



UNDER PRESSURE to keep it ticking

In a recent update Messerli *et al* described the effect of hypertension on the development of heart failure as the transition from hypertension to heart failure.



Most patients with hypertension can develop heart failure. In the Framing Heart Study hypertension preceded the development of heart failure in about 91% of new-onset heart failure during at least mean follow-up of 14.1 years. When other risk factors were accounted for, hypertension increased the risk for heart failure two-fold in men and three-fold in women. Multivariate analysis demonstrated a large population-attributable risk of hypertension for heart failure accounting for 39% of cases in men and 59% of cases in women. Patients with hypertension whom also had diabetes mellitus, myocardial infarction, left ventricular hypertrophy and valvular disease had an increased risk of heart failure. In the Framingham Heart Study, the life-time risk of heart failure was about 20% (one in five) in both sexes and this risk can double with a blood pressure of 160/100 mmHg as compared to a blood pressure of 140/90 mmHg.

Pathophysiology

Clinically hypertensive heart disease can be divided into four categories based on the pathophysiology and the clinical impact of hypertension on the heart:

Degree 1: Isolated diastolic dysfunction with no left ventricular hypertrophy.

Degree 2: Left ventricular diastolic dysfunction with concentric left ventricular hypertrophy.

Degree 3: Clinical heart failure (with dyspnoea and pulmonary oedema) with preserved ejection fraction.

Degree 4: Dilated cardiomyopathy with heart failure and reduced ejection fraction and eccentric left ventricular hypertrophy.

Diastolic dysfunction is much more common in hypertension than systolic dysfunction. Patients with heart failure with preserved ejection fraction have more left ventricular hypertrophy, more epicardial coronary artery lesions, coronary microvascular rarefaction and more myocardial fibrosis than control people. It has been described that isolated diastolic dysfunction with systolic



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blood pressure of ± 200 mm Hg, can trigger pulmonary oedema.

Decapitated hypertension

In patients with advanced heart failure the systolic blood pressure is usually low even in those patients who had hypertension. This condition has been named as 'decapitated hypertension' and can be observed in a previously hypertensive patient who now begins with progressive heart failure, the blood pressure starts to normalise and eventually becomes abnormally low. This decrease in systolic blood pressure is mainly due to a severely impaired pump function of the left ventricle despite compensatory peripheral vasoconstriction. These patients are difficult to manage as they cannot tolerate antihypertensive medications that are also used for the treatment of heart failure such as angiotensin-converting-enzyme inhibitors (ACE-I) and angiotensin-receptor blockers (ARB's).

If the patient recovers from heart failure the blood pressure rises and the patient may then again become hypertensive.

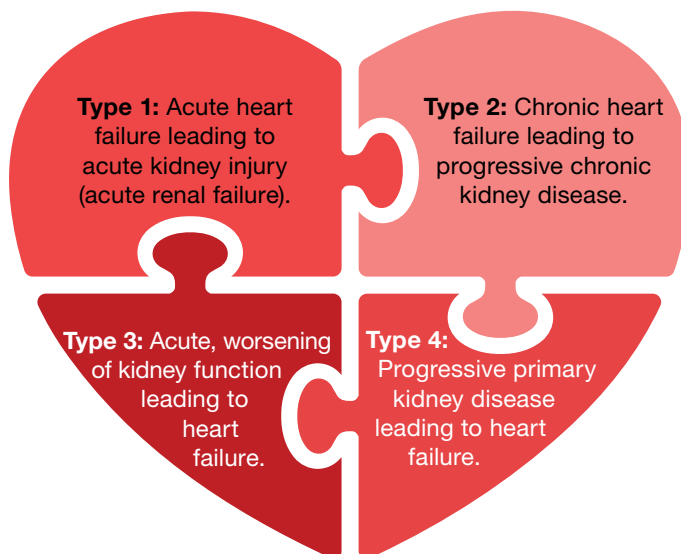
Blood pressure in heart failure

Hypertension with an elevated blood pressure incident may trigger heart failure onset. Many studies have shown that in patients with a high systolic blood pressure the prognosis and other outcomes are better than those with low blood pressures. It has been argued that the higher central aortic blood pressure associated with beta-blockade treatment could be an additional reason for their effectiveness in the treatment of heart failure as well as their lesser effect in hypertension without heart failure. The same phenomenon may be responsible for the heart rate lowering benefit of Ivabradine in heart failure as seen in the SHIFT trial.

