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Coronary Artery Disease in the Elderly

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1. Introduction

Cardiovascular (CV) disease is the most frequent diagnosis in elderly people and it is the leading cause of death in both men and women older than 65 years of age. The high morbidity and mortality from cardiovascular disease warrant aggressive approaches to prevention and treatment that have been shown to be effective in older patients. Increased emphasis is being placed on preventive strategies for cardiovascular disease the elderly and improving the quality of care using therapies that were not designed for them. Historically physicians are prone to more conservative and use less aggressive therapies. Nevertheless, given their high-risk status, the elderly with heart disease are also a group that is very likely to experience improvements in clinical outcomes and functional status with revascularization. However, they are also more likely to experience procedural complications, owing to age-related physiological changes, frailty, and comorbidities. As such, the decision on when to pursue revascularization in elderly patients, and if so, how to revascularize, is complex.

The limited representation of elderly patients in clinical trials has resulted in fewer data about the effectiveness of various strategies in this population. Moreover, the atypical clinical presentations of coronary artery disease (CAD) in elderly patients, and the consequent difficulty in diagnosis, have resulted in suboptimal implementation of treatment and secondary preventive measures by health care professionals. Increased investigation at both the basic level and clinical level is necessary to identify therapies that will benefit older patients on the basis of both the pathophysiology of age-related CV disease and the frequent presence of comorbid diseases.

It is important to assess the risk of the patient individually to provide the best treatment strategy. Decisions regarding medical therapy versus revascularization; PCI or CABG should be based not only on symptoms, severity of CAD, left ventricular function but in the context of other comorbidities, lifestyle, projected life span, and preferences. In hospitals without PCI capability reperfusion therapy with thrombolytic should be considered, regarding thrombolytic drugs especially in very old patients, streptokinase should be considered.

The purpose of this chapter is to explain the therapeutic approaches and considerations that must be taken when dealing with an elderly patient with CAD. To illustrate this we reviewed bibliographic databases such as medline and pubmed, with key words coronary artery disease, revascularization, thombolysis, coronary percutaneus intervention and elderly for our search.

Finally, we will demonstrate our experience in Chile with one of the few clinical trials in our country that includes the elderly as their main subjects of study, comparing different approaches of treatment towards CAD in this specific group of patients.

2. Epidemiology

The worldwide population of people 65 years of age and older are projected to increase to 973 million or 12 percent by 2030 and to 20 percent of the population by 2050. Most definitions of elderly are based on chronological age. The World Health Organization uses 60 years of age to define elderly whereas most classifications use the age of 65 years, but patients older than 75 years are more fragile.

Cardiovascular disease is the most important cause of death in both men and women in this age group. More than 80 percent of all deaths attributable to cardiovascular diseases occur in people older than 65 years with approximately 60 percent of deaths in patients older than 75 years old. High blood pressure, heart failure with preserved systolic function and multivessel disease are very common. Systolic blood pressure increases with aging, it occurs in one half to two thirds of people older than 65 years of age, and heart failure (HF) is the most frequent hospital discharge diagnosis among older patients. In addition, cardiovascular disease in the elderly usually is associated with other medical conditions given that eighty percent of people over 65 years old have at least one chronic medical condition, and half have at least two.

The prevalence and severity of CAD increases with age in both men and women. A significant number of people older than the age of 60 years have significant CAD with increasing prevalence of left main or triple-vessel disease. Evidence of myocardial infarction (MI), abnormal echocardiogram, carotid intimal thickness, or abnormal ankle-brachial index have been detected in 22 percent of women and 33 percent of men aged 65 to 70 years and 43 percent of women and 45 percent of men older than age 85 years. In addition, aging is associated to increased arterial stiffness and increased pulse pressure. There is an increase in fibrinogen, coagulation factors, platelet activity, increase in the levels of plasminogen activator inhibitor, resulting in impaired fibrinolysis. Inflammatory cytokines, endothelial dysfunction potentiate the development of atherosclerosis.

