



Current Treatment Options for Coronary Heart Disease

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Introduction

Coronary heart disease (CHD) becomes a major global public health problem since the last two decades. Although there has been recent decline in age-standardized cardiovascular mortality, the prevalence of CHD remains high due to increased life expectancy and changing in life-style of the population. CHD is the leading cause of death in the United States, responsible for nearly 20% of all deaths⁽¹⁾. Currently, CHD has been also the leading contributor for death and disability in developing countries. The World Health Organization estimates that CHD will account for 6% of the total global disease burden in 2020⁽²⁾.

The treatment for coronary heart disease aims to reduce the risk of mortality and morbidity as well as to reduce or eliminate angina pectoris, thus, allowing patients to return to normal activities. Ideally, these end points should be accomplished with minimal side effects and adequate long-term results. There are currently three well-established treatment options for CHD: medical therapy, coronary artery bypass grafting (CABG), and percutaneous coronary intervention (PCI). Throughout the last 2 decades, number of clinical trials has been conducted to compare those strategies. The last two options have been rapidly evolving. Both techniques have their own strengths and inherent weaknesses. Each is particularly beneficial in specific clinical settings. This article aims to review the evidences from the clinical trials which could provide a fair comparison for medical professionals in objectively choosing the best treatment option for patients with CHD.

Medical Therapy

The primary consideration in choosing pharmacological agents for treatment of CHD should be to improve prognosis. Aspirin and lipid-lowering therapy have been proved to reduce the risk of death and non-fatal myocardial infarction (MI) in both primary and secondary prevention setting. The data strongly suggest that cardiac events will also be reduced among patients with chronic stable angina. The ACC/AHA guidelines suggest that aspirin (75 to 325 mg daily) should be administered routinely to all patients without contraindications. Clopidogrel can be prescribed in those having absolute contraindication to aspirin⁽¹⁾. The Cholesterol and Recurrent Events (CARE) trial and Scandinavian Simvastatin Survival Study (4S) have established the benefit of aggressive lipid-lowering therapy for most patients with CHD, even when LDL levels are within the considered acceptable range for

patients in primary prevention setting. In addition, the Medical Research Council/British Heart Foundation (MRC/BHF) Heart Protection Study conducted in 20,536 high-risk adults in the United Kingdom revealed that adding simvastatin 40 mg to existing treatments reduced the rates of MI, stroke, or revascularization by approximately 24%. Angiotensin-converting enzyme inhibitors are also recommended for all patients with CHD and asymptomatic patients with CHD who also have diabetes or left ventricular systolic dysfunction. The Heart Outcomes Prevention Evaluation (HOPE) trial confirm that the use of ramipril (10 mg/day) can reduce the composite risk of cardiovascular death, MI, and stroke by approximately 25% in patients at high risk for or with current vascular disease without heart failure, regardless of age, sex, or coexisting disease. On the basis of their beneficial effects on morbidity and mortality, beta-blockers should be strongly considered as initial therapy for chronic stable angina, as secondary prevention in post-MI patients, and as a means to reduce morbidity and mortality among patients with hypertension. Long-acting or slow-release calcium antagonists are indicated to relieve symptoms in patients with chronic stable angina without enhancing the risk of adverse cardiac events. They are often preferable than long-acting nitrates for maintenance therapy due to their sustained effects. Short-acting nitrates do not lose their effect on symptom relief, but long-acting nitrates may produce tolerance^(1,3).

Coronary Artery Bypass Grafting

The first CABG to the right coronary artery using a reverse segment of saphenous vein was performed by Sabiston in 1962. Although the patient died due to cerebrovascular accident, the procedure itself was successful. DeBakey performed the first complete CABG as a bailout procedure after a carotid endarterectomy⁽⁴⁾. Subsequently, Favaloro in Cleveland Clinic refined the use of reversed saphenous vein grafts for coronary bypass. Kolessov and Green were the first who used internal mammary artery as bypass graft. Subsequently, the number of CABG has markedly increased. Currently, more than 500,000 operations are performed in the United States every year with excellent results⁽⁵⁾. Even so, many physicians still attempt to avoid recommending CABG to their patients. This may be in part a result of the perception that CABG is associated with high mortality risk. This perception has recently been challenged with large published studies demonstrating mortality risk of 1.2% to 1.7% for isolated CABG^(6,7). Some limitations of CABG include costs



associated with preoperative and postoperative care, the need for several days of hospitalization (including intensive care), rehabilitation, and delayed or inability to return to work quickly. Since the average patency time of venous bypass grafts is around 7 - 10 years; some patients may require repeat revascularization. In the mid-1990s two new surgical techniques have been introduced in attempts to reduce the invasiveness of the standard CABG procedure. Revascularization either on an arrested heart with peripheral cannulation through a small access incision (port access) or on a beating heart with a limited access approach (MIDCABG) becomes emerging. However, the lack of demonstrated benefit and significant technical challenge associated with the port access approach hamper its widely application. Similar restriction also happens to MIDCABG procedure since it is not only technically challenging but also its inability to perform complete myocardial revascularization. However, the recognition of improved outcomes in selected patients served as an impetus to develop off-pump coronary artery bypass (OPCAB) procedure as a treatment option for patients with multi-vessel CHD. Many other techniques, such as: complete arterial revascularization, mechanical anastomosis connector, robotic assist systems, stem cell implantation and genetic therapy for preventing vein graft disease are of current research interest.

