Definition of new targets in cardiovascular prevention from young into old age

In the perception of the public and many health workers, cardiovascular disease and mortality strike at old age so that borderline elevated cardiovascular risk factors do not require intervention in young or middle-aged people. The report by Thomas and colleagues disproves this attitude of complacency[1]. Among French patients aged 18–55 years, cardiovascular and coronary mortality were minimal if systolic pressure and serum total cholesterol were below 130 mmHg and 200 mg . dl$^{-1}$, respectively. In men, after adjustment for other cardiovascular risk factors including age and smoking habits, the risk of coronary mortality rose threefold if systolic pressure was high–normal (130–139 mmHg[2]). In the presence of hypercholesterolaemia (≥ 240 mg . dl$^{-1}$), the risk ratio further increased to 10 or 17 depending on whether systolic pressure was mildly (140–159 mmHg[2]) or more severely (≥ 160 mmHg[2]) elevated. Similar trends, albeit less strong, were observed in women.

The findings of Thomas and colleagues are in line with recent publications from the Framingham Heart Study[3,4]. These investigators reported a continuous increase in cardiovascular risk with higher systolic pressure[3]. As compared with optimal blood pressure, high–normal systolic pressure was associated with a risk factor adjusted hazard ratio for cardiovascular disease of 2·5 in women and 1·6 in men. According to the guidelines of the World Health Organization and the International Society of Hypertension[2] optimal blood pressure levels are less than 120 mmHg systolic and 80 mmHg diastolic, while high–normal blood pressure ranges from 130 to 139 mmHg systolic and from 80 to 85 mmHg diastolic. One decade ago, the Multiple Risk Factor Intervention Trial demonstrated a strong graded relationship in middle-aged men (35–57 years) between mortality from coronary heart disease and systolic pressure above 110 mmHg, diastolic pressure above 70 mmHg and serum cholesterol levels above 170 mg . dl$^{-1}$[5]. Systolic pressure was a stronger predictor than diastolic pressure[5].

How should the recent findings[1,3,5] impact on public health policies, clinical practice and research? From the public health point of view, prevention is better than cure. Among 17-year-old Flemish adolescents[6], we recently found that 4·5% had hypertension, 9·0% were overweight (body mass index >25 kg . m$^{-2}$), and 13·5% had a serum cholesterol concentration of 200 mg . dl$^{-1}$ or higher. If smoking and excessive alcohol intake were considered, 46·0% of the youngsters had one cardiovascular risk factor and 15·5% combined two or more risk factors. Prevention should therefore start at a young age. In Flanders, school attendance is compulsory until 18 years. Trained physicians examine the students at regular intervals. Unfortunately, the physical examination does not include blood sampling for the measurement of cholesterol and new directives are being implemented which place less emphasis on physical health. The professionalization of the armed forces in Western Europe has led to the disappearance of systematic health checks on young men. Health examinations of young adults may take place at the start of employment, during pregnancy, or when people subscribe to a mortgage or life insurance.

Governments carry responsibility for the health of new generations and should seriously consider implementing a systematic health examination of all young people before they leave school. Health checks of youngsters can be combined with environmental bio-monitoring for hazardous chemicals[6]. If systematically implemented, they would provide information that policy makers need for long-term planning and for monitoring secular trends in risk factors.

From the clinical point of view, it is important that hypertension and hypercholesterolaemia be diagnosed and treated according to international guidelines[2,7,8], which themselves should be based on evidence from clinical trials. The Framingham Heart Study showed a stepwise increase in the incidence of hypertension across three non-hypertensive
Among subjects below age 65, the proportion developing hypertension over 4 years was 5.3% of those with an optimal blood pressure and 17.6% and 37.3% of participants with a normal or high-normal blood pressure, respectively. Obesity and weight gain contributed to progression[4]. In Flemish subjects randomly selected from the population, the 10-year incidence of hypertension rose from approximately 15% in young adults (20–35 years) to 40% in middle-aged subjects (45–54 years)[9]. Current guidelines recommend repeating lifestyle advice and measuring blood pressure and blood lipids every 5 years in subjects who have a blood pressure less than 140 mmHg systolic and 90 mmHg diastolic and whose serum total cholesterol is less than 5.0 mmol·1⁻¹ (190 mg·dl⁻¹)[8].

