Screening for left ventricular systolic dysfunction in patients with stroke, transient ischaemic attacks, and peripheral vascular disease

Clinical heart failure is present in 0.4–2% of the population, and continues to rise as the population ages. Its impact is profound, accounting for 5% of all hospital admissions and 2% of all health expenditure. It has the greatest negative effect on quality of life of all chronic medical disorders and has a high mortality rate. In order to reduce the incidence of cardiac failure and all its consequences, we need to detect and treat presymptomatic left ventricular dysfunction (LVSD). We focus on a new way to screen for asymptomatic LVSD which is likely to be cost-effective.

LVSD is common and treatable, accounting for 8% of people aged 25–75 years; and 12% of 45–75-year-olds. Of the 8%, 4% are asymptomatic. Other surveys suggest the population prevalence of LVSD is 2.8–3.7%. The patients who appear to be at particularly high risk of LVSD are those with ischaemic heart disease, hypertension or diabetes, and smokers. However echocardiographic screening of all hypertensives, all diabetics and all smokers for LVSD would be a daunting and costly process. A more cost-effective approach might be to wait for the first presentation of a vascular episode, and to perform routine echo screening at that time. The first vascular episode could be either a myocardial infarction (MI), a transient ischaemic attack (TIA), a cerebrovascular accident (CVA) or peripheral vascular disease. In normal clinical practice, MI patients are nowadays screened for LVSD during their hospital admission, but patients who have had a CVA/TIA/PVD are not routinely screened for LVSD. Yet, the presentation with one vascular disease in the form of a stroke/TIA/PVD could be a golden opportunity to detect and treat LVSD, and so reduce the subsequent incidence of overt heart failure, and perhaps even sudden cardiac death.

One could even justify screening such patients from an entirely different perspective. It is well known that the main cause of death in TIA/CVA/PVD patients is cardiac death. Some of these deaths are probably due to fresh myocardial ischaemia/infarction, but many others could be ‘arrhythmic’ deaths due to LVSD, which might be preventable if LVSD was detected and treated. Indeed, it is rather ironic that we normally vigorously reduce cardiovascular risk factors of smoking, hypertension, and cholesterol in such patients, but currently ignore the much bigger risk factor of LVSD.

There is much circumstantial evidence to suggest that LVSD may be common in such patients. In the UK-TIA Study, 1% had overt heart failure; a further 8% had cardiomegaly on CXR. This cardiomegaly is most likely due to LVSD: indeed in SOLVD, LVSD was twice as common as was cardiomegaly on CXR. This suggests indirectly, that LVSD might be present in at least 20% of TIA patients. Hertzer et al. found that 29% of carotid endarterectomy patients had LV impairment on coronary angiography, and that around 40% of such patients had an elevated LV end-diastolic pressure. Importantly, 80% of Hertzer’s carotid endarterectomy patients who had LV dysfunction had had no prior MI to alert their doctor to the possibility of LVSD. Further support for the idea that LVSD might be common in stroke patients comes from a study of patients with asymptomatic LVSD where the risk of stroke increased by 18% for every 5% decrease in LV ejection. In a French study by Ricou et al., 10/102 acute stroke patients had LVSD on echocardiography. Similarly, in a study of Chinese stroke patients with coronary artery disease, 27% had LVSD detected by contrast ventriculography.

In peripheral vascular disease, Hertzer showed that 33% of patients referred for surgery had LV impairment on coronary angiography, and again an important point is that 80% of them had no prior MI to alert their doctor to the possibility of LVSD. Many other studies have examined this question and a low ejection fraction has been reported, with frequencies...
varying between 16–68% of PVD surgical candidates.\textsuperscript{17,18}

However, most of the above studies address what the LVEF (ejection fraction) is prior to surgery and what impact a low LVEF has on operative mortality. What we would like to know is the incidence of LVSD in all patients, irrespective of whether they are going for surgery or not. The vascular patient who is going for surgery is highly selected from a larger pool of patients. Indeed, LVSD is likely to be a strong factor excluding them from a surgical series of vascular patients. In summary therefore, there is much circumstantial evidence to suggest that both CVA/TIA and PVD patients have a high incidence of undetected LVSD. One might expect that about 10–35% of stroke/TIA/PVD patients have asymptomatic LVSD, which is currently neither noticed nor treated. We have recently begun a programme of screening CVA/TIA/PVD patients for LVSD. Our initial results show that 22% of these patients have LVSD (LVEF <40%), of whom 60% are asymptomatic. With such a common and treatable problem, screening for LVSD should be seriously considered.

