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Review

Unresolved issues in the management of chronic stable angina

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ABSTRACT

Chronic stable angina is a common and progressive disease which has a major impact on patient quality of life and imposes a high financial and medical burden on society. Given the range of agents now available, optimal medical therapy – which according to guidelines is the preferred option in the majority of patients with low-risk disease – offers the opportunity for effective control. However, recent studies suggest that management remains suboptimal in up to a third of patients and that physicians often underestimate the extent to which angina continues to limit patients' lives. A higher frequency of angina also relates directly to increased healthcare costs. These factors suggest the need for the development and implementation of appropriate guidelines, for tools to encourage the regular, systematic assessment of the management of chronic stable angina patients, and for improved means of communication between doctors and patients. Neither physicians nor their patients need to accept that a certain level of angina symptoms is unavoidable.

1. Introduction

Worldwide, coronary artery disease (CAD, also referred to as ischaemic heart disease, IHD) is the leading cause of death [1]. It is the largest contributor to the global burden of disease as reflected in disability-adjusted life years, a measure which combines premature mortality and the prevalence and severity of ill-health [2]. On this measure, the impact of CAD increased by 29% in the period 1990 to 2010. This reflects the worldwide shift in disease burden from infectious diseases, many of which can now effectively be controlled, to those chronic diseases associated with an ageing global population (Fig. 1).

The most frequent (and often the first) manifestation of stable CAD is chronic stable angina [3]. Chronic stable angina is defined by the ESC as follows: "Stable coronary artery disease is generally characterized by episodes of reversible myocardial demand/supply mismatch, related to ischemia or hypoxia, which are usually inducible by exercise, emotion or other stress and reproducible — but, which may also be occurring spontaneously. Such episodes of ischemia/hypoxia are commonly associated with transient chest discomfort (angina pectoris)." In the majority of developed countries, as many as 5% of adults aged over forty are affected [4]. Among men aged between 65 and 80 years, the prevalence is thought to be 12–14% [5]. Importantly, and contrary to a long-held assumption, many women also suffer stable CAD, with a prevalence of 10–12% for those between 65 and 80 years of age [5,6].

Angina arises from a mismatch between myocardial oxygen demand and the ability of the coronary arteries to deliver sufficient blood. Typically, this is due to the presence of atheromatous plaques restricting the lumen of epicardial coronary arteries. However, it is now increasingly appreciated that stable angina symptoms may also develop as a consequence of impaired vasodilation of the distal coronary microcirculation. This latter mechanism seems particularly prominent in women [6].

Management of chronic stable angina is multifaceted: it aims both to relieve symptoms and improve quality of life (QoL), and to reduce the risk of myocardial infarction, heart failure and death [5]. Pharmacological means of enhancing coronary blood flow and reducing myocardial oxygen demand are employed alongside physical means of relieving stenoses through percutaneous coronary interventions (PCI) or surgical coronary artery bypass. Attention is also paid to encouraging the modification of lifestyle factors that contribute to progressive atheroma, and

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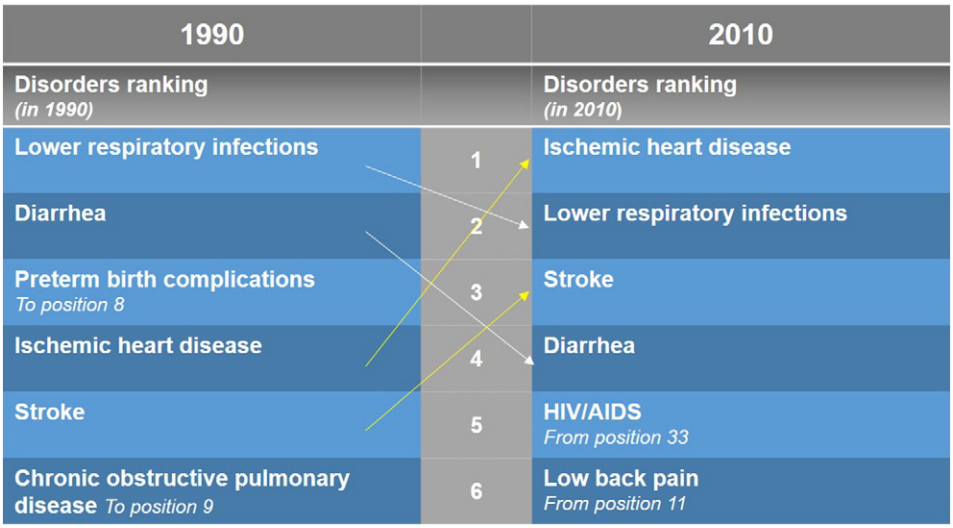

Fig. 1. Recent shifts in the global disability-adjusted burden of disease (top 6 diseases).
Adapted from Ref. [2].

to secondary prevention using statins (also widely used in primary prevention) and anti-platelet agents. Effective management requires the careful taking of a clinical history, the use of appropriate diagnostic tools and the thoughtful utilisation of revascularisation procedures when indicated to reduce mortality risk, or when stable angina symptoms prove refractory to pharmacological interventions.

