The return of silent ischaemia? Not really

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Patients with a positive but asymptomatic test for the detection of underlying ischaemia should be treated with the same commitment as those with a similar but symptomatic test

In a recent edition of Heart, Biagini et al.,1 in an observational study, looked at long term outcome in patients with silent versus symptomatic ischaemia during dobutamine stress echocardiography (DSE).2 They reviewed 931 consecutive patients who had DSE myocardial ischaemia in a single institution over a 12 year period (1990–2002), excluding a small further number who underwent revascularisation within two months of study. Mean follow up time was 5.5 years. The authors note that almost 70% of patients had no anginal type symptoms during their positive DSE, and that patients had a similar extent of myocardial ischaemia, whether with or without anginal symptoms. They report that “the annual cardiac death or myocardial infarction rate was significantly greater in patients with silent ischaemia when compared to those with symptomatic ischaemia on DSE, and that silent ischaemia was an independent predictor of these hard events”. It was noted that angiographic data were not available in the majority of cases, patients being divided into those with single and multivessel disease presumptively on the basis of DSE results.

SILENT ISCHAEMIA: "THE SILENT KILLER"

Silent ischaemia as a media (“Angina—tip of the iceberg”; “Silent ischaemia—the silent killer”; etc) and medical story extended for approximately 20 years from the early 1970s, and then gradually petered out with a reasonable degree of consensus having been achieved about its importance. Paul Wood, in 1950 in this journal, had described asymptomatic ST segment depression during exercise as “latent angina.”2 Silent ischaemia became a “top topic” in the 1970s in conjunction with the increasing use of ambulatory monitoring devices for clinical and research purposes. Reports appeared suggesting that transient episodes of silent ST segment depression occurred frequently during continuous monitoring in patients with coronary artery disease.3 Exciting initial reports raised the possibility that, if we could detect these “silent episodes”, and treat them, we could influence subsequent outcome, including heart failure, myocardial infarction, and cardiac death. Numerous subsequent publications, predominantly using ambulatory ST segment monitoring, detailed the frequency and characteristics of silent ischaemia during daily life, its relation to painful ischaemia, to exercise testing and with severity of coronary disease, and most importantly its prognostic significance. These findings would ultimately determine the place (or not) of ambulatory ST segment monitoring in routine clinical practice.

Silent ischaemia was shown to represent true ischaemia in various scintigraphic and other studies of patients with coronary artery disease.4-7 Approximately 70% of episodes of transient ST segment depression in patients with coronary disease occurred in the absence of symptoms, and comparison of silent and painful episodes of ST segment depression demonstrated similar pathophysiological mechanisms,5-7 with some reports suggesting that there was more ST segment change with angina, supporting the concept of the ischaemic cascade. Various theories were expounded as to why some episodes of ST segment change were silent and others painful, and have been well reviewed8; however, the majority of patients with coronary disease and predominantly silent ischaemia also had painful ischaemic episodes.

AMBULATORY ST MONITORING

From the practical clinical viewpoint, the relationship between ambulatory ST segment monitoring and exercise testing, our standard “ischaemia detector”, was key. Did ambulatory ST segment monitoring add significantly to the findings of exercise testing? In short, no. Transient (predominantly silent) ST segment change during ambulatory monitoring was shown to occur almost exclusively in those patients with a positive exercise test for ischaemia, particularly in those with a positive test at low workload,9 and was detected with significantly increased frequency in relation to increased severity of coronary artery disease.9 Indeed the ideal patient to study for the purposes of detecting and characterising silent ischaemia would have three vessel disease and a positive exercise test for ischaemia at low work load. This begged the question as to whether the detection of silent ischaemia by ambulatory monitoring was of practical relevance. We knew how to manage the patient with a positive exercise test at low work load (whether symptomatic or not) and significant three vessel disease, whereas the management, for example, of the patient with two vessel disease and a negative exercise test for ischaemia was a much more taxing issue (and where patients invariably would not have transient ischaemia during daily life).