3. Clinical presentation

After the age of 80, a minority of patients complain of chest pain. Symptoms like angina are less frequent, ischaemia is more likely to be silent and pain description differs from the classic substernal pressure. Symptoms may be described primarily as dyspnea, shoulder or back pain, weakness, fatigue or epigastric discomfort. Some patients describe symptoms with effort, but others may not, because of limited physical activity, mental impairment or altered manifestations of pain caused by diabetes or age changes. Symptoms may occur at rest or during mental stress. Silent ischaemia has been reported in 20 to 50 percent of patients 65 years or older. Treadmill exercise testing can provide information in patients able to exercise but the specificity is reduced because of a high prevalence of resting ST-T abnormalities on the ECG of elderly patients. Exercise results can be enhanced by the use of modified low-intensity exercise protocols. Stress echocardiography or nuclear studies are very useful in case of exercise limitation or ECG alterations. The presence of coronary calcifications is not a clear predictor of cardiac events. There is a high prevalence of

hypertension, diabetes, obesity, and inactivity in the elderly and efforts in improving diet and activity levels, smoking cessation, treatment of hypertension and diabetes, are better than screening with vascular imaging studies in the asymptomatic elderly.

4. Treatment

4.1 Medical therapy

In addition to life style changes and treatment of CAD risk factors, medical therapy is the main choice of treatment in most elderly patients, however revascularization, whether percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) should not be neglected only because of age, and should be indicated as recommended by the guidelines. Aspirin, clopidogrel, nitrates, beta blockers, calcium antagonists, ACE inhibitors, statins and partial free fatty acid inhibitors have demonstrated benefits. Precautions must be taken regarding renal and hepatic function, hypotension and interaction with other medications.

The U.S. Preventive Service Task Force recommends low doses of aspirin as primary prevention in men age 45 to 79 years old and women age 55 to 79 years old for prevention of myocardial infarction or stroke respectively when there are risks of MI or stroke but there is insufficient information regarding aspirin in primary prevention in the very elderly. For secondary prevention, there is strong evidence for the use of aspirin, given in low doses there is less risk of bleeding.

Nitrates, beta blockers, ACE inhibitors and angiotensin receptor blockers can exacerbate hypotension or postural hypotension in the elderly. Also, B-blockers may produce central nervous system (CNS) effects and calcium channel blockers, especially the dihydropyridines, can produce edema which is more frequent in the older patient. Verapamil can exacerbate constipation. Both beta blockers and nondihydropyridine calcium channel blockers should be avoided in the presence of sick sinus node disease.

Of the two early large primary prevention trials of lipid lowering with HMG CoA reductase inhibitors, one only enrolled men up to age 64 and the other had an upper age cutoff of 73 years of age. In the ALLHAT cholesterol study, both the pravastatin and usual care groups had a substantial decrease in cholesterol levels. The 9,6 percent difference in cholesterol levels between the groups was insufficient to produce significant reductions in deaths (14,9% versus 15,3%) and produced only a small, non-significant decrease in the rates of heart attacks and strokes in the statin group relative to usual care (ALLHAT Collaborative Research Group, 2002). The Lipid Lowering Arm of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT-LLA) tested the effects of lipid lowering in hypertensive patients up to age 79 years without increased lipids but with at least three additional CAD risk factors. ASCOT-LLA was stopped after 3.3 years because of a significant reduction in the primary end point of nonfatal MI and fatal CAD (Sever et al., 2003). Regarding secondary prevention, The Heart Protection Study demonstrated a 27% decrease in non-fatal MI and coronary death in patients older than 70 years of age. The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) a study with almost equal numbers of men and women aged 70 to 82 years who either had CAD or were at risk for cardiac events showed a significant reduction in mortality, nonfatal MI, and stroke (Shepherd et al., 2002). In summary, older patients should not be excluded from statin therapy, but caution must be taken in frail patients because of a higher risk of myopathy.

