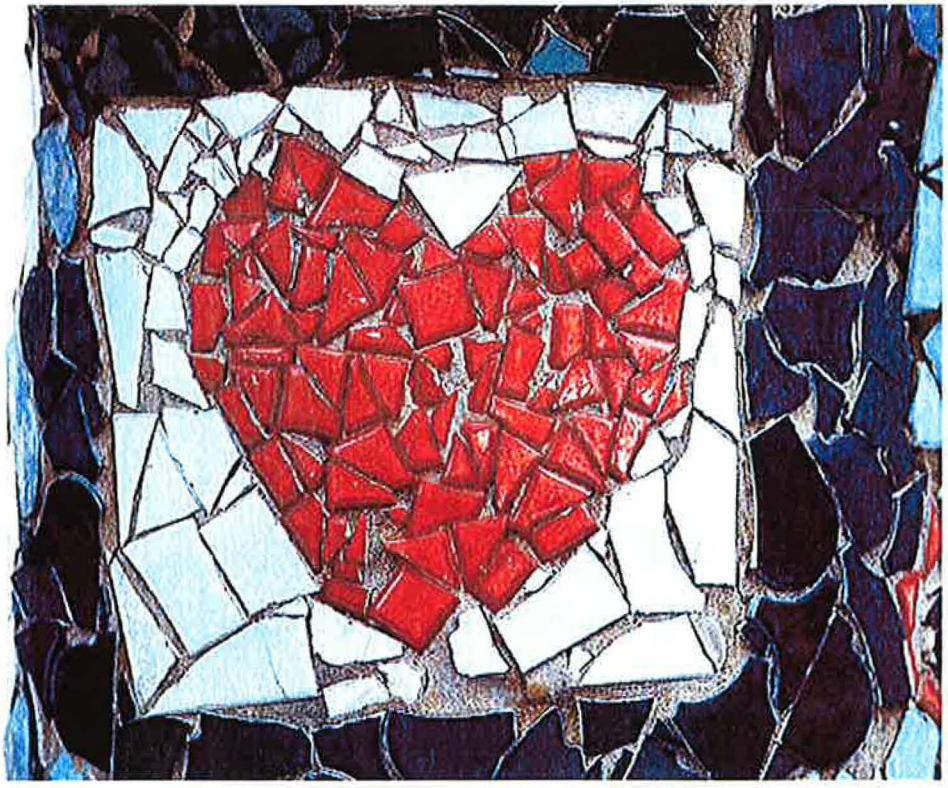
Presbycardia: Youthful Spirit, Aging Heart



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No off-label indications will be discussed.

The term "presbycardia" was introduced by Dr. William Dock in 1945. This term refers to the aging of the myocardium. His initial description was:

> Aging of the myocardium resembles aging of the accommodative mechanism of the eyes. Neither is apparent from gross or even histologic study, but only from functional tests. Presbyopia is revealed by failure to identify nearby objects or small type in the same way that myocardial aging is revealed by failure of the heart to sustain such stressors as high cardiac output, high arterial pressure, acute febrile illness or tachycardia (1)

Dr. Dock felt that the condition would be more widely appreciated if there was a good Greek word to indicate that age had altered the ability of the heart to meet its burden even though there was no significant structural change. Thus, the term presbycardia was coined.

Dr. Tinsley Harrison, who was the first chairman of the Department of Internal Medicine at UT Southwestern from 1944-1950 and a mentor of many physicians in Dallas was a firm believer in the syndrome first described by Dock, but disagreed with the terminology. He stated,

"when as is often the case one has students who are allergic to names of Greek or Latin origin, the term senile heart disease is perhaps simpler and equally descriptive. Such hearts represent the state of the myocardium, which is simply worn out because of too many birthdays... Unfortunately, the widespread and inaccurate usage of the term arteriosclerotic heart disease has tended to prevent a clear concept of the frequency and significance of the birthday heart" (1).

More recently Dorland's Medical Dictionary defines presbycardia as impaired cardiac function attributed to the aging process occurring in association with recognizable changes of senescent in the body and the absence of convincing evidence of other forms of heart disease (3).