Percutaneous Coronary Intervention

Werner Forssman inserted a catheter into his own basilic vein and threaded it to his right atrium for the purpose of 'intracardiac drug injection' in 1929. Later on, diagnostic cardiac catheterization was developed by Courmand, Sones, and Judkins. In 1964, Dotter and Judkins successfully dilated peripheral atherosclerotic lesions using progressively larger coaxial dilators. In 1974, Grüntzig developed the double lumen catheter and performed the first percutaneous dilation of a human coronary artery in 1977⁽⁸⁾. PCI is considered providing less invasive approach and offers shorter hospital stay or faster recovery. During earlier period, the quality of PCI was limited by lack of user-friendly and lesion-suitable technical equipment. Dissection and acute or threatened closure result in major morbidity. Mortality was sufficiently frequent and unpredictable. Therefore, in many institutions a staffed operating room was always kept empty for emergency surgery in case complications exist. The major limiting factor of PCI is the occurrence of restenosis in about 30–60% of patients, depending on clinical risk factors, lesion characteristics and technical aspects of the intervention⁽⁹⁾. Newer interventional techniques such as stents, directional, rotational, laser atherectomy, thrombectomy devices and drug-eluting stents (DES) have been introduced into clinical practice with better results.

Medical Therapy versus CABG

Three large randomized trials⁽¹⁰⁻¹²⁾, which included patients with stable angina and single - or multi - vessel CHD for either medical or surgical therapy, along with several observational studies and a meta-analysis⁽¹³⁾, have yielded consistent results and established

the role of CABG as a solid treatment option for CHD. CABG resulted in substantially lower mortality rates at 5-, 7-, and 10-years compared to medical therapy. Patients with left main coronary artery disease, three-vessel CHD with impaired left ventricular function, diabetes mellitus, and unstable angina pectoris derive the greatest benefit from CABG.

Medical Therapy versus PCI

Two randomized clinical trials^(14,15), including low-risk patients who were randomized to either medical therapy or PTCA, have been published. Mortality rates were similar in both groups. Patients who underwent PTCA were more likely to be free of angina. In the Asymptomatic Cardiac Ischemia Pilot trial⁽¹⁶⁾, patients with CHD who were free of angina and had evidence of ischemia on electrocardiography or stress testing were randomized to either medical therapy or revascularization (percutaneous or surgical depending on the operator). Patients who underwent revascularization had lower mortality, MI, and hospitalization rates than the medically treated patients. The Medicine, Angioplasty or Surgery Study was a three-arm trial that compared PTCA, medical therapy, and CABG using LIMA graft in patients with isolated severe proximal LAD stenosis⁽¹⁷⁾. There were no differences in mortality risk or MI among all three groups. Patients who underwent CABG or PTCA were more likely to be symptom-free than those medically treated. Repeat revascularizations were higher in the PTCA and medically treated groups. In the Atorvastatin Versus Revascularization Treatment trial⁽¹⁸⁾, low-risk patients who were randomized to aggressive lipid-lowering therapy with atorvastatin tended to have fewer ischemic events than those who received angioplasty along with usual medical care. A recent randomized trial involving 2,287 patients who had objective evidence of MI and significant CHD at 50 American and Canadian centers demonstrated that PCI did not reduce the risk of death, MI, or other major cardiovascular events when added to optimal medical therapy in patients with stable CHD⁽¹⁹⁾.

PCI versus CABG

Several randomized trials, comprising more than 5,000 patients, have compared PCI and CABG in the management of single- and multi-vessel CHD^(17,20-27). Despite differences in design and inclusion criteria, several conclusions can be drawn from these trials, in addition to two meta-analyses performed later^(28,29). There were no significant differences in mortality or combined endpoint of death and non-fatal MI between PCI and CABG. Patients undergoing initial PCI are more likely to require repeat revascularization (either CABG or PCI) than patients undergoing initial CABG. Initial costs are lower in the PCI group but tend to equalize later, owing to the increased repeat revascularizations. More importantly, patients with treated diabetes mellitus seem to have better survival from initial CABG than PCI. Recent long-term follow-up results have been published^(30,31). More recent data emphasize previous findings and confirm the similar survival achieved by both strategies, except in the diabetic patients who



benefit more from initial CABG. They also show that the rates of repeat revascularization tend to become similar for both strategies on long-term follow-up, probably due to late vein graft failure in the CABG group. The Stent or Surgery trial has demonstrated an early survival advantage for CABG (32). This finding is supported by recent meta-analysis from 13 trials with 7,964 patients (33). When compared with PCI, CABG is associated with lower 5-year mortality, less angina, and fewer repeat revascularizations. CABG provided a survival advantage at 5 - 8 years for patients with multi-vessel CHD, and at 4 years for diabetic patients.

The recent development of anti-proliferative DES is a major breakthrough in preventing restenosis after initial PCI. DES prevents neointimal proliferation, thereby, decreasing restenosis and repeat revascularization. Randomized trials using both sirolimus-and paclitaxel-eluting stents have shown significant reductions of repeat revascularization in target lesion. A meta-analysis confirms these aggregate reductions in repeat revascularization, but it does not detect any mortality benefit (34). Although several different drug-eluting stents are under investigation, sirolimus and paclitaxel account for the majority of existing clinical data, and are now commercially available. Clearly, not all of DES is promising. At least three clinical trials with alternative drug formulations have been discontinued due to poor effects. The long-term effects of DES implantation remain unknown. The growing use of DES not only produces clinical benefits for certain patients, but also creates financial crises for many health care systems. DES cost 3 - 7 times higher than their uncoated predecessors.

Conclusion

Despite increased popularity of PCI, CABG remains an important treatment option for CHD. Further evidence on long-term efficacy and safety of some DES, especially in high-risk subgroups, is warranted. Meanwhile, intensive communication between medical professionals who involve in providing medical care, in term of objectively choosing the best treatment option for specified patients with CHD, is of highly necessary. One can be sure that most of the patients with CHD will benefit from each treatment options that continue to advance and improve.

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