Intensive insulin treatment of diabetic patients with myocardial infarction is highly cost-effective

See page 733 for the article to which this Editorial refers

As the variety of treatable diseases increases, so too does the health budget. As most communities have a limitation on the further expansion of health budgets, cost-effectiveness of different treatment modalities has become increasingly important.

The calculations used for costs and savings differ, hampering comparison between different treatments. One example of such a discrepancy is the question whether future costs in a saved life period should be included in the comparison. This is discussed in the paper by Albrand et al., in which the cost effectiveness of intensive insulin treatment after acute myocardial infarction in patients with diabetes mellitus is estimated.

Patients with type 2 diabetes have an increased morbidity and mortality from ischaemic heart disease. In a recent paper from Hafner et al., it was shown that patients with type 2 diabetes without known ischaemic heart disease had the same risk of myocardial infarction and cardiovascular death as non-diabetic patients with known ischaemic heart disease. This and other findings suggest that patients with type 2 diabetes have a latent arteriosclerosis, and should be treated more aggressively according to guidelines for secondary prevention.

In patients with signs of ischaemic heart disease the mortality risk for the type 2 diabetic patient is considerably higher than for the non-diabetic patient. In several studies it has been shown in patients with acute myocardial infarction, that type 2 diabetics have a mortality twice that of non-diabetics. In
these studies the diabetics comprises 10–20% of the myocardial infarction population, but presumably there is a substantial proportion of undiagnosed diabetes\cite{5}. This was also demonstrated in a study of patients admitted electively to coronary angiography. Twenty-five percent had known diabetes, but a further 13% had diabetes and 16% had impaired glucose tolerance, defined by an oral glucose tolerance test\cite{6}.

A major challenge is how to treat this high-risk group of diabetic patients with myocardial infarction. In general the patients should be treated like non-diabetics, using thrombolysis and aspirin, statins, beta-blockers\cite{7} and ACE-inhibitors\cite{8}. All of these interventions have been demonstrated to exhibit a relative risk reduction of at least the same as in non-diabetics, implying a considerably higher absolute risk reduction. The cost-effectiveness of these interventions in diabetic patients has not been established, but in general they will be considerably more cost effective than for the non-diabetic patients.

In DIGAMI a further mortality reduction was shown. In this study type I and II diabetic patients with acute myocardial infarction were randomized to intensive insulin treatment or conventional treatment. The patients were otherwise treated according to up-to-date standards during the study period, thus 68% received beta-blockers, and 31% ACE inhibitors.

A substantial reduction in mortality in favour of the intensive treatment was demonstrated, with an absolute risk reduction of 11% after a mean of 3.4 years\cite{9}.

In the paper by Albrand et al.\cite{1} in this issue the question of cost effectiveness of the treatment in the DIGAMI study is addressed, calculating the incremental cost per life-year and quality-adjusted life-year gained. Using this method the cost per life-year gained using intensive insulin treatment was Euro 16 900, and the cost per quality-adjusted life-year gained was above Euro 24 100. Excluding the increased cost due to the extended life expectancy, the total cost decreased to Euro 1000 per life-year gained and Euro 1500 per quality-adjusted life-year gained.

In the paper, comparison is drawn with other interventions, such as road investments which cost Euro 50 000 per life-year gained. Even ACE-inhibitor intervention in patients with post myocardial infarction heart failure has a cost per life-year gained of approximately Euro 6000, excluding the costs due to the extended life expectancy\cite{10}.

Another way of looking at comparative cost effectiveness using different treatment regimens is absolute risk reduction. Using this method, intensive insulin treatment of myocardial infarction in type 2 diabetics has a high ranking with an absolute mortality-risk reduction of 11% (during 3.4 years) compared to 3% (during 5 years) of statin intervention in patients with ischaemic heart disease\cite{11} and 5% (during 1-3 years) of beta-blocker treatment in heart failure patients\cite{12}.

Thus, intensive insulin treatment in type 2 diabetic patient with acute myocardial infarction seems very cost-effective and with a putative large gain in saved years. One drawback is the small dimension of the DIGAMI study; the DIGAMI 2 study is presently being carried out on a larger scale, including more thorough investigations of mechanistic explanations and health economic issues.

Until results from the large scale DIGAMI 2 study appears, type 2 diabetic patients with myocardial infarction should be treated according to modern standards with thrombolysis, aspirin, beta-blockers, ACE inhibitors and statins, and the implementation of an intensive insulin treatment regimen should be considered.

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References


\[9\] Malmberg K. Prospective randomised study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. DIGAMI
What have we learned from the recent large trials in acute coronary syndromes without ST-segment elevation?

See European Heart Journal Supplements Suppl C which accompanies this issue

Following DeWood’s observation in the late 1970s that intracoronary thrombosis was a key mechanism in the pathophysiology of acute myocardial infarction[1], the focus throughout the 1980s and into the early 1990s in acute cardiovascular research was centered around reperfusion therapy. The GISSI[2] (Gruppo Italiano per lo Studio della Streptochinasi nell’Infarto miocardico) and ISIS[3] (International Study of Infarct Survival) groups ushered in the era of the large, simple mortality trial of fibrinolysis in acute myocardial infarction. Data available on tens of thousands of patients from the large acute myocardial infarction trials then allowed investigators to examine issues far beyond the primary questions of these trials and led to an explosion of published information regarding the care of these patients, spanning disparate topics such as prognostic predictors[4], anticoagulation parameters[5], stroke[6], regional differences in treatment[7] and cost-effectiveness[8]. Secondary analyses from the GUSTO-I (Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded coronary arteries) trial have led to over 100 peer-reviewed publications and have offered a complete database on caring for the acute myocardial infarction patient[9].

During this 15-year period of intense investigation of acute myocardial infarction, there was growing recognition that there existed a much larger group of patients presenting to hospitals throughout the world with acute chest pain without the dramatic findings of ST-segment elevation. This group of patients was typically older and had more co-morbidity than the group of patients with acute ST-segment myocardial infarction and was categorized under the general heading of unstable angina/infarction without ST-segment elevation. Much less investigation was being performed in these patients, in part due to the heterogeneity of the presenting symptoms and signs and in part due to a lack of knowledge regarding the seriousness of the disease. Unlike the patients presenting with ST-segment elevation on the electrocardiogram, this other group of patients had much more diverse and much less dramatic clinical presentations. This group was more likely to have a less urgent, less focused initial medical evaluation and to be admitted to the hospital for observation (i.e. to ’rule-out myocardial infarction’) rather than being treated with aggressive therapies.

Recognition of the magnitude of this neglected group of patients shifted the clinical research focus. The large trials with glycoprotein (GP) IIb/IIIa inhibitors, low molecular weight heparins and specific antithrombin therapies carried out in this patient population in the late 1990s—most notably the platelet GP IIb/IIa inhibitors—have provided the data to update the knowledge base on the care of these patients, much like the fibrinolytic mega-trials allowed in the early 1990s.

Moderate- to large-scale trials have now been performed in the patient group with unstable coronary syndromes testing antithrombin therapies[10–14], antiplatelet therapy[15–18] and interventional management strategies[19,20]. Collectively, these trials have randomized tens of thousands of patients and have provided insights into patient management issues far beyond whether or not a particular therapy is of benefit to them.

Data from these trials have been instrumental in revising the terminology used to describe these