SCOPE OF THE PROBLEM

Elderly people are the fastest growing segment of the United States population. In the 1979, Dr. Jere Mitchell presented Medical Grand Rounds on the aging heart. At that time it was estimated that approximately 23 million people were over the age of 65 and it was projected that 31 million would be over the age of 65 by the year of 2000. Currently, over 10 million persons are over the age of 80 in the United States.

The prevalence of cardiovascular disease in older adults is dramatic. Over 85% of women over the age of 80 and 80% of men over the age of 80 have some sort of underlying cardiovascular disease including coronary heart disease, heart failure, stroke and hypertension. The prevalence of cardiovascular disease is much greater in men at a younger age, but becomes equal with age. Women surpass men in terms of

cardiovascular disorders once they reach the age of 80. Although cancer remains a leading cause of cardiovascular mortality, cardiovascular deaths are greater than cancer related deaths in those individuals age 75 to 84 and those over the age of 85. Another way to view this is in terms of the proportion of deaths attributable to cardiovascular disorders. This proportion increases with age. In those individuals under the age of 85 less than half of all deaths may be attributable to coronary disease where as in those individuals greater than 85, cardiovascular disorders account for the majority of causes of death.

There are many cardiovascular disorders that occur in the older population. A major problem is heart failure, typically heart failure with preserved ejection fraction (or diastolic heart failure). The incidence of heart failure is greater in men than in women overall, but women over the age of 85 are more likely to have heart failure. Atherosclerotic coronary artery and valvular heart disease are common. Nearly all elderly Americans are hypertensive and up to 15% have cardiac conduction disorders.

The varieties of disorders that occur in the elderly include the same sorts of disorders that might be found in an older home. An older home frequently has plumbing, electrical and mechanical issues. Examples of plumbing abnormalities include atherosclerotic disease of the coronary arteries, valve and vasculature. Electrical problems are illustrated by atrial fibrillation and sinus node dysfunction. Mechanical issues include systolic dysfunction and heart failure with preserved ejection fraction.

The underlying pathophysiology in these situations includes myocardial cell hypertrophy and fibrosis. This fibrosis and focal calcification can alter the conduction tissue giving rise to conduction block. Atherosclerotic risk factors are modified and influenced by age. In addition, the older patient has altered hemostatic factors to injury and altered responses to healing leading them to respond differently from younger patients in the presence of cardiovascular stressors.

HOW OLD IS ELDERLY?

It is very difficult to interpret how old an elderly patient is. In the late 1970's an elderly patient was generally one who had reached the age of 65. Over the ensuing 30 years, the elderly patient keeps getting older and older. In the current cardiovascular literature, the term elderly generally refers to those over the age of 75 or 80. In some studies there is an advanced class of patient, "the very elderly patient", who is usually over the age of 85 or 90.

Patients of these age ranges have traditionally been excluded from clinical trials. This makes it very difficult to know whether application of therapies known to be beneficial in younger patients is appropriate in the other patient. Fortunately, there are now some data from controlled trials and registries to help guide decision making in the cardiovascular care of the elderly patient.

INTERSECTION OF CARDIOVASCULAR CARE AND PATIENT

How we take care of elderly patients depends not only on their underlying cardiovascular disease, but also on the value placed on the quality as well as the quantity of life. In many patients prolongation of life is not the goal; rather, the quality of life and the ability to function independently is extremely important. In these individuals improvement in quality of life is the primary goal. Dr. Melvin Cheitlin of University of California San Francisco has stated "that the prolongation of life for any meaningful length of time is not as important as the release in symptoms and improvement of the quality of life".

Many elderly patients have disorders other than cardiovascular disease that impact care and decision making. In order to effectively care for the elderly patient, we must understand the following principles of medical ethics: 1) Autonomy (respect for patient preferences); 2) Beneficence (acting commensurate with the patient's best interests); 3) Nonmalfeasance (doing no harm) and 4) Justice (fairness in distribution of resources) (4). Technological advances in cardiology have advanced greatly in cardiology and we must use them judiciously and follow these principles.

