The following Expert Roundtable Discussion was held on April 6, 2011. Dr. Andrew Duxbury from the University of Alabama at Birmingham moderated the topic “Cardiovascular Disease and Aging” with Drs. Jerome L. Fleg from the National Heart, Lung, and Blood Institute, Marian Limacher from the University of Florida, and Michael W. Rich from Washington University-St. Louis participating.

The discussion focused primarily on: (1) increase in aging population and the expectation of increased incidence of cardiovascular disease, (2) worldwide increase in obesity, (3) the roles of cardiologists and primary care physicians in treating increasing numbers of patients, (4) forecasting the use of technology in treating the elderly population, (5) primary prevention of cardiovascular disease including legislative changes in the food industry, (6) pharmaceutical advances and consideration of polypharmacy incurred by elderly and heart failure patients, (7) the unabated epidemic of diastolic heart failure, (8) guideline modifications for the elderly, including use of ICDs, (9) some lack of an evidence base for clear treatment of the elderly and the need for trials specifically for the aging population, and (10) proposed changes to the health care system. 

TRIALS DISCUSSED: CHARM, I-PRESERVE, PEP-CHF, TOPCAT

COMPOUNDS DISCUSSED: anacetrapib, torcetrapib, apixaban, rivaroxaban, warfarin, dabigatran, amiodarone, dronedarone, candesartan, irbesartan, spironolactone, perindopril

From the University of Alabama at Birmingham, Birmingham, AL1; National Heart, Lung, and Blood Institute, Bethesda, MD2; Division of Cardiovascular Medicine, University of Florida, Gainesville, FL3; Washington University-St. Louis, St. Louis, MO4

Address for correspondence: Andrew Duxbury, MD, Division of Gerontology and Geriatrics, University of Alabama at Birmingham, 1530 3rd Ave. South, 201CH19, Birmingham, AL 35294
E-mail: ADUXBURY@aging.uab.edu

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in some recent surveys to have at least blunted the improvement in longevity and in cardiovascular event rates that had been occurring up to this point. I think that it’s a major question as to whether or not we are able to stem the tide of increasing obesity. I believe there are some recent data that this increase seems to have leveled off, but at a rate that is still very unhealthy, with two thirds of the adult population being overweight and one third being obese. The elderly are not immune to this; the same trend is occurring in the elderly population as well.

It’s unclear as to whether we are able to continue to have reductions in cardiovascular event rates. A lot of it will depend upon our ability to control both obesity, the metabolic syndrome, which goes along with the increased obesity rates, and the traditional risk factors: hypertension, lipid problems, diabetes. I think it remains to be seen as to whether those event rates are going to continue to go down or whether they will level off, or even go up. The treatment of hypertension and dyslipidemia has, thus far, had a major beneficial impact on CV events and mortality.

DR. DUXBURY: Dr. Limacher, have you got anything to add to these somewhat pessimistic views?

DR. LIMACHER: I would like to emphasize that when we talk about heart disease in the elderly, we should consider that women comprise a larger proportion of the elderly than men. As such, heart disease becomes a burden of elderly women even more so than elderly men, if we talk about absolute numbers. I also wonder if some of the gains we’ve had in cardiovascular disease prevention may change as the influx of the increased risk factors and obesity in the population emerges into this age range.

DR. DUXBURY: Certainly, I know from the point of view of the geriatrician we’ve certainly seen improved gains in health in general in the elderly. The chance of an older person being dysfunctional or unhealthy is actually going down and has been going down steadily. However, the absolute numbers of elderly are so great that it’s overwhelming those decreases, so the total number of individuals with disabilities is actually going up.

DR. FLEG: Another point to be made is that the greatest increase in the population among the elderly is those over 85. By 2050, those numbers will have more than doubled from 2010, from 1.9% to 4.3%. So that’s something to keep in mind, because it’s the group that obviously has the highest burden of cardiovascular disease. It’s also the group for whom we have the smallest evidence base in terms of knowing how to treat.

