

# Management of Hypertension in Patients Presenting with Ischemic Heart Disease: Review of Current Literature

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## ABSTRACT

Ischemic heart disease (IHD) is a major global health issue with a prevalence of 1,655 in 100,000 population. One of the major risk factors and progression factors of IHD is hypertension. Hypertension is marked by an increase in baseline blood pressure over 140/90 mmHg. Hypertension possesses the ability to induce hypertension-induced organ damage (HMOD), which increases the risk of morbidity and mortality in IHD. It is known that hypertension is the major contributing factor to morbidity and mortality in IHD. The management of hypertension has advanced in the past decade and newer drugs have been used and researched. New guidelines have emerged for blood pressure control in the general population as well as in the cardiovascular disease population, including IHD. The aims of blood pressure control in the CVD population focus on preventing further CVD events and reducing disease progression. Thus, this review aims to review the latest management of hypertension, especially in the settings of patients with IHD.

**Keywords:** hypertension; ischemic heart disease; literature review.

## INTRODUCTION

Ischemic Heart Disease (IHD) is a major global population health hazard, presenting as the most prevalent cardiovascular illness in the world [1]. Furthermore, cardiovascular illness was the top three cause of mortality globally in 2013, with an overall mortality rate of 222.9 per 100,000 population [2]. IHD affects approximately 126 million individuals with a prevalence of 1,655 in 100,000 people [3]. With this extremely high prevalence, over 9 million deaths are present in association with IHD. This figure will continue to rise by trend and cause further health problems in the future thus requiring further advancement in research.

One of the major risk factors for IHD is hypertension, marked by increased blood pressure on baseline. Other than that, hypertension also presents as a major contributing factor to disease progression and increases morbidity and mortality rates in IHD [4]. One of the reasons is the progression of the atherosclerotic process in patients with hypertension. Studies have shown that hypertension increases the risk of complications through multiple mechanisms of organ damage, resulting in a higher risk of mortality in IHD [5]. Thus, the management of hypertension, especially blood pressure control, is crucial in the management of IHD.

Blood pressure control intervention has been greatly advancing in the past decades. Newer drugs and approaches have been used with newer guidelines emerging. One of the latest guidelines from the European Society of Cardiology (ESC) that was released in October 2024 has several changes in recommendation from the former guidelines [6]. This ensures more effective hypertension management in general and also in patients with comorbidity, such as IHD. With this being set, this review aims to renew the current management of hypertension in patients presenting with IHD.

## REVIEW CONTENT

### 1. Hypertension

Blood pressure (BP) in the normal human body lies around 90/60 until 120/80, however, in such a condition named hypertension, it exceeds that level. Based on the latest definition, Hypertension is a condition where the systolic BP  $\geq$  140 or diastolic BP  $\geq$  90 (ESC). The pathophysiology of hypertension involves a multifactorial and complex interplay multiorgan such as the renal, neural, vascular, and hormonal [7]. Nevertheless, some other factors like genetics, behavioural, psycho-socio-economic, and environmental also played a part in the regulation of BP itself.

Based on the cause of hypertension, it could be classified into two groups, 1) Essential hypertension, a condition that the leading cause is unknown, also called primary hypertension, 2) Secondary hypertension, the source of this condition is clear (8). A survey study conducted to monitor the prevalence of hypertension revealed that from 1990 until 2019, the amount of hypertension doubled from 650 million to 1.28 billion (9). A study by Mills in 2021 (10) displayed data showing that more people in the low to middle-income group (1.04 Billion) suffer from hypertension compared to the high-income group (349 Million). That study also revealed that the increasing number of hypertension with the variations of its spread is correlated with the change in lifestyle especially involving unhealthy diets and sedentary life (10). In terms of its treatment, the

number of drugs used worldwide to treat hypertension has increased almost double from 2010 to 2021 (11). Regarding the diagnosis of hypertension, a grading system was made to help determine the management end goal. Based on the ESC 2018 guidelines, the grading system includes 1)normal blood pressure 2)prehypertension 3)hypertension grade I 4) Hypertension grade II 5) Hypertension grade III, and 6) Isolated Systolic hypertension. This grading system is displayed in Table 1. Most of the patients who suffer from hypertension are asymptomatic, however, this does not mean the patient is safe from any circumstances. The effect of hypertension is seen throughout many organs in the body, such as renal damage, heart failure, stroke, sexual dysfunction, blindness, aneurysm, and many more [12].