CARDIOVASCULAR DISORDERS IN THE ELDERLY

I will review three common disorders that occur in the elderly patient and discuss the approaches to clinical management. There are many cardiovascular disorders that influence older patients but I have selected aortic stenosis, atrial fibrillation and atherosclerotic coronary artery disease with acute myocardial infarction for review today.

AORTIC STENOSIS.

Aortic stenosis is an increasingly common problem in the elderly. While bicuspid aortic valve disease and rheumatic etiologies may be more common in the young patient, those individuals over the age of 70 will typically have degenerative or atherosclerotic aortic valve disease. The typical risk factors for aortic stenosis include not only coronary artery disease, lipid disorders, diabetes, hypertension, and renal disease. Age is the most potent risk factor for aortic stenosis. Age is used as an exclusion to aortic valve replacement in some studies leading to the concept of age discrimination in cardiac care.

A small study was published on a British cohort of patients in the late 1990s reporting cardiac outcomes in 391 octogenarians, 93 nonagenarians and 6 centenarians (5). The cause of death was cardiac in nearly half the patients and vascular another 17 patients. Interestingly, in this particular cohort the likelihood of a cardiac condition causing death declined with age. In the 6 individuals who were over 100, they did not die from underlying cardiovascular disease. If one looks for underlying atherosclerosis or calcification using CT scanning in the elderly, coronary artery calcification is extremely common. It increased with age and is present in nearly all individuals over the age of 90.

Aortic valve calcification increases with age from 42% in octogenarians to 63% in nonagenarians and 86% in centenarians. Significant aortic valve stenosis was seen more commonly in the patients in their 80s and 90s.

Survival with symptomatic aortic stenosis in the absence of surgery remains poor. Unfortunately very little data is available comparing the outcome of elderly to younger patients. In one series 277 patients with significant aortic stenosis and who were greater than 80 years old were studied (6). Slightly over half of the patient population was male. At the time they underwent valve surgery, their aortic valve area was 0.7 cm^2 consistent with critical aortic stenosis. Coronary artery disease was present in 47%. Only about 20% of these patients underwent aortic valve surgery over a two and a half year period. One hundred and seventy seven deaths were seen over this time period. When you look at survival in these patients, you can see that aortic valve replacement resulted in a marked improvement in survival up to five years after surgery. Initial one year survival was nearly 90% declining to 67% at the five year mark. For those individuals not undergoing aortic valve replacement survival was 50% at one year declining to 20% at five years (Figure 1).