4.1.1 Considerations when prescribing medications in older patients

- Knowledge of collateral effects of cardiovascular medications, specially hypotension, bradicardia or exacerbation electrical conductance defects.
- Knowledge of non cardiac medications its effects and drug interaction with cardiovascular drugs.
- Loading doses should be reduced.
- Body surface area should be used to estimate dose (loading and maintenance).
- Estimate glomerular filtration to guide dosing of medications.
- Consider lower doses with hepatically cleared drugs.
- Time between dosages should be adjusted.
- Assess non adherence of medications.
- Assess adequate financial coverage.

4.2 Revascularization

4.2.1 Cabg vs pci

There is increased experience with both PCI and CABG in older patients. Half of all PCI and CABG procedures are performed in patients older than 65 years of age, with one third of coronary artery revascularization procedures performed in patients older than 70 years of age.

The Bypass Angioplasty Revascularization Investigation (BARI) trial of patients with multivessel disease included 39% patients between the ages of 65 and 80 (BARI Investigators, 2007). It demonstrated that this group of patients had a higher early morbidity and mortality after CABG compared with PCI but greater angina relief and fewer repeat procedures after CABG. Stroke was more common after CABG (1.7% versus 0.2%, $p = 0.015$). Heart failure or pulmonary edema were more common after PTCA (4.0 versus 1.3%, $p = 0.011$) and the 5-year survival rate was more than 80 percent for both procedures, with no difference between both treatments in non-diabetics but lower than in younger patients.

The Northern New England Cardiovascular Disease Study Group included nearly 1693 patients older than the age of 80 years who were treated for two or three vessel disease, found better in-hospital mortality and short-term survival for PCI versus CABG. For those surviving past 6 months, survival was better for patients who underwent CABG. PCI data were from bare metal stent implants, and CABG data were from on-pump procedures in more than 85 percent (Dacey et al, 2006).

Elderly patients who require PCI are more likely to have complex, multivessel disease requiring multilession interventions, than their younger counterparts. Nonfatal complications with procedures increase with age. PCI is associated with a slightly less than 1 percent risk of permanent stroke or coma, and CABG is associated with a 3 to 6 percent incidence of permanent stroke or coma in patients older than 75 years of age. Interventions on calcified plaques are associated with increased frequency of periprocedural complications, decreased procedural success rates and inadequate stent expansion and increased rates of restenosis. Tortuous and calcified vessels increase the difficulty of coronary device deployment and the risk of complications, including those with vascular access. Decreased vasodilatory response to nitroglycerin, increased plasma levels of activated coagulation factors and thrombin-antithrombin complexes are higher in older than in younger adults and platelet reactivity is also enhanced. These changes contribute to increased risk of acute thrombosis.

As stated before, the metabolism of many drugs is reduced and renal drug clearance is also compromised with increasing age. The decline in renal function affects the

clearanceofanti-thrombotic drugs used in patients undergoing PCI, such as low-molecular-weight heparin and glycoprotein (GP) IIb/ IIIa receptor inhibitors, and might, in part, explain the increased risk of bleeding seen when these agents are used in the elderly. Renal protection from contrast to prevent renal failure must be taken in consideration with pre and post procedure hydration with saline solution and the use of the lower dose of isosmolar contrast.

Regarding CABG in the postoperative period, longer durations of ventilatory support, greater need for inotropic support and intraaortic balloon placement, greater incidence of atrial fibrillation, bleeding, renal failure, perioperative infarction, infection, stroke and delirium are seen in older patients compared with younger patients. The duration of disability and rehabilitation after procedures is usually longer, the risk of postoperative cognitive impairment in older patients detected with neuropsychological testing has been estimated as 25 to 50 percent after CABG. Depression is not uncommon as the need for prolonged hospitalization and home-assistance after discharge. The potential need for extended hospitalization, in-home assistance and depression after surgery should be assessed. Therefore there is an increase in mortality and morbidity especially during the first 30 days.

