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Cost-effectiveness of medical, endovascular and surgical management of peripheral vascular disease☆

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ABSTRACT

Peripheral arterial disease (PAD) is responsible for 20% of all US hospital admissions. Management of PAD has evolved over time to include many medical and transcatheter interventions in addition to the traditional surgical approach. Non-invasive interventions including supervised exercise programs and antiplatelets use are economically attractive therapies that should be considered in all patients at risk. While surgery offers so far a clinically and economically appropriate option, the improvement of percutaneous transluminal angioplasty (PTA) technique with the addition of drug-coated balloons offers a reasonably clinically and economically attractive alternative that will continue to evolve in the future.

1. Introduction

Admissions for peripheral artery disease (PAD) have been increasing and are currently responsible for approximately 20% of all U.S. hospital admissions. Data analysis of over 2 million hospital admissions for PAD between 2001 and 2007 showed that the choice of treatment has dramatically changed, with a 78% increase in endovascular procedures, and a concomitant decrease in open bypass and amputations [1]. That trend was associated with a change in the distribution of cases among different specialties involved in performing them. Between 1998 and 2005, there was a 6-fold drop in peripheral procedures performed by interventional radiologists (5.6% of all cases in 2005), with a 3-fold increase for interventional cardiologists (29% of all cases), and a 2-fold increase for vascular surgeons (43% of all cases) [2]. The number of interventional laboratories that have the capability to do peripheral vascular interventions is rapidly growing, with many fellowship programs now offering additional training in these techniques. Advances in technology, use of bare metal stents and atherectomy, and intravascular imaging have helped to increase success and reduce complications. It is estimated by industry that peripheral interventions will grow an average of 8% per year over the next 4 years [3].

1.1. Cost effectiveness analysis and decision making

The primary goal of cost-effectiveness analysis is to evaluate different health care intervention options in common terms so that policy and other decision makers can be informed of the most efficient method of producing extra health benefits from among the alternative ways that health care dollars can be distributed. The metric used to assess incremental cost effectiveness is the Incremental Cost-effectiveness Ratio (ICER). An ICER is defined as the ratio of incremental costs to incremental health benefits of treatment 1 compared to treatment 2, or ICER = (C1 – C2)/(HB1 – HB2); where C1 and C2 are cost for treatments 1 and 2, respectively and HB is the health benefit of treatments 1 and 2, respectively [4].

The ICER defines the cost that should be assumed for gaining one unit of output. In other words, if one of the alternatives is the usual practice, then it will tell us how much it will cost to gain a unit of outcome when moving from the usual practice to a new alternative. The health benefit may be measured in any sensible unit, such number of MIs averted, but most studies use the conventional option of measuring clinical benefits as either the number of added life-years (LYs) or quality adjusted life years (QALYs) [4,5]. Both of these approaches require estimation of life expectancy with and without the intervention being considered.

When assessing whether a treatment is cost effective, a requirement for threshold can arise when policy makers seek a benchmark to compare different treatments and judge different studies. In general, wealthier countries may be willing to pay more (i.e. accept higher threshold) for a given treatment than poorer countries [4,6]. In the United States, a cost-effectiveness ratio <$50,000 per LY or QALY is frequently regarded as economically attractive, in part because it approximates the cost of providing

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chronic hemodialysis to patients with renal failure, at a cost that meets willingness-to-pay through Medicare [4]. Conversely, a cost-effectiveness ratio of >$100,000 per added LY or QALY is frequently regarded as economically unattractive. The range between these two benchmarks is the gray zone in which there is no consensus on whether a treatment is economically acceptable [4]. While the benchmarks may be viewed as informative, there is actually no scientific basis for any threshold above which a treatment would be viewed as not cost effective.

2. Factors that impact the costs of peripheral vascular disease management

There are many factors that may impact the cost of vascular interventions. In a study assessing the cost of peripheral procedures at the Brigham and Women's hospital from 1990 through 1995, the cost of these interventions was noticed to be higher with advance age ($1345, $P = 0.02$), the presence of CAD ($1287, $P = 0.05$) and female gender ($1461, $P = 0.03$). The presence of complications was associated with a substantial increase in cost with additional cost estimated for fatal systemic complications of $11,675 ($P = 0.004$) and for nonfatal systemic complications of $9345 ($P < 0.001$) [7].

The extent and severity of PAD also have a substantial impact on the cost of treatment. While treatment of a patient with stage IIa PAD by Fontaine criteria (i.e., with a pain-free walking distance of more than 200 m) costs about $650 per year, treatment of a patient with stage IV PAD (defined by ischemic tissue necrosis) costs $9353 per year. Similarly critical leg ischemia (PAD stages III–IV) is on average $4478 more expensive than the treatment of intermittent claudication (PAD stage II disease) [7,8]. This also holds true for the costs of a specific therapeutic/invasive procedure; for example, the costs for percutaneous transluminal angioplasty (PTA) are much greater for patients with critical ischemia and tissue necrosis than for patients with disabling claudication secondary to higher complication rates and longer hospital stays [9]. Another consideration is that amputation has been shown to be about twice as expensive as a limb salvage strategy with either interventional or surgical methods and for both acute and chronic limb threatening ischemia [10].