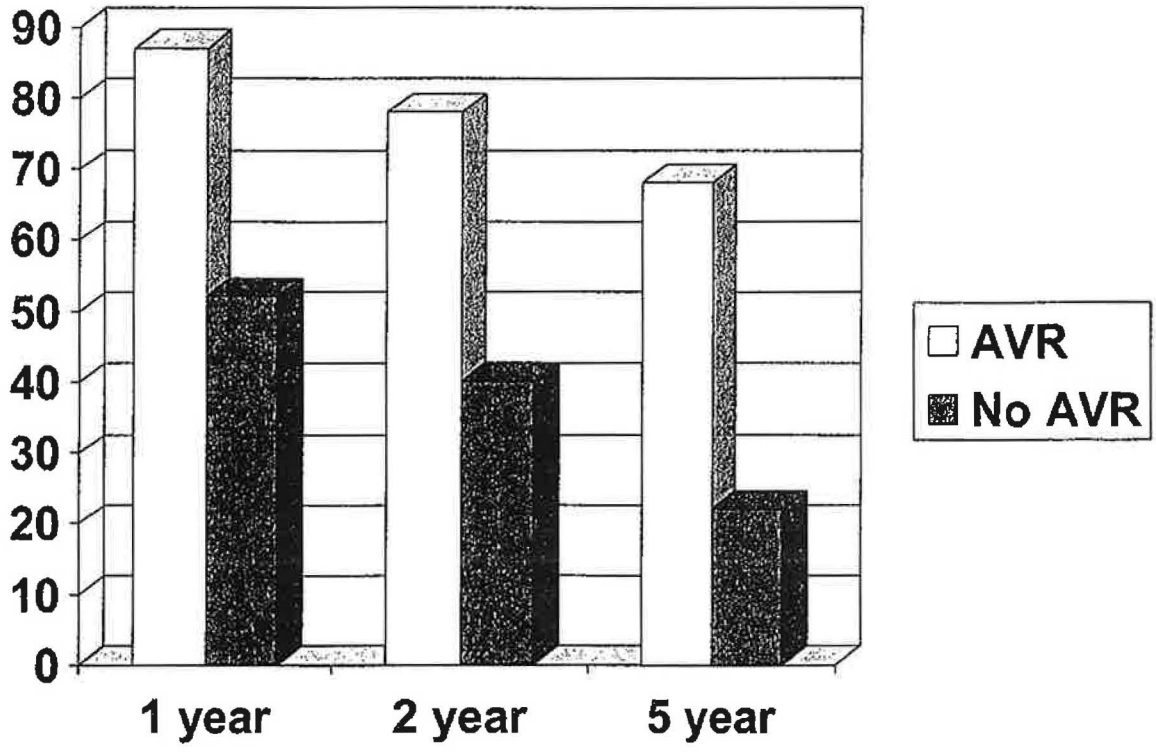

Figure 1.

Deciding to refer the elderly patient with aortic surgery remains a significant problem. Preliminary data from the University of Michigan demonstrates that only about 50% of patients with severe aortic stenosis on echocardiography ultimately are referred

for cardiac surgery. While some of this may be related to other comorbidities, it is likely that some patients are not being cared for properly.

Decision making in the management of these patients is difficult. In a one year retrospective cohort of patients with aortic stenosis greater than 60 years of age, nearly 90% of patients undergoing aortic valve replacement were alive one year after the operation while only 55% of patient's not undergoing aortic valve replacement were alive (7). Postoperative complications are relatively similar among all ages rather than increasing with age. The most common reasons for not offering surgery to patients include comorbidities and age.

Since coronary disease is commonly seen in the elderly patient with aortic stenosis it has been presumed that the association of the two entities would lead to decreased survival postoperatively. A small amount of data is available from Scandinavia. In this cohort 94 patients with a mean age of 82 years and preserved ejection fractions presented with critical aortic stenosis (8). The majority were in functional class III or IV for heart failure and slightly over half of them underwent combined surgery (coronary artery bypass grafting and aortic valve replacement) while 42 underwent isolated aortic valve surgery. Early mortality rates, those less than 30 days, demonstrated a slightly lower mortality rate of those undergoing the combined procedure. This persisted out to three years when the mortality rates were on the order of 20% in both patient groups.

Importantly, elderly individuals who undergo aortic valve surgery for aortic stenosis not only live longer but they have a good quality of life. This occurs regardless of whether or not the aortic valve has been replaced as an isolated surgery or it is combined with coronary artery bypass surgery. The majority of these patients also return home with a small proportion may live in an extended care facility.

Early mortality rates vary dramatically between studies. Fortunately, we now have data on a series of older patients who have undergone both aortic valve replacement and those with aortic valve replacement plus coronary artery bypass grafting.. Perioperative death rates are higher in those with combined aortic valve replacement and bypass surgery. Some patients, however, will not do well after undergoing aortic valve replacement. Risk factors for adverse outcomes include history of heart failure, hypertension, pulmonary hypertension, preoperative hemodynamic instability and severe systolic dysfunction.

Aortic valve replacement for aortic stenosis in the elderly improves mortality; it is reasonably tolerated along with bypass surgery and is associated with an improved sense of well-being and function. Moreover, it is associated with living independently. Surgery may be withheld due to physicians overestimating the likelihood of adverse outcomes. Two nice databases, the Society of Thoracic Surgery Database and Euroscore, can give us useful information to help guide the patient in the decision making process. Both databases have websites (sts.org and euroscore.org) that may be accessed by health care providers as well as consumers to calculate an individual's risk with cardiac surgery.

