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EDITORIAL

The heart in hypertension

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Hypertension (HT) is a leading cause of mortality and morbidity affecting over a quarter of the world's adult population (estimated to be around one billion adults worldwide) and this number is forecast to increase to over 1.5 billion by 2025 [1]. It is estimated that there were in excess of 10 million deaths annually related to HT [2]. HT affects practically every organ of the body both at the micro and macrovascular level and these effects are responsible for the increased mortality and morbidity associated with HT. There are many organ-specific changes caused by HT and these have been referred to as "hypertension mediated organ damage (HMOD)", and specific examples of HMOD include hypertensive retinopathy, nephropathy, left ventricular hypertrophy (LVH) and neurovascular changes including stroke and dementia [3].

The heart is a major organ that is affected by HT, being directly exposed to the high blood pressure (BP). One of the most striking and perhaps the earliest effect of HT on the heart is LVH. It has been suggested that around 36–41% of all hypertensives have LVH [4]. The extent of LVH is related predominantly to the duration of HT and the levels of elevated BP. LVH initially occurs as a compensatory process that represents an adaptation to increased ventricular wall stress. Besides this raised BP, many other pathophysiological processes such as sympathetic overdrive [5] activation of the renin angiotensin aldosterone system (RAAS) [6], insulin resistance [7], tissue-related factors such as endothelins [8], genetic and racial predisposition [9] and levels of dietary salt intake [10] have all been implicated in the causation and progression of LVH in patients with HT.

There are extensive data demonstrating the poor prognosis of patients with hypertensive LVH with increased cardiovascular events and death [11]. Indeed, patients with LVH have been shown to have a twofold to fourfold higher rate of cardiovascular events independent of other risk factors such as age, hypercholesterolaemia, diabetes, etc. [12]. Patients with LVH are also at a higher risk of developing strokes [13], cognitive impairment [14], atrial fibrillation [15], ventricular arrhythmias [16] and sudden cardiac death [17]. It is likely that LVH is simply a surrogate for the severity of HT, given that the extent of LVH depends on the BP control and duration of HT. However, the changes in the left ventricle at the macro and microscopic level would by themselves lead to some of the other complications such as arrhythmias, AF-related strokes, etc.

There are other changes that occur in the heart secondary to LVH. The stiff hypertrophic LV increases the diastolic pressure within the LV and can lead to diastolic dysfunction. HT and LVH are major risk factors for the development of heart failure with preserved ejection fraction (HFpEF) [18]. HT is also a major risk factor for heart failure with reduced ejection fraction (HFrEF). Patients with a concentric hypertrophy usually develop HFpEF, whereas those with an eccentric (dilated) phenotype develop HFrEF, reflecting the different pathological processes in both these types of heart failure. In the Framingham study, the presentation of 91% of patients with new heart failure was preceded by the development of HT [19]. Nevertheless, it should be noted that not all patients with HFpEF have evidence of LVH and many elderly patients with LVH do not have signs and symptoms of HFpEF [20].

The diastolic dysfunction and raised diastolic pressures can also lead to increase in left atrial pressure and over time results in enlargement of the left atrium and other structural changes in the left atrial wall [21]. The structural remodelling and deposition of fibrous tissue in the left atrium cause disruption between the myocytes and electrical bundles and potentiate the formation of multiple micro

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re-entrant circuits that are pathognomonic of AF [22]. All these changes, along with the activation of the RAAS and heightened sympathetic activity in HT, create the substrate required for the initiation of atrial fibrillation and HT is indeed a major risk factor for atrial fibrillation [23]. The severity of LVH also contributes to the formation of AF. For example, it has been shown that for every 1 standard deviation increase in LV mass, the risk of atrial fibrillation increased by 1.2-fold [15].

On a microvascular level, the increased shearing forces of HT can lead to endothelial activation and dysfunction [24]. The endothelial activation is both a cause and an effect of HT. Conditions such as diabetes, hyperlipidemia, smoking, etc. can cause endothelial dysfunction, which leads to defective nitric oxide production by the endothelium which, in turn, can lead to impaired vasodilatation and hence HT. HT on its own can also lead to endothelial dysfunction due to the increased shear force exerted on the vessel wall that the endothelium is exposed to. This can promote the formation of atheroma and indeed HT is a major risk factor for myocardial infarctions and cerebrovascular accidents [25]. Studies have shown that even modest increases in BP (stage 1 HT) are associated with an increased risk of cardiovascular events [26].