Risk assessment should be evaluated with the Society of Thoracic Surgeons risk model (STS score) or (EuroSCORE). Nielssen et al, in 2006 published a study that compared these two risk algorithms for CABG. Risk factors for all adult patients undergoing heart surgery at the University Hospital of Lund between 1996 and 2001 were collected prospectively at preoperative admission. The study included 4497 coronary artery bypass-only operations and the average age was 66.4 ± 9.3 years (range 31 to 90 years). In this study the EuroSCORE had a significantly better discriminatory power to predict 30-day mortality than the STS risk algorithm for patients undergoing coronary artery bypass.

The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation trial (COURAGE) proved that the addition of PCI to optimum medical therapy did not reduce long-term rates of death, nonfatal MI, and hospitalization for ACS in patients with stable angina but showed that patients with severe angina who received PCI had greater improvements in angina symptoms and quality of life within the first 36 months than those who received medical therapy alone (Boden et al, *2007)*. Among the patients over the age of 65 years, a similar lack of benefit of PCI was shown (OR 1.10, 95% CI 0.83–1.46). In a subgroup analysis of 314 patients, studied with nuclear perfusion, PCI significantly reduced the rate of ischaemia in those with 10% or more of myocardium at risk. In this group, there was a lower risk of death and MI. An assessment of ischemic burden might be useful when deciding between invasive and medical management (Shaw et al, 2008).

In the trial of Invasive versus Medical Therapy in Elderly Patients (TIME), patients 85 years and older, with chronic angina who were refractory to at least two antiangina medications, were randomly assigned to an invasive strategy (PCI or CABG) or to conservative medical therapy (TIME Investigators, 2001). The analysis demonstrated a decreased severity of angina in both groups, but death, non fatal MI or hospital admission for acute coronary syndrome was 19% in the invasive group versus 49% in the conservative group. In the Alberta Project for Outcomes Assessment in Coronary Heart Disease (APPROACH), in which the health status of 21,573 patients with CAD treated with PCI, CABG surgery, or medical therapy was measured, among the 6,181 patients aged 70 years or older the improvements in health status observed with coronary revascularization was better at four years than in those patients treated medically, even in patients over 80 years of age (Graham et al, 2006).

ACC/AHA Coronary Artery Bypass Surgery and PCI Guidelines conclude that age alone should not be used as the sole criterion when considering revascularization procedures. Individualized prognostic information based on multiple clinical factors and respect for patient preference in the decision-making process has a clear role.

5. Acute coronary syndromes

About 60 percent of hospital admissions for acute myocardial infarction (AMI) occur in people older than 65 years, and account for approximately 85 percent of deaths caused by AMI. With increasing age, the gender composition of patients presenting with AMI changes from predominantly men in the middle age, to an equal number of men and women and a majority of women in patients older than 80 years of age. Mortality is higher in older women than in older men with AMI, as are adverse outcomes with thrombolytics, and glycoprotein (GP) IIb/IIIa inhibitors. As age increases, there are more patients with functional limitation, heart failure, prior coronary disease, renal insufficiency and patients with prior revascularization. Fewer older patients present with chest pain or ST elevation on ECG within 6 hours of symptom onset.

5.1 Thrombolysis

Most randomized clinical trials of thrombolysis have enrolled few patients older than 75 years of age. In a study of 14,341 of Medicare patients older than 65 years with ST elevation MI or left bundle bunch block, treated with thrombolytics there was a significant reduction of mortality at one year, but with 1.5 rate of intracranial hemorrhage. The Fibrinolytics Therapy Trialists´ found a 15% percent reduction in mortality in patients older than 65 years, and there were 34 lives saved per 1000 patients. This result was more effective than in younger patients in whom 11 lives were saved per 1000 patients. Some studies that include patients up to 75 years of age have demonstrated that fibrinolytic, antiplatelet, and antithrombin therapy is associated with a survival advantage compared with placebo that may be similar to than that seen in younger patients. The Global Utilization of Streptokinase and Tissue plasminogen activator for Ocluded coronary arteries-I (GUSTO I) found a significant absolute reduction in mortality with thrombolysis, specially with plasminogen activator in patients 65 to 85 years of age. In patients older than 85 there was a beneficial trend with streptokinase. Finally, in a registry of Swedish Hearts Intensive Care Admissions, in a group of 6,891 patients 75 years and older, fibrolytic therapy was associated with a 13% relative reduction in the composite of mortality and cerebral bleeding complications at one year. Complication of minor and major bleeding, intracranial bleeding and transfusion rates are higher in older patients compared with younger patients with all agents and some subgroups may not have an overall benefit from use of thrombolytics. Those with high risk for ICH include patients older than 75 years, women, African Americans, small size, prior stroke, systolic blood pressure >160 mm Hg. Fibrin-specific agents such as tissue plasminogen activator are also associated with increased stroke risk caused by ICH in the older than 75 year age group. Improper dosing of antiplatelet, antithrombin agents or combinations with low-molecular-weight heparins or GP IIB/IIIa inhibitors increase as well the risk of bleeding. Even with dose adjustments, however, the risk of bleeding appears increased in older patients.