DR. RICH: In addition to limits in the size of the cardiology workforce, there are also, I believe, deficits in training in that fellows coming through current cardiology training programs are often inadequately prepared to take care of truly elderly patients with multiple comorbid conditions. I think that many practicing cardiology fellows are even uncomfortable with addressing some of these problems in the geriatric population, and would often prefer pushing them off on the PCPs and the geriatricians. In reality, that’s not going to be feasible. I think that cardiology is going to have to be competent in dealing with multiple problems in order to provide optimal care for the increasing number of older people with cardiovascular disease.

DR. DUXBURY: Dr. Fleg, do you have anything to add?

DR. FLEG: Just that the number of cardiology fellows probably is not going to increase, certainly, at the same rate that the incidence or the prevalence of cardiovascular disease does. I think it’s clear that the primary care physicians, i.e., family practitioners, and internists are probably going to end up delivering a greater proportion of that care than they currently do. Currently they treat a lot of cardiovascular disease. Often, the cardiologist sees the patient...
initially and then refers them back to their family practitioner or internist. I think that we'll see an even greater proportion of the population of elderly patients being treated by their primary care physicians.

**DR. DUXBURY:** I'm going to ask you all to get out your crystal balls and look at the next 20 years. Do you see a kind of push away from high tech interventional cardiology—stents and valve replacements—back to a more low-tech medical treatment of cardiovascular disease coming, simply because of the various strains on the health care system?

**DR. RICH:** I don't think that there is likely to be a decline in utilization of technology in cardiology, but what I would hope to see is a more circumspect application of technology, such that more consideration is given to lifestyle factors, the impact of technology on quality of life, and the effects of comorbid conditions on the risks and benefits of technology-based interventions. Most importantly, incorporating individual preferences and lifestyle goals into the decision-making process is crucial.

I think that we're likely to see an increase in use of technology, as more data become available, evaluating efficacy and safety in older patients. As technology improves, complications tend to decline and more and more older patients become potentially eligible to benefit from these procedures. I would just like to see more circumspect application of these technologies, particularly in people over age 80 or 85.

**DR. LIMACHER:** Yes, I would say that there is an opportunity for increasing methodologies. The recent reports that catheter-based valve replacement is working are particularly attractive to the elderly individual with significant symptoms, but a lot of comorbidities. Your point about the new technologies being applied appropriately is very pertinent.

**DR. FLEG:** I think that the amount of money that both the American government and public is willing to put into health care is going to be a major driver for some of these factors. We now have guidelines that suggest that patients even with mild heart failure will benefit from cardiac resynchronization therapy, and yet the cost of putting one of these devices in everybody who could potentially benefit is going to be very burdensome. The same with ICDs, I think that we will see a greater emphasis on cost-effectiveness and judicious application of technology. Some of it is going to depend upon how much the American public is willing to spend in terms of the percentage of GDP that goes to health care.

I would also like to see a greater emphasis on primary prevention, because it's much less costly to prevent some of these conditions from occurring than to treat them after the fact. Greater emphasis should be placed on diet and physical activity, even among the elderly, a group in whom the attitude, “You're too old to exercise” has often been widely prevalent. We really know better than that. I'm hopeful that resources will go into not just interventional and noninterventional cardiology, but also into primary prevention, especially conditions such as hypertension.

**DR. DUXBURY:** Let's stay with the idea of primary prevention, I am well aware that a healthy elder comes from a healthy middle-aged adult, who comes from a healthy young adult, who comes from a healthy teen, who comes from a healthy child, who comes from a healthy infant. To produce the healthy elder who is free of significant atherosclerotic and cardiovascular disease requires lifelong choices. What kinds of things do you think need to happen to significantly impact atherosclerotic and cardiovascular disease rates?

**DR. FLEG:** I think that some steps are already being taken. A lot of these are going to have to be at the societal level, because individuals can only do so much if the environment is not conducive. The current move to reduce the sodium intake of foods is actually going to be legislated. There is already a large taskforce that has recommended a reduction in the average dietary sodium intake to 1500 mg/day, and probably that will be reflected in requirements for the food industry. Less sodium in the food, fewer calories, less saturated fat, and less high fructose corn syrup—all of these things could be major positive factors in terms of reducing the incidence of cardiovascular disease by reducing both hypertension and obesity. I think that, similar to what we've done with smoking, it should be possible to accomplish some of these changes in the diets of Americans.