Given the other medical problems in the elderly, some will have unacceptably high risks of adverse outcomes with conventional cardiac surgery. Ongoing research trials are investigating the use of percutaneous aortic valves for the treatment of aortic stenosis. These valves may be placed from the femoral or apical approach and may offer high-risk patients an opportunity to reduce their symptoms.

ATRIAL FIBRILLATION

Another problem that occurs frequently in the elderly is atrial fibrillation. This disorder which is reaching nearly epidemic proportions in older adults is associated with a higher likelihood of embolic complications as well as a higher likelihood of bleeding complications in the older patient. The decision to institute anticoagulation therapy varies by the person and it is unknown whether rate control versus rhythm management is the best strategy in the elderly. Stroke increases with age, with over 17% of the population over the age of 80 and nearly 14% of women over the age of 80 suffering a stroke. For those individuals over the age of 80, approximately one third of all strokes may be attributed to underlying atrial fibrillation.

Current epidemiologic information suggests that atrial fibrillation increases with age increasing from about 0.5% in the patient's age 50-59 increasing up to 9% in the octogenarian. The age adjusted prevalence of atrial fibrillation is increasing over time when data from the last few decades has been examined. This increase is presumed to be due to better management of other underlying disorders,

In the past, common risk factors for atrial fibrillation included rheumatic heart disease, hypertension, coronary artery disease, pericardial and thyroid disease. In the current era, additional risk factors have been identified. These additional risk factors include diabetes, heart failure and valve disease, sleep apnea and pulmonary hypertension. Atrial fibrillation has most recently been described to be more common in sedentary individuals. Echocardiographic risk factors for atrial fibrillation include left atrial enlargement, increased wall thickness, depressed myocardial infarction and decreased flow velocities in the atrial appendage.

Atrial fibrillation is a problem because it leads to inconvenient and bothersome symptoms, which may wax and wane over time, decreased functional capacity, and more importantly increases the risk of stroke. The attributable risk of atrial fibrillation for stroke increases with age and is associated with an increased mortality risk. In a study 300 patients who were hospitalized for various disorders, the relationship of atrial fibrillation to patient outcome was examined (9). Approximately one-third of the patients developed atrial fibrillation while in the hospital. Individuals developing atrial fibrillation had a markedly increased mortality rates at 30 days, one year, five years and ten years with a median survival of 1.2 years compared to those who did not develop atrial fibrillation (6 year median survival). Thus, atrial fibrillation is a marker for abnormal outcomes.

There are many studies testing the hypothesis that warfarin reduces the risk of embolic events in those individuals with atrial fibrillation (10, 11). The pattern of atrial fibrillation does not seem to matter as the stroke risk is elevated in those individuals with paroxysmal, persistent, and permanent atrial fibrillation. In these trials evaluating the role of warfarin in the prevention of stroke in patient with atrial fibrillation, there were different target ranges for warfarin. These studies showed a reduction in the risk of embolic events. The degree of protection varied from trial to trial possibly in part due to the different patient populations as well as the target anticoagulant ranges. In a recent study evaluating patients over the age of 75 with atrial fibrillation who were willing to take warfarin, the yearly risk of having an embolic event decreased from 3.8% to 1.8% in those taking warfarin as opposed to aspirin (12)

Subsequently, several strategies have evolved to help us quantitate the risk of stroke have been examined. The most common criteria quoted are called the CHADS Risk Criteria (13). This is commonly used in the older patient with atrial fibrillation. In this scoring system, the primary risk factors for embolic events are shown including prior stroke or transient ischemia attack, advanced age (including those over the age of 75), hypertension, diabetes and heart failure (Figure 2). You simply count how many of these risk factors an individual has to determine their score. The investigators looked at a cohort of patient to examine stroke risk versus CHADS score. In this population of over 1700 patients, the adjusted stroke rate increases directly with the CHADS score. Thus, if you are a young patient who has no risk factors your adjusted stroke rate is about 1.9% per year. However, if you have four risk factors, your adjusted stroke risk increases up to 8.5% per year (Figure 3). This led to the derivation that if your CHAD score is 2 or greater you should be treated with oral anticoagulants since the risk of embolization exceeds the risk of significant bleeding. Those individuals with a score of 0 may be treated with aspirin as prophylactic therapy.