5.2 Antithrombotic agents

Trial data shows that aspirin reduces mortality in patients older than 70 years and is recommended for routine administration to older patients with acute MI, although older

patients have been less likely to receive aspirin than younger patients in routine clinical practice. The addition of clopidogrel to aspirin reduces major events, with similar absolute reductions in patients younger and older than 65 years. In the Clopidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT), a chinese megatrial with almost 46,000 MI patients, with 11,934 patients older than 70, in which half of the patients were treated with clopidogrel and the other half with placebo, there was a 9% reduction in the composite end point of death, reinfarction and stroke without an increase in serious bleeding. It also showed a significant reduction in mortality in the patients treated with clopidogrel (COMMIT Collaborative Group, 2005). Patients were treated with 75 mg. of clopidogrel without the 300 milligrams loading dose. Low- dose of aspirin (≤ 100mg.) should be used when combined with clopidogrel. Prasugrel is not recomended in patients over 75 years and there is not enough information on the safety about ticagrelor. GP IIb/IIIa inhibitors appear efficacious in older patients but in patients over age 75 years when given in combination with thrombolytics there is an increased risk of bleeding. Bleeding is about twofold greater in older patients undergoing PCI who receive GP IIb/IIIa inhibitors compared with patients who do not, with intracranial bleeding as the most common site of fatal bleeds.

Antiplatelet and antithrombin agents have narrow therapeutic windows dosing should be based on weight and renal function. Prospective observational analyses have shown that more than 40 percent of patients with acute coronary syndromes receiving unfractionated heparin, low-molecular-weight heparin, or GP IIb/IIIa inhibitors receive at least one dose in excess of guidelines. Factors associated with excess dosing were older age, female sex, renal insufficiency, low body weight, diabetes mellitus, and congestive HF. Bleeding increased relative to the degree of excess dose and to the number of agents administered in excess. Mortality is higher and length of hospital stay is longer in patients administered excess dosing and there is a close relation between bleeding and mortality. Women had twofold higher rates of major bleeding than men and are three times more likely to receive excess GP IIb/IIIa doses than men. Approximately 25 percent of the bleeding risk was attributable to excess dosing in women versus 4.4 percent in men. A randomized, controlled clinical trial for treatment of acute MI with PCI with eptifibatide administration has also reported increased bleeding resulting from lack of dose adjustment for reduced renal function (Kirtane et al, 2006). Fondaparinux and bivalirudin have shown less risk of bleeding in patients with ST-elevation MI (STEMI) and non-STEMI, including the elderly.

Primary angioplasty in experienced centers is associated with improved outcomes compared with thrombolytic strategies in elderly patients with STEMI. Even when mortality is reduced with primary PCI compared with thrombolytic therapy, in-hospital mortality of patients older than the age of 75 years is estimated to be fivefold higher than patients younger than 75 years, and 1-year mortality is 7-fold greater. Achieving revascularization within 90 minutes is less likely in older patients with delays in diagnosis and/or transport to experienced centers. Acute procedural success rates are also somewhat lower than in younger MI populations, there are increased risk of bleeding, complications including those at the access site, increased transfusion requirements and contrast-mediated renal dysfunction. However, PCI is preferred to fibrinolysis as a reperfusion option for elderly patients who experience STEMI.