2. The continuing burden of stable angina

Data from clinical trials and from observational registries are consistent in suggesting that annual mortality rates among stable CAD patients are between 1.2% and 2.4% and that the annual incidence of cardiac death is between 0.6% and 1.4% [5]. While the annual death rate from stable CAD appears to be decreasing, the prevalence of diagnosed CAD does not show a similar downward trend. It is likely that the reduction seen in mortality – without a corresponding decrease in prevalence – reflects improved prognosis for patients with stable CAD [5].

Morbidity is also a major consideration when evaluating the stable CAD burden. A review in 2007 suggested that between 10% and 30% of CAD patients with stable angina continue to experience symptoms despite treatment [7]. Although more recent studies are few, available data suggest that the proportion of treated patients continuing to experience symptoms is at the higher end of this range, and that many suffer impaired QoL as a consequence. Data from the studies reported below also suggest that those responsible for the care of stable angina patients underestimate the burden of poorly controlled disease. On the other hand, it is always important to appreciate that some patients may overestimate their symptoms and that some symptoms reported by patients may be only vaguely related to true angina.

The CADENCE (Coronary Artery Disease in gENeral practiCE) study, conducted in 207 Australian primary care practices representative of the country as a whole, set out to determine the adequacy of everyday angina management [8]. All patients had a history of stable angina and were recruited consecutively by general practitioners, irrespective of the reason for initial consultation. Of the 2031 patients, 29% experienced one or more attacks per week as recorded by the Seattle Angina Questionnaire (SAQ), and 7% had daily episodes. These patients had greater physical limitations and worse QoL (24% and 27% lower SAQ scores respectively, $p < 0.05$) when compared with those with minimal angina (angina less than once a week over the preceding four weeks).

In the same study, the likelihood of experiencing angina at least weekly was significantly associated with female sex and the presence of heart failure or peripheral artery disease. However, of greater practical importance for the optimisation of care was that the adequacy of angina treatment appeared to vary considerably from one practice to another. In 14% of clinics, there were no stable angina patients who experienced symptoms at weekly or greater frequency. In contrast, in 18% of practices more than 50% of such patients had angina attacks at least once a week.

These findings are largely supported by an observational study from Spain involving 2039 stable angina patients (73% male, mean age 68 years) seen during routine follow-up visits to 419 cardiologists in the period 2009–10 [9]. Of the 66% who had revascularisation, stable angina recurred in 59%. Despite the use of beta blockers in 78%, long-acting nitrates in 53%, calcium antagonists in 40%, ivabradine in 11% and trimetazidine in 7%, half the 2024 patients whose data were analysed remained symptomatic and, as a result, had impaired QoL. Thirty-nine percent (of the overall population of 2024) reported between one and three attacks per week over the previous four weeks, and 11% reported more than three attacks per week. The remaining 50% had fewer than one attack per week and were regarded as asymptomatic.

Among more than seven thousand patients with self-reported CAD who completed the SAQ while in the care of the Department of Veterans Affairs, 22% of those with frequent symptoms were receiving no anti-anginal medication and 33% were receiving only one class of anti-anginal drugs (many of which were being taken at lower than the recommended dose) [10].

A further issue concerns the success rate of coronary revascularisation in eliminating angina symptoms in patients with stable CAD. Randomised clinical trials [11–14], registry data [15], and meta-analysis [16] have consistently shown that about 30% of patients revascularised for stable CAD continue to experience angina symptoms. Importantly, this seems to occur independently of the choice of procedure (PCI vs CABG) and of the deployment of drug-eluting stents.

Collectively, these findings indicate a clear need for improved medical management of stable angina. This is required not only as a means of reducing the impact of stable angina on QoL but also as a way of reducing healthcare costs. Using data from the MERLIN-TIMI 36 trial, Arnold et al. investigated the relationship between stable angina frequency and resource utilisation among 5460 stable outpatients who completed the SAQ four months after an acute coronary syndrome and were then followed for an additional eight months [17]. Absence of