Figure 2. CHADS Risk Criteria

CHADS Risk Criteria	Score
Prior stroke or TIA	2
Age > 75 years	1
Hypertension	1
Diabetes	1
Heart Failure	1

Figure 3. Stroke rates based on CHADS score

Patients (1733)	Adjusted Stroke Rate	CHADS
120	1.9 (1.2-3.0)	0
463	2.8 (2.0-3.8)	1
523	4.0 (3.1-5.1)	2
337	5.9 (4.6-7.3)	3
220	8.5 (6.3-11.1)	4
65	12.5 (8.2-17.5)	5
5	18.2 (10.5-27.4)	6

The lowest effective intensity of anticoagulation was ultimately derived from the variety of blood thinning trials. Trials aimed at an INR of 1.5-2.0 did not demonstrate a significant reduction in embolic risk. The INR ratio of 2 to 3 seems to protect against embolic events while minimizing bleeding risk (that increases significantly over an INR of 3.

Oral anticoagulants are often withheld from elderly patients due to the perceived risk of falling. The risk of falling and its attendant risk of significant bleeding appear to be overestimated by physicians. We need to improve our ability to assess the risk of significant bleeding and understand better the optimal monitoring strategy of warfarin.

ATHEROSCLEROTIC CORONARY ARTERY DISEASE

The number of diagnosed heart attacks increases with age, although the ratio of myocardial infarction in men versus women varies with age. The most common age for men to present with heart attacks is between the ages of 45-64 whereas women are much more likely to present when they are over the age of 75. The older patient presenting with acute coronary syndrome is more likely to be female, have diabetes and hypertension and have a history of prior cardiac events.

Almost all studies show that increasing age is associated with decreased utilization of invasive cardiac procedures. There is a concern that standard pharmacologic therapies may be underutilized in older patients. In the past few years there have been various trials and registries published examining the outcomes of older patients with

coronary artery disease. The Crusade Initiative studied over 50000 patients. 5557 patient's greater than 90-years-old who represent the older elderly cohort and 46270 who were 75-89 years old (elderly) who had suffered a non-ST elevation myocardial infarction (14). These patients were examined for adherence to standard treatments as well as cardiovascular outcomes. Many patient variables on presentation were associated with death including reduced systolic blood pressure, heart failure, renal insufficiency, elevated troponin, diabetes, obesity and elevated heart rate. Interestingly enough, dyslipidemia and prior angioplasty were associated with improved outcomes.

Acute Therapy	Adjusted OR (95% CI)
Aspirin	**0.65 (0.58-0.73)**
Beta-blocker	**0.67 (0.61-0.74)**
Heparin	**1.06 (0.96-1.17)**
Catheterization in 48 hours	**0.70 (0.64-0.77)**
Glycoprotein IIb/IIIa	**1.24 (1.12-1.38**
Cath plus IIb/IIIa	**0.94 (0.84-1.06)**

Figure 4. Outcomes in the elderly according to therapy given.

Many therapies that we administer in the hospital are viewed to be standard of care for the patient with myocardial infarction. Very few of the studies evaluating the efficacies of these therapies were performed in the older patient. These acute therapies include aspirin, beta-blocker administration, and intravenous heparin, acute catheterization for determination for anatomy and subsequent therapy and use of glycoprotein 2b3a inhibitors (Figure 4) (14). The use of glycoprotein 2b3a inhibitors is largely limited to adjunctive care in patients undergoing percutaneous interventions. Even in older patients, the use of aspirin, beta-blocker and catheterization was associated with a reduced mortality rate. The Crusade investigators looked at the adherence to therapies. In patients who are over the age of 90 and those that are between 75 and 89, the more likely you are to have received one of these therapies, the lower your mortality rate.