HT is associated with platelet activation and platelets from patients with HT have been shown to demonstrate increased adhesiveness [27, 28]. The level of platelet activation has been demonstrated to correlate with HMOD [27, 29]. The changes in HT also fulfil the criteria of the Virchow's triad leading to a hypercoagulable state. This explains the preponderance of thrombotic strokes rather than haemorrhagic strokes in patients with HT, although the vessels are exposed to high pressures and this has been referred to as the "thrombotic paradox of HT" [30].

Strict BP control has been demonstrated to reduce cardiovascular mortality and morbidity. It has been shown that lowering BP reduces risk of a myocardial infarction by 20–25%, of stroke by 35–40% and by 50% for heart failure [31]. Many of the HT-related changes have been shown to be reduced or even completely reversed by lowering BP [3]. In the heart, regression of LVH has been shown to occur with BP reduction. Patients who demonstrate greater LVH reduction have been shown to have much better prognosis and fewer cardiovascular events than those whose LVH remained the same with the worst prognosis in those where new LVH developed or where the LVH worsened on treatment [32]. Some group of antihypertensive medications such as angiotensin converting enzyme inhibitors (ACEI) have been shown to cause more LVH regression than other classes of drugs [33]. Treating HT has also been shown to improve endothelial function and reduce platelet activation, which could also explain the improved cardiovascular outcomes [34]. Treating HT has also been shown to significantly reduce the risk of heart failure and the incidence of new onset AF [35, 36]. Blockers of the RAAS such as ACEI and angiotensin receptor blockers have been shown

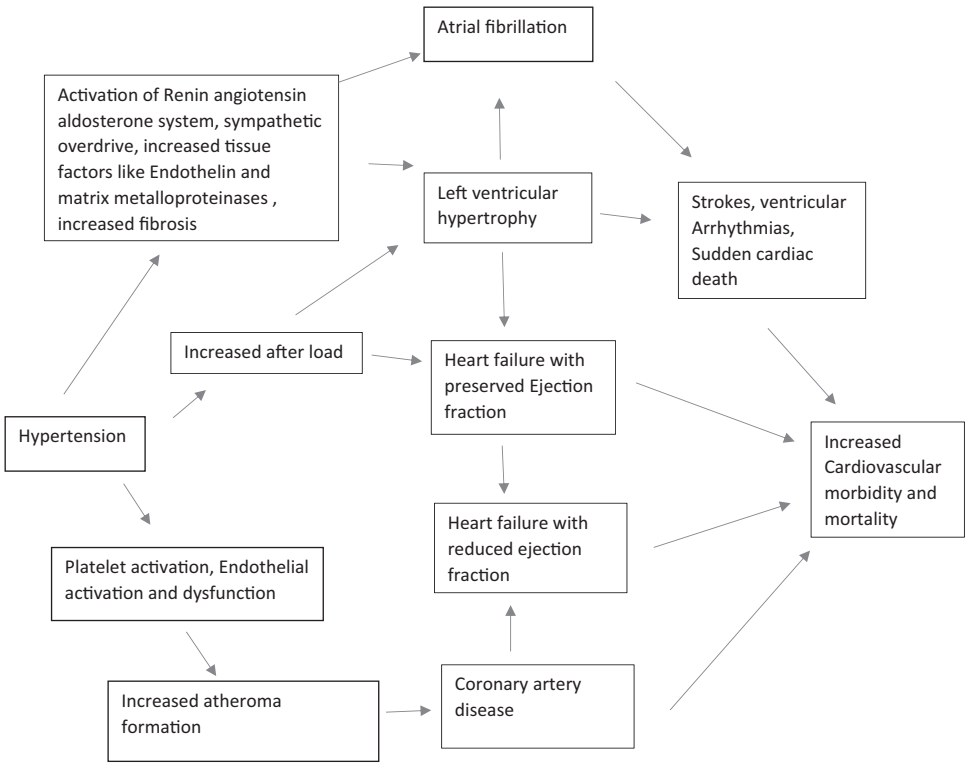

Fig. 1 Effects of Hypertension on the heart and cardiovascular system. The various pathophysiological effects of hypertension on the heart leading to increased cardiovascular morbidity and mortality.

to be superior to other classes of antihypertensive drugs in reducing the incidence of new onset AF in some subgroups of hypertensive patients such as those with LVH [37].

The heart is one of the major organs that is affected by HT. Figure 1 shows the various inter-connected pathophysiological processes at play, as a result of HT which ultimately results in increased cardiovascular morbidity and mortality. Strict BP control can reverse many of the deleterious effects of HT on the heart. Early detection is therefore a key in picking up these changes such as LVH at an early stage. Convincing asymptomatic hypertensive patients to strictly adhere to medications is challenging but is worthwhile spending that time and energy to persuade them about the importance of lowering BP as it can significantly improve their overall prognosis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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