weight gain. Clearly we are learning more about novel risk factors predisposing to cardiovascular disease, but there is much to be gained by vigorously controlling those that have been shown to be modifiable.

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The role of pharmacological stress echo for evaluating chest pain in women

See page 145 for the article to which this Editorial refers

The assessment of chest pain is generally easier and more accurate in men than in women. The nature of the chest pain is a better determinant of coronary artery disease in men[1], such that an exercise ECG adds little diagnostic information in a man with typical chest pain. A false-positive exercise ECG result is far more likely in women, more so as the pre-test likelihood of coronary artery disease falls. Alternative diagnostic modalities have been developed and the main contenders are myocardial perfusion imaging and stress echocardiography.

Myocardial perfusion imaging has been established considerably longer than stress echocardiography. Earlier studies using planar imaging highlighted the problems with soft tissue attenuation, particularly in women. More recent techniques, for example using technetium-99m sestamibi and simultaneous acquisition of perfusion and function (gated SPECT), have improved the specificity considerably[2]. Not only can the technique provide evidence of underlying ischaemic heart disease but several excellent studies attest to its prognostic capabilities in men and women[3–5].

Exercise echocardiography was initially demonstrated as a useful non-invasive test in men with suspected coronary artery disease. Results in women have been less concordant, partly due to smaller populations and different referral patterns. More recent studies show it to be more specific than exercise

ECG in women[6] and as accurate as, or slightly better than, exercise thallium scintigraphy[7]. Pharmacological stress echocardiography is also an effective tool for diagnosis and prognosis in women with chest pain[8–10], although single vessel disease may be missed[11].

Women with either atypical or typical chest pain are relatively straightforward to diagnose[12]. The most difficult, and by far the largest, group falls between these categories, that is women with an intermediate likelihood of coronary artery disease. Although myocardial perfusion SPECT has been shown to add incremental prognostic information even after clinical and exercise information is known[4] the role of stress echocardiography in the evaluation of chest pain in women is less well defined.

In this issue, Dodi and colleagues sought to establish criteria for the clinical use of exercise ECG and pharmacological stress echocardiography in women with chest pain of unknown origin[13]. Moreover, they set out to determine whether stress echocardiography might play a useful role as a first diagnostic screening test in this patient population. They studied 244 women referred with chest pain. As a group, the pre-test likelihood of coronary artery disease was >70% in 40% patients. Patients underwent bicycle exercise ECG and pharmacological stress echo (with high dose dipyridamole in 171 and dobutamine in 73) in random order and on different days.

Several important facts emerged, some new and some worthy of re-emphasis. First, there were no major complications with pharmacological stress echo, even with atropine co-administration. A positive exercise ECG was found in 95 patients (37%), although only 30 patients had a positive result at a rate–pressure product of <20 000. Thus, the greater proportion of positive tests occurred at higher workloads where false-positive results are more likely. Furthermore, exercise was submaximal in 33 patients, a group recognised to be at greater risk of future cardiac events.

The stress echo was positive in far fewer patients (n=33, 14%). Of these, the majority (61%) had wall motion abnormalities. In those with a negative stress echo (n=211), 48 (23%) developed isolated ST segment changes. Tables 1 and 2 examined clinical variables and the test result. Only hypertension was more frequent in patients with a positive exercise ECG compared with patients with a negative response. In contrast, patients with a positive stress echo had a worse cardiovascular risk profile.

Fourteen patients had a cardiac event during a follow-up period of 36 ± 18 months. There were 10 (10%) events in patients with a positive exercise ECG compared with 11 (33%) events in patients with a positive stress echo. Events were very infrequent and similarly so in patients with a negative exercise ECG (1·7%) or negative stress echo (1·4%), although patients who exercised submaximally had an event rate of 6·1%.

Univariate predictors of hard cardiac events were, in descending order, peak stress wall motion score index, positive stress echo, positive ECG at rate–pressure product <20 000, ECG changes during stress echo and family history of coronary artery disease. However, multivariate analysis showed that a positive stress echo was the only covariate independently associated with hard cardiac events (OR 40·1; 95% CI 4·3–377·5; $P=0·0012$). Of note, negative exercise ECG and stress echo predicted a good and similar event-free survival. Event-free survival for a positive exercise ECG but at a high rate–pressure product was not dissimilar. Survival was worse for patients with a positive stress echo than those with a positive ECG, even in the low rate–pressure product subgroup.

Dodi *et al.*[13] have shown that pharmacological stress echo provides incremental prognostic information to that derived from exercise ECG. What is more important are the clinical guidelines that can be inferred from the study. Worthy of re-emphasis is that patients with a negative exercise ECG have a good prognosis, provided an adequate workload is achieved. A negative stress echo carries a similarly good prognosis. Although positive exercise and stress echo tests predict future cardiac events, there was a ten-fold difference in odds ratio, favouring stress echo. The incremental prognostic power of pharmacological stress echo reinforces earlier work from Heupler *et al.*[14], who found similar results with exercise echo. There is no evidence to favour either dipyridamole or dobutamine as the pharmacological stressor.

Much practical information can be derived from this study. Although the prognostic value of a positive pharmacological stress echo is superior to exercise ECG, they have similar negative predictive value. Exercise ECG is more readily available and cheaper and should be the initial test for evaluating chest pain in women and, if negative, should be the only test. Obvious exceptions are patients unable to exercise and patients with uninterpretable resting ECGs. Patients with a positive exercise ECG should be investigated further, with coronary angiography in high risk patients and by either stress echo or myocardial perfusion imaging in intermediate risk patients.

Although there is no head-to-head comparison of the prognostic value of stress echo and myocardial perfusion imaging in women, it is likely that they perform similarly. However, whereas myocardial

perfusion imaging has been in existence as a validated investigational technique for many years, stress echo has a significantly shorter history and is being developed as a new service in many hospitals. Any new service should be carefully and prospectively evaluated before assuming that the diagnostic accuracy is similar to that reported in the literature from institutions with a special interest in the field.

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Predictive value of electrocardiographic markers for autonomic nervous system dysfunction in healthy populations: more studies needed

See page 165 for the article to which this Editorial refers

In this issue Whitsel *et al*.[1] looked at the predictive value for primary cardiac arrest of low heart rate variability and a large QT interval index taken together in a population of enrollees in a large health plan. The rationale behind this nested case-control study is based on the fact that both heart rate variability and QT index are electrocardiographic markers of the autonomous nervous system function and sympathovagal balance[2–4].

Where do we stand on each of these markers with respect to their predictive power and usefulness in both patients and the population at large? Since the pioneering paper from Kleiger *et al*.[5] showing that depressed heart rate variability increased the risk of mortality in a cohort of 808 patients who survived an