Getting older people to exercise may be a little bit tougher, but again I think there are things that can be done in terms of public service announcements on TV, radio, billboards, etc. Maybe even inducements, in terms of lower insurance rates and things of that sort if you're in an exercise program; I think interventions like this could go a long way towards helping to reduce the risk factors that cause and exacerbate cardiovascular diseases that we treat.

**DR. LIMACHER:** I would like to also support that notion. It’s really going...
to take more institutionalized effort, whether it’s governmental or even more broadly in the workplace and community to change behaviors early on before they reach the elderly stage. Right now, we don’t make it easy for people to live healthy lifestyles. Legislative changes in the diet, and tackling the food industry head-on, really gives us the best chance of getting people back to healthier lifestyles.

DR. DUXBURY: Let’s switch now to some medical treatments. One of the developments of the last year is the availability of dabigatran as a substitute for warfarin for anticoagulation in atrial fibrillation. The use of this drug may result in fewer of the very complex clinical problems that anticoagulation can pose in the elderly.

DR. RICH: Dabigatran is a major advance in our management of people with atrial fibrillation, roughly 50% of whom are over the age of 75; the numbers are expected to increase to 50% over the age of 80 by mid-century. Dabigatran has some advantages, in terms of ease-of-use, and it doesn’t require constant monitoring of the INRs. It doesn’t require as many dietary restrictions, has fewer drug interactions, although there are interactions with amiodarone and dronedarone. However, despite these advantages, there are very few data on use of dabigatran in people over the age of 80 or 85. So we will need to continue to collect post-marketing data with respect to potential bleeding complications and other adverse events. In addition, there is the potential for overdosing if clinicians don’t consider renal function. The recommended dose of dabigatran is 150 mg BID in individuals with an estimated creatinine clearance of greater than 30 cc/min/1.73 m², but the dose should be reduced to 75 mg BID if the creatinine clearance is 15 to 30 cc/min/1.73 m², and dabigatran should not be used at all if the creatinine clearance is less than 15 cc/min/1.73 m².

DR. FLEG: I would point out that dabigatran is costly, about $5 a pill.

DR. RICH: It is costly, but most insurance carriers have been willing to cover it with reasonable co-pay. The co-pay has been higher than for warfarin, which is available generically, but most patients are willing to pay more in order to get the increased convenience of dabigatran. From the insurance company’s perspective, the reduced cost of monitoring partially offsets the price of the drug.

DR. FLEG: I’m not convinced that the cost is not a factor in the elderly population. The other concerns are the twice-a-day dosing, which may reduce the adherence rates. Also the fact that, even though we usually see the lack of monitoring as a plus, it is also a negative in that you don’t know where you are in terms of anticoagulation protection.

I think that like with many other drugs, longer term, follow-up with real world experience with the drug is going to be necessary to put it in its rightful place. However, it is an alternative for older people who are unwilling to be bothered with follow-ups with warfarin.

DR. DUXBURY: There are some other drugs in the pipeline that may be useful in the area of atrial fibrillation and anticoagulation. Two other drugs, rivaroxaban and apixaban, which are factor Xa inhibitors, may be useful in atrial fibrillation, but also as prophylaxis and treatment of deep vein thrombosis and pulmonary embolism.

DR. FLEG: Another promising category of drugs are the CETP inhibitors, which are for use in treatment of lipid problems, particularly low HDL cholesterol. Regulation of lipids, as well as blood pressure control, are the most promising approaches to prevention in this population, as well as in younger patients. The first drug in this class was torcetrapib, but we had a poor experience with it. It had some aldosterone agonist effects and raised blood pressure. It actually caused an increase in morbidity and mortality rather than the decrease everyone expected, despite the favorable lipid effects. There is a new one, anacetrapib, which has just undergone a large clinical trial that was not endpoint related, but the drug caused impressive increases in HDL cholesterol and reductions in LDL cholesterol without adverse changes in blood pressure seen with torcetrapib. So I think that anacetrapib and other drugs in its category to increase HDL cholesterol more effectively than any of the current drugs that we have available, will be a major step forward in preventing cardiovascular disease for all age groups, including the elderly.

DR. LIMACHER: What we do also need to pay attention to is the polypharmacy that most older patients incur. Every new condition gets a new drug and few practitioners have the time or energy to review every medication that has been prescribed by the patient’s providers, and then determine whether the initial indication is still in play.