The most common reasons cited to withhold catheterization were comorbidities and other advanced disorders, which may include memory disorders, renal failure or cancer. Advanced age was an exclusion for catheterization (an interesting observation for

a study with a purpose of evaluating care in elderly patients). Those patients with "do not resuscitate orders" did not undergo catheterization.

In another study, the prescription of aspirin, beta-blocks, statin and cardiac catheterization were examined in patients presenting with myocardial infarction. This trial looked at patients less than 70 years, between 70 and 80 years and greater than 80-years-old (15). While aspirin use was given in all patient subgroups, there was a drop off in those individuals greater than 80. Similarly beta-blockers were less commonly used in the older age groups possibly due to side effects or due to underlying conduction defect. There was a significant reduction in prescription of statin therapy. The biggest discrepancy in the prescription of therapies for the patients is for cardiac catheterization.

Until the last few years it has not been clear whether or not early invasive management resulted in improved outcomes following non ST elevation myocardial infarction. In the study by Bach et al, patients randomly assigned to early invasive management who were over the age of 65 fared significantly better than those who did not undergo catheterization (16). Obviously those who do not undergo cardiac catheterization will not undergo subsequent either percutaneous intervention or coronary artery bypass grafting.

Older patients are more likely to suffer recurrent myocardial infarction after presenting to the hospital for acute coronary syndromes (17). This increase in myocardial infarction is decreased by the application of percutaneous coronary intervention or CABG during the index hospitalization. This is true across all age groups and in fact there is a larger absolute reduction in subsequent myocardial infarction in those individuals over the age of 80. Revascularization reduces the risk of death also in those elderly individuals who present with acute coronary syndromes. There is frequently significant concern regarding the risk of stroke with the use of multiple antithrombotic therapies in this population. Fortunately, there is no significant data suggesting increased stroke rates in older patients who undergo percutaneous intervention/ bypass surgery versus those who do not undergo revascularization.

The positive message of improved outcomes with aggressive management of acute coronary syndromes must be tempered by the risk of bleeding in this population. In fast, percutaneous coronary intervention may be withheld because of the concern of the risk of bleeding in elderly patients. Aging is associated with increased tendency towards bleeding and adverse responses to antithrombotic agents. This can be due to increased anticoagulant proteins and clotting factors as well as a diminished local vascular response to injury with loss of vascular integrity. There is also a decrease in fibrinolytic capacity with age as well. In cardiovascular disorders there are a variety of different antithrombotic therapies or risk factors that are associated with increase in bleeding risk. These include aspirin, heparin, clopidogrel, glycoprotein 2b3a inhibitors and catheterization. In the Crusade Initiative, older patients had increased bleeding risk. In addition, the more antithrombotic risk factors you have, the greater your risk of bleeding.

Bleeding risk post catheterization can be quantitated in various ways including looking at access site bleeding, blood transfusion, major bleeding or minor bleeding. In this a cross sectional study of elderly patients receiving various antithrombotic therapies, bleeding risk does increase across all ages and is noted for all types of bleeding. This bleeding risk is important because those individuals that have major bleeding following a myocardial infarction also have increased mortality rates (Figure 5) (18). Thus, aggressive management of myocardial infarction is generally good in the elderly unless bleeding occurs.