Furthermore, as larger long term prognostic studies came rolling in, it became clear that, when comparing stable coronary patients with
transient ischaemia (silent or painful), versus no transient ischaemia during daily life at baseline, there was little difference in outcome for hard events (death and myocardial infarction), 10–13 any differences being predominantly in soft, physician influenced, end points such as revascularisation. This is not particularly surprising, as it has been clearly shown that many acute cardiac events result from plaque rupture of lesions not previously severe enough to cause ischaemia. 14, 15 we know that if stable coronary disease patients are followed in the long term, subsequent cardiac events usually correspond with the (acute) development of significant lesions distant from the site of the original ischaemia inducing lesion. 15

ASYMPTOMATIC POSITIVE DSE

So what of the publication by Biagini et al,1 and the somewhat surprising finding that an asymptomatic positive DSE is prognostically of greater long term significance than a symptomatic positive DSE. The authors make two important observations which likely explain the findings of significance noted in their report; firstly the two groups of patients were managed differently, in that 50% of symptomatic DSE patients (145/288) underwent coronary revascularisation compared to 27% of patients (174/643) with silent DSE ischaemia, during follow up, despite the extent of ischaemia at baseline being similar. This potential management bias in effecting the statistical findings is confirmed by the fact that the authors have shown that revascularisation was of prognostic benefit in both groups. Secondly, and as importantly, is that, following the decision to predominantly treat such “asymptomatic” patients medically, this group received significantly less “cardioprotective therapy” than those patients with symptomatic ischaemia during DSE. During follow up, patients with symptomatic ischaemia were significantly more likely to have received aspirin (82% v 52%), β blockers (70% v 43%), and statins (85% v 41%) than those with silent ischaemia, despite the fact that all patients had a positive DSE. All these agents have been shown to be of long term prognostic significance in the setting of stable coronary artery disease. Thus patients with a positive but asymptomatic DSE in this study were significantly less likely to receive a statin, aspirin, or β blocker, or to undergo revascularisation over a mean 5.5 year follow up. From our present knowledge, this would more than adequately explain the finding of long term prognostic significance of not having, compared to having, anginal symptoms during a (moment in time) positive DSE.

WHERE ARE WE WITH (SILENT) ISCHAEMIA IN 2005?

If a patient has a positive DSE, they are likely to undergo coronary angiography, on the basis that the DSE is being undertaken to point towards the likelihood and rough extent of coronary artery disease. The presence or absence of symptoms in association with a positive DSE, from the clinical management viewpoint, should not influence the decision whether to proceed or not with delineation of the coronary anatomy, the extent of ischaemic area being of more importance in terms of initial risk stratification. If there is coronary disease, patients will be commenced on aspirin, a statin, possibly a β blocker, and likely an angiotensin converting enzyme (ACE) inhibitor; 16 treatment with such medications should be commenced even if patients do not undergo angiography. Following angiography, the decision to intervene will be on the basis of symptoms, coronary anatomy, left ventricular function, and extent of ischaemic area on DSE, and our accepted understanding of high risk groupings. We know that revascularisation with bypass surgery relieves symptoms, and is of prognostic benefit in certain coronary disease distribution subgroups, but in most cases would not, in isolation, influence long term prognosis—this needs to be dealt with by modification of lifestyle and the compliant use of prognostically proven medications. Angioplasty and stenting, beneficial in symptom relief, still has to show prognostic benefit. Despite a lack of scientific justification, the increasing likelihood is that patients will undergo percutaneous revascularisation of even asymptomatic single vessel disease (with evidence of reversible ischaemia) on the basis of “can-do”, and “must be beneficial”. Only time will tell.

We have efficient tools, such as DSE, to detect coronary disease. It seems reasonable, considering the attrition rate from coronary disease in the western world, not to guess the coronary anatomy, but to delineate it if such a test points towards significant disease, whether the patient is asymptomatic or not. The coronary anatomy is a very important link in risk stratification. We have increasingly effective intervention means to relieve symptoms, and increasing means to maximise outcome, intervention-wise, in some high risk cases, but always with proven medications. Finally the study by Biagini et al emphasises the importance of treating a positive but asymptomatic test for the detection of underlying ischaemia with the same commitment as a similar but symptomatic test. This is on the basis that, clinically and prognostically, silent ischaemia is painful ischaemia without pain, but we can also reasonably conclude that, in the setting of coronary disease, and from all available evidence, silence, while not always golden, is no more important than pain.

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