The Global use of strategies to open Occluded Coronary Arteries (GUSTO) IIb trial was one of the first to report that PCI is superior to fibrinolysis among all age groups, and in particular that this strategy has the greatest benefit in the elderly, when all age groups are compared (Angioplasty Substudy Investigators, 1997). The National Registry of Myocardial

Infarction (NRMI)-2, evaluated 38,787 patients in which the treatment was performed within 12 hours of onset symptoms with either an intravenous thrombolytic agent or PCI. Of these, 10,2% were treated with streptokinase or anistreplase, 77,1% were treated with alteplase and 12,7% underwent primary PCI. In patients with STEMI who were aged 75 years, this study demonstrated that there was a lower risk of the combined end points of death and nonfatal stroke with primary PCI than with fibrinolysis, owing primarily to a higher rate of intracranial bleeding (2.5%) observed in the fibrinolysis group (Tiefenbrunn, 1998). In the Senior Primary Angioplasty in Myocardial Infarction (Senior PAMI) study, PCI was superior to thrombolytic therapy from ages 65 to 79 with no advantage of primary PCI over thrombolysis in those older than 80 years of age (Grines, 2005).In the observational setting, the Global Registry of Acute Coronary Events (GRACE) showed lower adjusted in-hospital mortality (or 0.62, 95% Ci 0.39–0.96) for primary PCI compared with fibrinolysis among 2,975 patients with STEMI who were aged ≥70 years (Mehta, et al, 2004). The Tratamiento del Infarto Agudo del Miocardio en Ancianos (TRIANA) compared primary PCI and fibrinolysis in very old patients (mean age 81). It enrolled 266 patients, 134 allocated to PCI and 132 to fibrinolysis, both groups were well balanced in baseline characteristics, and it demonstrated that recurrent ischemia was less common in PCI-treated patients (0.8 vs. 9.7%, P< 0,001). No differences were found in major bleeds. A pooled analysis with two previous reperfusion trials performed in older patients showed an advantage of PCI over fibrinolysis in reducing death, re-infarction, or stroke at 30 days (Bueno, et al, 2010**).** Finally, in a meta-analysis of 22 randomized trials (n= 6,763) evaluating the effects of primary PCI versus fibrinolysis, de Boer et al showed a mortality reduction favoring primary PCI in all age strata, as well as reductions in the risk of repeat MI and stroke.

Regarding non STEMI, it is the most frequent manifestation of CAD and represents the largest group of patients undergoing PCI. Despite the advances in medical and interventional treatments, the mortality and morbidity remain high and equivalent to patients with STEMI after the initial month. The ultimate goals of angiography and revascularization are mainly twofold: symptom relief, and improvement of prognosis in the short and long term. Different trials have shown that an invasive strategy reduces ischaemic endpoints mainly by reducing severe recurrent ischaemia and the clinical need for revascularization. The most recent meta-analysis of 3 randomized trials with a follow up of 5 years, showed a 19 % relative reduction in non fatal MI and death. This difference was mainly driven by reduction in MI. In these trials between 12,5% to 18,8% of the patients were over 75 years old, most of them in the high risk group, in whom the invasive therapy had the greatest effect. (Fox, 2010)

6. Drug eluting versus bare metal stents

Randomized controlled trials and pooled analyses of randomized trials in which drug eluting stents (DES) and bare metal stents (BMS) have been compared demonstrate similar acute and intermediate survival and MI outcomes among nonelderly patients. Elderly patients enrolled in these trials has been small and no dedicated randomized comparison trial of DES to BMS has been performed among patients aged >65 years. In a study of 71,965 elderly patients (mean age 75 years) undergoing PCI, in those in whom DES were used, there was lower adjusted mortality (HR 0.83, 95% Ci 0.81–0.86) than contemporary controls undergoing BMS implantation. DES-treated patients were also less likely than controls to undergo revascularization procedures within 2 years after PCI and had fewer hospitalizations for MI. In an analysis of 262,700 Medicare patients (mean age 73 years) treated at 650 hospitals from 2004

to 2006, recipients of DES (83% of whom were aged over 65 years) had lower risk adjusted mortality (HR 0.75, 95% Ci 0.72–0.79) and risk of MI (HR 0.77, 95% Ci 0.72–0.81) than BMS-treated patients, but had minimal differences in rates of repeat revascularization or bleeding.