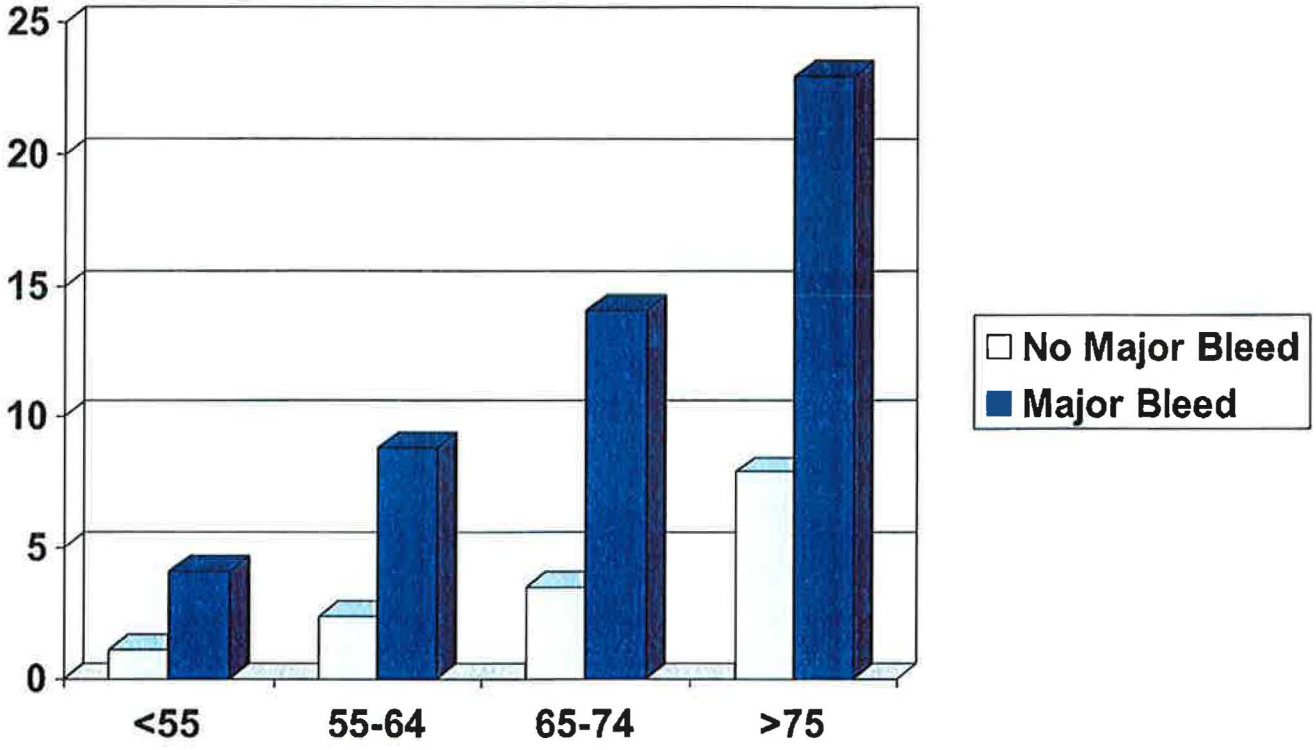

Figure 5. Risk of mortality associated with bleeding post myocardial infarction

SUMMARY

Insufficient data is available to help us guide therapies of cardiovascular disorders in the elderly patient. These studies should examine the selection and dosing of therapies for treating aortic stenosis, atrial fibrillation, and coronary disease. Since complications are more common in the elderly patient, we need better information on the management of these complications and how to decrease their occurrence.

Until more information is available, it should be recognized that symptomatic elderly patients with aortic stenosis should undergo aortic valve surgery. This therapy results in an improvement in survival as well as improved quality of life. Comorbidities

may limit surgery in some patients; percutaneous aortic valve surgery may represent a viable alternative for this group in the future.

The hazard of atrial fibrillation is largely related to the risk of stroke. Warfarin is the most effective therapy known to reduce the risk of stroke, but is associated with increased bleeding risk in the elderly. The risk: benefit assessment for most elderly patients favors systemic anticoagulation and we need to be not only more liberal in prescribing this therapy but more vigilant in monitoring its safety.

Management of the elderly patient with myocardial infarction should include the standard therapies used in younger patients. Cardiac catheterization with percutaneous coronary intervention performed after presentation for myocardial infarction results in improved outcome in these patients. Prescription of standard preventative therapies including aspirin, beta blockers, and statins is not optimal in the older patient. Improving use of these medications will likely improve patient outcomes.

Presbycardia will be seen in increasing numbers over the next few decades. Aggressive thoughtful care can result in improved patient outcomes and quality of life.

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