DR. DUXBURY: Adherence to complex medical regimens, and trying to simplify and create medical regimens that the average patient can handle is a major clinical problem we have to deal with.
DR. FLEG: This is particularly true in heart failure, where we keep adding drugs. Every few years there is a new class of drugs. The typical patient with systolic heart failure would by evidence-base now be on an ACE inhibitor or ARB, a beta blocker, and now probably an aldosterone antagonist, plus of course diuretics and possibly digoxin.

DR. LIMACHER: We have a similar problem with coronary disease. Everybody is on five different agents just for their coronary disease, and they don't have just coronary disease. Many of them are on lipid or blood pressure lowering drugs, as well as on anti-diabetic therapy or treatment for arthritis.

DR. DUXBURY: One of the chief problems is the relatively healthy older patient who is in their 80s who develops some substernal chest pain, and ends up in the emergency room, and has not been taking any medications. They may be sent home on a nitrate, an ACE inhibitor, a beta-blocker, and a statin. Four days later, they can't get out of bed because they have no blood pressure. I think that there is room within all of our specialties to recognize that there is the interaction of medications, and the real world, particularly in the elderly, is not always what it would be in the textbook.

DR. FLEG: Yes, in fact, Mike was part of the group that had an editorial in JACC about the limitation of guidelines. First of all, there are few data in people over the age of 80 in almost any of our guidelines except for hypertension. Even in younger elders, there may be differences in the efficacy of much of our guideline-based therapy compared to younger adults. Mike, you might want to comment on that with regard to both heart failure and other conditions.

DR. RICH: Yes, as already pointed out, heart failure is the classic polypharmacy condition. Patients can be on five, six, or seven drugs for heart failure, not to mention all of the drugs they're on for their various other problems. It's been well documented that the potential for drug/drug interactions increases exponentially with the number of medications a person is taking. A recent article looking at medications in a heart failure population found that the average number was in excess of ten per patient. That virtually guarantees that there are going to be some drug interactions. Additional concerns include the ability of patients to understand and adhere to the medication regimen. These issues are further complicated by the high costs of medications and inadequate insurance coverage through Medicare Part D.

In addition to prescription medications, older patients are often taking non-prescription drugs and supplements that can cause adverse interactions. For example, non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to arthritis in older patients, but these drugs may counteract the effects of ACE inhibitors and diuretics and may also contribute to worsening renal function.

There is a strong need to develop better strategies for optimizing drug therapy in older adults, minimizing the number of medications prescribed and ensuring that all active medications are indicated and appropriate. A common scenario is that a patient is started on a proton pump inhibitor (PPI) while in the hospital and the drug is continued more or less indefinitely with no clear indication for its use.

DR. FLEG: In addition to the drug-drug interactions, I would also point out the drug/patient interactions because of the greater predilection to adverse reactions in the elderly; volume depletion, electrolyte disturbances, reduced renal function, orthostatic hypotension—these are just some of the issues that we need to deal with in older patients with cardiovascular disease. You can't just treat them like a 50-year-old patient by the guidelines because, as Dr. Duxbury pointed out, they may not be able to get out of bed due to drug-induced orthostatic hypotension or other side effects. The usual simple adage of “start low and go slow” is certainly relevant in terms of the way to titrate older patients. First establish the need for the drug and then titrate it much more gingerly than one might in a 50 or 60 year old.

DR. LIMACHER: Yes, I think that begs the question of incomplete provider education. We emphasize evidence-based guidelines so much that the condition gets treated and not the patient. If we were to focus our guidelines, that we don't need to slam everybody with five drugs the instant they have a diagnosis, and approach them individually, we might be better prepared to monitor the effects and side effects of each treatment. I think there should be more attention paid to careful initiation of treatments on an individual basis rather than simplistically emphasizing implementation of guideline recommendations across the board.

DR. DUXBURY: I’d like to stay with the issue of congestive heart failure for just a moment. Because certainly there have been a number of studies that point out that it’s the diagnosis that’s probably the most costly to the healthcare system in regards to the elderly, as

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- Michael Rich, MD
it tends to come with multiple relapses and readmissions. We are all familiar with patients who are in the revolving door of a hospital, rebalancing of fluids, and discharge home. Back again several weeks later completely decompensated and on and on it goes. Do any of you have strategies on how to kind of best manage this disease to minimize this kind of revolving door acute care treatment?