Cardiorenal syndrome

The heart and the kidneys are targets for the detrimental effects of longstanding hypertension and their structure and function progressively become impaired. Therefore, heart

Recently the most common types of cardiorenal syndrome have been classified as:



failure and renal failure commonly co-exist in the same patient. There are different interactions between these two organs.

Clinically, when renal failure develops in heart failure, regardless of the type, the effect on the treatment becomes complicated. The presence of the cardiorenal syndrome drastically limits the therapeutic armamentarium. The renal failure itself as well as the different types of therapies for heart failure all contributes to a greater risk of hyperkalemia.

Pickering syndrome

Pickering described multiple episodes of acute pulmonary syndrome (flash pulmonary syndrome) hypertension and bilateral atherosclerotic plaques of the renal arteries. This syndrome can be classified as cardiorenal syndrome type 3.

Antihypertensive treatment to reduce the risk of heart failure

Beta-blockers are the cornerstone in the treatment of heart failure with a solid base of trial evidence, but in the prevention of heart failure in the treatment of hypertension they are no better than any other antihypertensive drug. In the ALLHAT trial on the treatment of hypertension, the treatment arm that was given, the alpha blocker, doxazosin, had to be stopped prematurely due a doubling of the rate of heart failure development.

The thiazide-like diuretics such as chlorthalidone (the SHEP trial) and Indapamide (the HYVET trial) reduced the risk of heart failure highly significantly.

Thomopoulos *et.al.* published a large meta-analysis of 68 purely hypertension randomised clinical trials on the treatment of hypertension. They standardised the effect to a reduction of 10mmHg systolic blood pressure and 5mm Hg diastolic blood pressure over a period of five years. For this minimal reduction of blood pressure the relative risk reduction of heart failure was: RRR 48% (95%CI: 31-61%) with an absolute risk reduction of heart failure of 16 (95%CI: 10-19) per 1 000 treated and a number-needed-to-treat of 63 (95%CI: 51-94). Hypertension treatment reducing blood pressure 10/5 mmHg over five years could prevent 16 cases of heart failure per 1 000 treated, an effect as significant and similar to the reduction of stroke and much more than the reduction of coronary artery disease.

In a separate meta-analysis, the same group scrutinised all 68 trials and could only find 36 trials that had heart failure as an end-point. The relative risk reduction of these 36 trials was: RRR 37% (95%CI: 25-48%) very similar to the reduction of stroke. Heart failure and stroke reductions were significantly related to systolic blood pressure, diastolic blood pressure and pulse pressure reductions. In head-to-head comparisons, calcium antagonists

were inferior in preventing heart failure, but when other drugs were used concomitantly, this inferior effect disappeared. They concluded their results by stating that blood pressure lowering effectively reduced the risk to develop heart failure. It is, however, also true that the trial based-evidence for the prevention of heart failure due to hypertension is not as large as for other cardiovascular outcomes as almost 50% of hypertension trials did not evaluate heart failure outcome.

Antihypertensive therapy in heart failure patients with persisting hypertension

A more common clinical problem is heart failure with a too low blood pressure. However, sometimes a heart failure patient will be on an ACE-Inhibitor (or ARB), a diuretic and a beta blocker and yet still have an elevated blood pressure. There are no outcome data from randomised clinical trials for these circumstances. The suggestion is that these patients be given a vasodilating beta-blocker such as Carvedilol and the combination sacubitril/valsartan combination when available. The reasoning behind it is to improve diastolic and microvascular function.

Conclusion

- 1** Hypertension is common and the most important contributor to the development of heart failure.
- 2** The transition from hypertension to heart failure progresses through specific stages.
- 3** Diastolic dysfunction in hypertension is common and precedes heart failure.
- 4** Treating hypertension is a powerful mechanism to reduce the risk of developing heart failure and they decelerate this transition, but not all drugs are equally effective. Diuretic such as indapamide and chlorthalidone seems to have an edge over the other drugs in reducing the risk of heart failure.

References are available on request. 