3. Cost effectiveness of noninvasive therapy

3.1. Cost effectiveness of exercise programs

Exercise therapy was shown to be associated with improve symptoms and increased walking distance in PAD. A cost-effectiveness analysis comparing an exercise program to PTA showed that although at 3 months, PTA was more effective than exercise therapy and resulted in an additional 38 m, it did that at an additional cost of $6719, for an ICER of $177/m. At 6 months, however, exercise was more effective than PTA, resulting in an additional 137 m walked, and costs less ($61 less per meter gained). Therefore, exercise rehabilitation at 6 months is more effective and costs less than plain PTA, and is therefore cost saving [11]. However, it should be noticed that in this study exercise program was compared to PTA before the introduction of new techniques including drug-eluting stents (DES), drug-coated balloons (DCB) and woven nitinol stenting.

A supervised exercise program seems to be superior to simply motivating patients to exercise. The supervised exercise therapy (SET) in the Exercise Therapy in Peripheral Arterial Disease (EXITPAD) study was shown be more effective than 'go home and walk' advice (WA) for patients with intermittent claudication in regards of walking distance (620 m SET vs. 400 m WA) and quality of life (QALYs: 0.71 SET vs. 0.67 WA) making it cost effective with an ICER for cost per extra meter on the 12-month treadmill test of € 4.08 [12].

3.2. Cost effectiveness of antiplatelet agents

The use of antiplatelet agents was shown to be effective in reducing the risk of vascular occlusion in a wide range of patients with PAD. A meta-analysis of 8000 patients built from 46 randomized trials of antiplatelet therapy versus control and 14 randomized trials comparing one antiplatelet regimen with another showed that antiplatelet therapy (chiefly aspirin alone or aspirin plus dipyridamole) produced a highly significant ($P < 0.0001$) reduction in vascular occlusion, with the largest absolute reductions among patients at highest risk of occlusion and smaller but still significant absolute reductions among lower risk patients. Also, antiplatelet therapy in patients with PAD produced a significant 25% reduction ($P = 0.002$) in the incidence of vascular events (non-fatal MI, non-fatal stroke, or vascular death) [13]. Giving the compelling evidence of the benefit of aspirin in patients with PAD, no economic assessment was performed to compare its use to placebo.

The Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance (CHARISMA) trial that originally randomized 15,603 patients with either clinically evident cardiovascular disease or multiple risk factors for cardiovascular disease to receive clopidogrel plus low-dose aspirin or low-dose aspirin alone showed no significant difference in the composite of MI, stroke, or cardiac death [14]. However, a subgroup analysis including 9478 patients with

Table 1
Cost-effectiveness of non-invasive versus invasive management of peripheral vascular disease.

Author	Comparison	Primary outcome	Results	Cost effectiveness
Treesak et al. [11]	Exercise vs. PTA vs. none.	Absolute claudication distance at 3 and 6 months.	At 3 months, PTA was more effective than exercise therapy and resulted in an additional 38 m. At 6 months, however, exercise was more effective than PTA, resulting in an additional 137 m walked.	At 3 months, PTA was more effective than exercise therapy and resulted in an additional cost of $6719, for an ICER of $177/m. At 6 months, however, exercise was more effective than PTA, resulting in less costs ($61 less per m gained).
Van Asselt AD [12]	Supervised Exercise Therapy (SET) vs. Walking advice (WA).	Walking distance	Median walking distance was 620 m for exercise vs. 400 m for walking advice group.	Mean total costs were higher for SET than for WA (3407 versus 2304 Euros). ICER for cost per extra m was € 4.08 and € 28,693 per QALY.
Chen et al [16]	Aspirin vs. aspirin and clopidogrel in patients with cardiovascular disease	Composite of death, myocardial infarction and stroke	Adding clopidogrel use was associated with a reduction in the primary outcome at 28 months (6.9 vs. 7.9%, $P = 0.048$)	ICER was $36,343 per LY
Squires et al [17]	Naftidrofuryl oxalate vs. cilostazol	Logarithm mean of maximal walking distance	Cilostazol was superior in increasing the mean of maximal walking (0.181 to 0.762) vs. (0.108 to 0.337).	Naftidrofuryl oxalate, had an ICER of around £6070 per QALY gained when compared with no vasoactive drug, whereas cilostazol was associated with ICER of >£ 20,000 per QALY gained when compared with no vasoactive drug [17].

Abbreviations: PTA = percutaneous transluminal angioplasty; SET = supervised exercise therapy; WA = walking advice; ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life years; LY = life year.

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