DR. FLEGG: Well, Mike Rich actually had the first definitive study of overall disease management of elders with heart failure with a multi-pronged approach, so Mike, maybe you should comment on that first.

DR. RICH: There have now been many studies evaluating heart failure disease management (HFDM). In contrast to many other studies in cardiovascular medicine, many of the HFDM studies focused on elderly patients. Meta-analyses of these trials have shown that multi-disciplinary HFDM interventions reduce readmission rates by 20–30% and improve quality of life.

However, it’s worth noting that despite significant reductions in heart failure mortality rates and length of stay over the past 20 years, 30-day readmission rates have actually increased.

In my opinion, the increased readmission rate is in part a direct consequence of decreased length of stay; that is, patients are being discharged prematurely before their heart failure has been adequately treated. This situation is particularly germane to older adults. A common scenario is that a patient is admitted with heart failure and looks and feels much better after modest diuresis. There is then a tendency to discharge the patient fairly quickly, despite the fact that the patient is still significantly volume overloaded. In my view, the patient would be better off staying an extra day or two to complete normalization of volume status and optimization of medical therapy. The transitional care process is also woefully inadequate. Patients are often discharged without an adequate understanding of what they’re supposed to do after they get out of the hospital in terms of their medications, diet, and activities. The problem is then further compounded by inadequate follow-up.

One of the things we learned from our early work in this area is that having direct contact with the patient within the first 24 to 48 hours of discharge is absolutely critical for ensuring successful transition back to the home environment. All too frequently, patients are given a handful of prescriptions and a long list of instructions at the time of hospital discharge. They may or may not get the prescriptions filled, but even if they do get them filled, they may also have a bag of medications that they were taking prior to coming into the hospital. Unsure which medications to take, they’ll often take their old medications in addition to whatever new ones were prescribed. Obviously, this increases the risk for drug interactions and adverse outcomes, including early readmission.

Older patients with frequent admissions are at risk for subsequent readmissions, and these patients require high quality transitions in care, including follow-up within 24 to 48 hours of discharge. Ideally, this should include a home visit by a home health nurse, preferably a nurse with experience managing older heart failure patients. If this is not feasible, at the very minimum a telephone follow-up call from someone familiar with the patient’s diagnoses, prescribed medications, and discharge instructions is essential for ensuring a smooth transition.

Another important point is the issue of fluid intake. Older people often hear, or are told by well-meaning family, that they should drink eight or ten glasses of water every day. Many heart failure patients think that because they’re taking large doses of diuretics, they need to drink even more. This of course leads to re-accumulation of fluid and is an under recognized but very significant contributor to early re-hospitalization. Avoidance of excess fluid intake needs to be addressed very plainly in the patient’s discharge instructions and during subsequent follow-up.

DR. FLEGG: Another issue I think we need to deal with is the current epidemic of heart failure with preserved ejection fraction, also known as diastolic heart failure. This is a disorder for which we still have no evidence-based therapy. This type of heart failure occurs in probably at least half of elderly people who have heart failure as opposed to a younger population in whom most heart failure is due to systolic dysfunction. In the very elderly, especially in very elderly women, the percentage may be as high as two-thirds to three-quarters of heart failure being due to diastolic dysfunction.

We also know that about half of heart failure hospitalizations occur in this group, and that, even though their mortality is somewhat less than in systolic heart failure, their hospitalization rate is just as high. Many of those hospitalizations are due to comorbid conditions, but just because these patients have preserved systolic function doesn’t mean that they stay out of the hospital. This is a group in whom we’re going to need to develop some evidence-based therapy. Then of course, we’ll have to deal with all the issues that Dr. Rich raises.

DR. DUXBURY: So, Jerry, can you comment on some of the ongoing trials in management in individuals with heart failure and preserved ejection fraction?