The articles published by Thomas et al.[1] and the Framingham Investigators[5,4] challenge these recommendations. Vasan and colleagues proposed monitoring individuals with high-normal blood pressure once a year and those with normal blood pressure every 2 years[4]. Because the incidence of hypertension and hypercholesterolaemia depends on many factors, such as age[4,9], weight gain[4], lifestyle and genetic predisposition[9], clearly, additional research including cost-effectiveness analyses, is required to determine the optimal strategy for screening adults without hypertension or hypercholesterolaemia. In the not so distant future, genetic characteristics will certainly allow refining of risk stratification and a better-targeted administration of preventive and therapeutic measures.

Current guidelines advocate drug treatment for stages 2–3[7] or grades 2–3[2] of systolic hypertension (≥160 mmHg). An alternative analysis of the Framingham data suggested that the incidence of cardiovascular mortality was independent of systolic pressure for all pressures below the 70th percentile for specified age- and sex-classes and sharply increased with a systolic pressure higher than the 80th percentile. This level was approximately 160 mmHg in older (65–74 years) men and 170 mmHg in women of similar age[10]. Secondary prevention trials[11,12] included high-risk patients with borderline or no elevation of blood pressure, but angiotensin-converting enzyme inhibitors or matching placebos were administered on top of other antihypertensive drugs, so that the true underlying blood pressure remains unknown. In PROGRESS[13], the older definition of normotension included what is currently labelled as mild systolic hypertension[2,7], and perindopril alone did not affect outcome. Clinical trials should be mounted according to a descending blood pressure gradient. If both high-normal blood pressure and mild systolic hypertension require treatment, in our experience[9], approximately 50% of all currently untreated elderly subjects (≥60 years) must be offered antihypertensive drug treatment. A decision to treat must mean that some other health care will not be funded. Thus, there is a priority to first investigate whether older subjects with mild uncomplicated systolic hypertension can benefit from therapy for the primary prevention of cardiovascular events to such extent that the costs to society would be balanced by increases in longevity and quality of life[14].

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References

A prediction rule for left ventricular dilatation post-MI?

See doi:10.1053/euhj.2001.2820 for the article to which this Editorial refers

Left ventricular remodelling after acute myocardial infarction results in a number of topographic and functional changes in the left ventricle in response to the abrupt loss of myocytes. The initial trigger for the increase in left ventricular size is the loss of contractile shortening and subsequent stretching of the infarct and peri-infarct zones, both of which increase regional wall stress. The increased wall stress is the driving force that stimulates ventricular remodelling including dilatation, hypertrophy and activation of extracellular matrix which begins the repair process. Left ventricular remodelling is traditionally divided into an early phase and a late phase. The early phase is confined to the infarct zone and consists primarily of infarct expansion. The late phase involves changes in the entire myocardium and may continue for months until the distending forces are counterbalanced by the restraining forces conferred by the tensile strength of the reparative collagen scar. The factors that determine the magnitude and duration of this dynamic remodelling process are multiple, but important among them are the size and location of the initial infarct, the patency and time to restoration of antegrade flow in the infarct-related artery, neurohormonal activation (sympathetic nervous system and the renin-angiotensin-alderosterone system) and the ability of the extracellular matrix to form a stable, mature collagen scar. The outcome of these complex interactions is either stabilization of left ventricular size, haemodynamic compensation and preservation of ventricular function or progressive left ventricular dilatation, haemodynamic decompensation, deterioration in contractile function and development of heart failure.

The implications of early left ventricular dilatation have been clearly shown in a number of studies in man and in infarct models in experimental animals[1–5]. Even small increases in left ventricular size early after myocardial infarction are associated with increased risk for adverse complications including cardiovascular death, recurrent non-fatal infarction and congestive heart failure[6]. Moreover, end-systolic left ventricular size has been demonstrated to be a more powerful predictor of clinical outcome post-infarction than either coronary artery anatomy or ejection fraction[1], and provides further incremental prognostic information over and above that ascertainable from statistical modelling of baseline demographics and cardiac risk factors alone[6]. Importantly, left ventricular dilatation is associated with concomitant ventricular distortion resulting in a mechanically disadvantageous shape, increased regional systolic and diastolic wall stress and compromised ventricular ejection performance.

In a proportion of survivors of acute myocardial infarction, left ventricular dilatation may be progressive because of a continuous imbalance between the distending forces and the strength of the reparative process. Delayed myocyte loss from apoptosis may also contribute to this prolonged disequilibrium. Thus, left ventricular dilatation begets left ventricular dilatation, and currently there is no simple accepted means of reliably identifying patients at high risk for developing left ventricular dilatation. Progressive dilatation is associated with deteriorating pump function and also a high risk for experiencing serious adverse cardiovascular events including sudden cardiac death, re-infarction, heart failure and embolic stroke[4,7,8]. Left ventricular dilatation post-infarction