7. Our experience in chile

We performed a study randomised, retrospective comparing DES versus BMS in elderly patients 75 years and older who underwent PCI. The clinical setting was STEMI in 40 percent of patients, non STEMI in 25 percent, stable angina in 24 percent and silent ischaemia in 11 percent. The purpose of this study was to determine whether the use of DES was associated with less mortality, MI (fatal and non fatal), angina and hospitalization of cardiac causes. One hundred and forty six patients were analyzed in which DES and BMS were implanted between the years 2003 and 2007, with a median follow up of 5.2 years. Twenty nine patients were selected in the DES group and 26 in the BMS group. The groups were comparable according to age, gender, risk factors, symptoms, ejection fraction, number of vessels affected and number of stents implanted (Table 1).

CHARACTERISTICS	BMS	DES	P
Nº OF PATIENTS	26	29	
PREVIOUS MI	6	6	NS*
DIABETES	9	14	NS*
HYPERTENSION	23	20	NS*
HIGH CHOLESTEROL	14	20	NS*
AGE	79,8	79,4	NS**
MALE	15	14	NS*
TOBACCO	2	3	NS*
PREVIOUS PCI	4	9	NS*
1 VESSEL DISEASE	12	13	NS*
2 VESSELS DISEASE	5	6	NS*
3 VESSELS DISEASE	9	10	NS*
LVEF > 50%	17	16	NS*
1 VESSEL TREATED	18	20	NS*
MORE THAN 1 VESSEL TREATED	8	9	NS*

* Chi-squared ** T- Student
NS: statistically non significant LVEF: left ventricular ejection fraction

Table 1. Baseline Characteristics

Both groups were compared according to global mortality, mortality of cardiac disease, presence of angina, MI and hospitalizations because of a cardiac disease. As shown in table 2, in this group of elderly patients in which a DES was implanted there were no differences in global mortality, MI and angina when compared to the group of patients in which a BMS was implanted. However, there was statistical significant less hospitalization because of cardiac disease and a tendency to less mortality because of cardiac disease.

	BMS	DES	P
Nº of patients	26 (100%)	29 (100%)	0,9767
Global Mortality	9 (34,6%)	11 (38%)	0, 8117
Mortality of Cardiac disease	7 (26,4%)	3(10%)	0,98
Angina	3 (11, 5 %)	4 (13, 7 %)	NS
MI	2 (7, 6 %)	3 (10, 3 %)	NS
Hospitalization because of cardiac disease	9 (34, 6%)	5 (17, 2%)	0,0001

Table 2. Results

8. Rehabilitation

The feasibility and improvement with intensive exercise interventions have been shown for both the frailest elderly residing in the community as well as in the nursing home. The Cardiac Rehabilitation in Advanced Age (CR-AGE) trial compared hospital-based cardiac rehabilitation with home-based cardiac rehabilitation in cognitively intact patients from ages 46 to 86 with recent MI (Marchionni et al., 2003). Similar improvement in total work capacity and health-related quality of life was seen with home-based rehabilitation compared with hospital-based rehabilitation in all age groups without improvement in the control group. The improvement, however, was somewhat smaller in the group older than age 75. Benefits decreased over time after hospital rehabilitation but were maintained with home cardiac rehabilitation. Complications were similar across groups, whereas costs were lower in the home rehabilitation group.