DR. FLEGG: There have been several trials in this disorder that have been unsuccessful: CHARM, looking at the ARB candesartan; I-PRESERVE looking at the ARB...
irbesartan; PEP-CHF, looking at the ACE-inhibitor perindopril; and some smaller trials as well. The NHLBI is sponsoring the TOPCAT trial, using a cheap and old generic drug, spironolactone, the aldosterone antagonist, in people who have heart failure and preserved systolic function. The minimum age is 50, our mean age in the trial is about 70, and we do have a sizeable number of patients who are over the age of 80. We have enrolled more than 50% women, which is also representative of the heart failure community.

The trial is going to be continuing for another two years; by that time, we will have an answer as to whether this drug works. Certainly, the aldosterone antagonists have been very effective drugs in systolic heart failure. One would anticipate that given their anti-fibrotic effects and the stiff heart and cardiac fibrosis characteristic of individuals who have diastolic heart failure, these drugs should be beneficial. Thus, we are hopeful that TOPCAT will have a positive result.

**DR. RICH:** There is one other point that I want to make, which is that guidelines need to incorporate some of the issues we’ve discussed related to polypharmacy and the effects of aging on the heart and vasculature as well as the kidneys and liver. There are some circumstances for which guideline recommendations should be modified for patients of advanced age.

The use of ICDs is a prime example; the current guidelines don’t distinguish use of ICDs by age, despite the fact that there is no compelling evidence that ICDs are beneficial in people over the age of 80. In fact, observational studies and a recent meta-analysis failed to show a significant benefit of ICDs in people over the age of 80. Nonetheless, the guidelines suggest that any person who meets criteria for an ICD, regardless of age, should be offered a device. In other words, if a person is 93 years old and meets criteria for an ICD, the physician who doesn’t offer a device may be considered non-compliant with the guidelines and guilty of practicing substandard care.

**DR. FLEG:** I would go a step further and say that we need to do a better job of including more very elderly and elderly with comorbidities in our clinical trials, so that we actually do have an evidence-base to be able to make appropriate decisions in this age group. I think we’re moving in that direction. There are many fewer trials now that have upper age cut points than was the case say 15 or 20 years ago, but we still generally tend to choose the healthier people, those with the fewest comorbidities, to enter the clinical trials. So we end up with a relatively “pure” group that can more easily address the question or the intervention that we’re looking at. The downside of this is that the results then are not generalizable to the real world of elderly patients.

**DR. RICH:** I completely agree.

**DR. DUXBURY:** I often see people within a year or so of the implantation of an ICD, which was implanted for somewhat dubious reasons and they have many other comorbid diseases. We’re looking at it as prolonging suffering at this point rather than prolonging active or healthy life. We can get into these very long discussions of turning them off.

My last question to everybody is, in an ideal world, and we know we do not live in an ideal world and we have a health care system that is very definitely in flux, what changes do you see that the system needs to make to better support the treatment of cardiac disease in older adults? If you could change two or three things to make the system serve those needs, what do you think they would need to be?

**DR. FLEG:** I think Dr. Rich has already pointed out one. Better hospital to home transitions I think would be a major step in terms of decreasing the need for re-hospitalization. Perhaps individualizing when a patient goes home, particularly an elderly patient and making sure that the infrastructure is set up for early follow-up, and proper and prompt filling of prescriptions and all the things that are necessary in order to keep the patient out of the hospital.

Another thing I would also mention, with the new health care system providing coverage for preventative Medicare visits, is a greater emphasis on prevention, to hopefully keep people from developing these diseases.

**DR. RICH:** I also think that there is a serious misalignment between the amount of time that it takes to provide high quality health care services to an older adult and the reimbursement for that time for both the physician and other health care providers. I recognize that this is sort of “pie in the sky,” but I think that reimbursement should be shifted to increase the number of RVUs for providing care for complex procedures in older patients who clearly require more time. Physicians cannot be expected to spend the additional time needed to provide patient-centered care if they don’t receive some compensation for it. This is not in any way a cardiology-specific issue. It applies to cardiology, but it applies to every major area of medicine and surgery as well. Providing optimal care to older patients simply takes more time.

**DR. DUXBURY:** With that, I would like to thank all of our panelists for joining me today in this informative discussion of cardiovascular disease in the elderly.

The views expressed by Dr. Fleg are his own and do not necessarily reflect those of the National Institutes of Health or the Department of Health and Human Services of the United States.
REFERENCES


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