012, Cleveland Clinic was ranked one of America’s top 4 hospitals in U.S. News & World Report’s annual “America’s Best Hospitals” survey. The survey ranks Cleveland Clinic among the nation’s top 10 hospitals in 14 specialty areas, and as the top hospital in three of those areas.

Same-Day Appointments
Cleveland Clinic offers same-day appointments to help your patients get the care that they need, right away. Have your patients call our same-day appointment line, 216.444.CARE (2273) or 800.223.CARE (2272).
U.S. News Ranks Cleveland Clinic One of America’s Best Hospitals

Geriatric Care Ranked No. 4

Cleveland Clinic has been ranked among America’s top hospitals since U.S. News & World Report began its annual survey of “America’s Best Hospitals” in 1990.

The 2012 survey ranks Cleveland Clinic No. 4 overall and among the nation’s top 10 hospitals in 14 specialty areas. Cleveland Clinic is ranked as America’s best hospital in three of those specialty areas.
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