In summary, what to consider when approaching to the older patient with CAD:

1. Morbidity and mortality in the elderly with CAD and CAD treated medically or with revascularization increases with age, especially in patients older than age 75 years.
2. Special care must be taken regarding medications, dose, collateral effects, drug interactions and interaction with other comorbidities.
3. Clinically recognized CAD or heart failure confer the greatest risk for cardiac death and warrant aggressive secondary prevention strategies.
4. In STEMI patients
   - In hospitals where direct PCI can be performed rapidly by experienced operators, PCI has an advantage over thrombolysis.
   - In hospitals without PCI capability reperfusion therapy with thrombolytic should be considered, regarding thrombolytic drugs especially in very old patients, streptokinase should be considered.
   - Avoid combinations of GP IIb/IIIa inhibitors with thrombolytics. In case of low molecular heparins and thrombolytics, lower doses as recommended can be used.

- The use of antiplatelet and antithrombotic drugs is recommended according to the guidelines but a careful evaluation of the bleeding risk should be taken.
- For non STEMI patients the same care with antiplatelets and antithrombotic drugs must be taken and the same recommendations of the guidelines regarding invasive or conservative approach must be taken.

5. Decisions regarding medical therapy versus revascularization: PCI or CABG should be based not only on symptoms, severity of CAD, left ventricular function but in the context of other comorbidities, lifestyle, projected life span, and preferences.
6. In case of PCI the patient and family must be aware of the risks but some are less explained by the physician, especially lower success, renal failure, prolonged hospitalization and bleeding. The radial approach should be preferred in order to diminish this last complication.
7. In case of CABG prolonged hospitalization because respiratory, renal, central nervous system or infectious conditions and special home care should be emphasized.

9. Conclusion

CAD in the elderly is more severe and is accompanied by a high rate of comorbidities. There are a few trials that include a significant number of older patients, therefore there is little information on how to optimize treatment in this age group. There are age-associated pathophysiological changes as well different comorbidities. Physicians tend to be more conservative and use less aggressive therapies, although it has been proven that these patients have greater benefits with aggressive therapy but also complications are more common. The elderly with CAD are also a group that is very likely to experience improvements in clinical outcomes and functional status with revascularization. The decision on when to perform revascularization in elderly patients and how to revascularize, is difficult. More than one in five patients treated with percutaneous coronary intervention (PCI) are aged ≥75 years and the proportion of elderly individuals in the population is growing. Although a slight advantage of surgical over percutaneous revascularization might exist for elderly patients with multivessel coronary disease, surgical revascularization should remain an option for a selected population of elderly patients with few comorbidities.

10. Future directions

Increasing emphasis is being placed on preventive strategies for CAD in older patients and improving the quality of care using current therapies that were not designed for the elderly. A major limitation is the lack of understanding of the mechanisms underlying many age-related cardiovascular changes or diseases. Increased investigation at both the basic level and clinical level is necessary to identify therapies that will benefit older patients on the basis of both the pathophysiology of age-related CV disease and the frequent presence of comorbid diseases. Caring for patients near the end of their lives is different than caring for patients with longer life expectancies. Research and training will be necessary to achieve coordinated care for the older patient, and both medical and social factors must be considered to provide optimal care.

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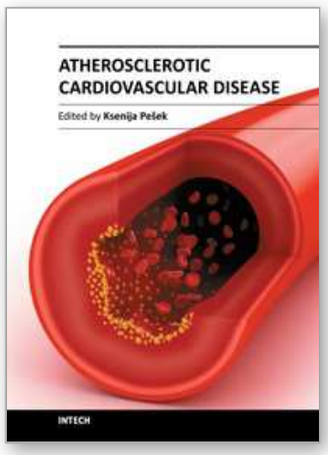

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Cardiovascular diseases (CVD) are still one of the leading causes of death in the world. The book Atherosclerotic Cardiovascular Disease is a contribution to the application of new knowledge in the area of cardiovascular diseases. The book comprises six chapters divided in three subsections, starting with the General Considerations of Cardiovascular Disease, through Diagnostic Techniques, and Specific Therapy.

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