Echocardiography is a reliable, non-invasive method of determining ventricular function. In comparison with nuclear cardiology, visual estimation of ejection fraction by echo has the most reasonable agreement with RNEF (radionuclide ejection fraction).\textsuperscript{19} Furthermore, echocardiography is free of radiation exposure. Despite this, there is an obvious limitation with using echocardiography to screen stroke, TIA and PVD patients: patients with these diseases are commonly smokers and smoking-induced lung diseases severely restrict the ability to obtain clear images. Additionally, echocardiography requires highly skilled personnel to perform the technique and to interpret the results.

The value of the electrocardiogram (ECG) in identifying LVSD has been studied in heart failure patients by Davie et al., who showed that LVSD is very unlikely in a patient with a normal ECG, which means that LVSD screening could be concentrated towards patients with abnormal ECGs. If screening is restricted to those with major ECG abnormalities (atrial fibrillation, previous MI, LVH, LBBB or left-axis deviation) the incidence of LVSD increased from 18% to 37% in the series of Davie et al.\textsuperscript{20}

There is conflicting data about the value of chest X-ray (CXR) in identifying LVSD. The Framingham Study and the VHef Trial showed that cardiomegaly appeared more commonly in patients with ejection fractions below 35%.\textsuperscript{21} In the SOLVD study, LVSD was twice as common as was cardiomegaly. Nevertheless CXR may be useful for identifying LVSD patients when combined with other screening methods.

Evidence suggests that noradrenaline and natriuretic peptides may be elevated in LVSD, before any clinical evidence of heart failure occurs.\textsuperscript{22} In the SAVE and SOLVD studies, measuring atrial natriuretic peptide was a sensitive way of identifying LVSD, especially N-terminal ANP.\textsuperscript{23,24} Recent data suggest that BNP is a more sensitive and specific neurohormone to use when diagnosing LVSD.\textsuperscript{25} Choy et al. found in MI patients that BNP was 84% sensitive for identifying LVEF <35% (using BNP > 4 pmol/l).\textsuperscript{26} The sensitivity of BNP may be increased by combining it with the ECG. McDonagh et al. found BNP was 77% sensitive and 87% specific for identifying LVSD, with higher sensitivity achieved in patients over 55 years.\textsuperscript{27} The main aim in screening is to optimize sensitivity, so that patients will not be missed. Therefore BNP should probably be used to prescreen, before the ‘gold standard’ test of echocardiography, rather than using BNP information on its own to make the final diagnosis of LVSD. It is possible that BNP prescreening might reduce the echo burden by 60%, while only picking up LVSD in every second patient undergoing echocardiography. This is likely to be more cost-effective than performing echocardiography in all patients but only identifying LVSD in 20%.

Asymptomatic LVSD is both common and treatable with ACE inhibitors, which means that we ought somehow to be identifying these patients. A cost-effective way of screening for asymptomatic LVSD might be to restrict screening only to those patients who already had had one vascular episode in the form of either a transient ischaemic attack, a stroke, or overt peripheral vascular disease. Echocardiography is a reliable method of diagnosing this. Prescreening using BNP with or without an ECG, may reduce the number of people needing echocardiograms. Identifying and treating LVSD in these patients may even be a more cost-effective way of reducing their high incidence of cardiac death than by controlling their conventional risk factors of hypertension, smoking and cholesterol.

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References
4. Ho KK, Pinsky JL, Kannel WB, Levy D. Epidemiology of