**TABLE 1:** ESC 2018 Hypertension Classification [8].

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	And	<80
Normal	120 - 129	And/or	80 - 84
Upper range of Normal	130 - 139	And/or	85-89
Grade I	140 - 159	And/or	90 - 99
Grade II	>159	And/or	100 - 109
Grade III	> 179	And/or	> 109
Isolated Systolic Hypertension	>139	And	< 90

## 2. Ischemic Heart Disease

Ischemic heart disease (IHD) is a heart condition, especially in the coronary artery that involves the mechanism of atherosclerosis that leads to a lack of oxygen supply to the heart muscle [13]. The usual symptom that the patient felt is angina, a pain in the chest region that spreads to the shoulders, jaw, neck, or back. Other symptoms that are also common are cold sweats, light-headedness, and dyspnoea [14]. IHD pathophysiology involves the mechanism of plaque buildup in the coronary artery, with stenosis of the artery as the final stage of this complex process [15]. Risk factors for IHD can be divided into modifiable and unmodifiable risk factors [16]. Modifiable risk factors include smoking, sedentary lifestyle, hypertension, diabetes, obesity, and dyslipidemia and unmodifiable risk factors include male gender, older age, and family history of IHD.

The reason IHD is still one of the heart conditions to be studied is due to the fact that it is one of the leading causes of morbidity and mortality in the world. An epidemiological study from the Global Burden of Disease showed approximately 126 million (1,655 in 100,000) people affected by IHD with a total of nine million deaths being caused [3]. It is known that men are more prone to this disease compared to women, but women with the age over 65 years have the same risks as men [17]. The risk of IHD is also increasing with age, as the mortality of

this disease rises from the age of 60 years old onwards [16].

## 3. Hypertension in Ischemic Heart Disease

Hypertension is a major risk factor for many cardiovascular diseases, including stroke and IHD. One study in India shows that hypertension is associated with six to eight times increased risk of ischemic heart disease in the population [18]. Even though hypertension has a strong association with ischemic heart disease, blood pressure control is still low, as shown by the low control rate of blood pressure in the Indian population with hypertension. One study assessing blood pressure as a predictor for cardiovascular risk shows that uncontrolled blood pressure is associated with a 25% attributable risk for CHD [19]. Another similar study shows a more specific predictor for blood pressure, with a 49% attributable risk of CHD in patients with blood pressure of over 115 in systolic and 75 in diastolic [20]. Another study shows that hypertension produces a 1.3-fold increase in the risk of IHD in the Indonesian population [21].

The variation of results shows that the risk is associated with multifactorial conditions, with lifestyle such as smoking and physical activity, also other comorbidities, such as dyslipidemia play a role in contributing to the development of IHD [22].

A pooled analysis of 97 prospective cohorts done in 2014 shows that body mass index (BMI) as well as another indicator of obesity and metabolic syndrome is associated with a higher risk of CHD [22]. An increase of 5 kg/m<sup>2</sup> of BMI is associated with a 1.27 hazard ratio (HR) for coronary heart disease (CHD). Other mediators such as cholesterol are also associated with 1.21 HR for coronary heart disease. However, this study revealed that the most important mediator for coronary heart disease among other metabolic mediators is the presence of uncontrolled blood pressure with 31% mediated risk for CHD. This shows that hypertension is an important mediator in the risk factor of CHD in the general population.

Hypertension also presents as a major contributing factor for disease progression in IHD. High blood pressure is associated with a higher risk of cardiovascular events in patients with a history of CVD [23]. The major long-term effects of hypertension rely on the ability of high blood pressure to orchestrate hypertension-mediated organ damage (HMOD) [24]. One of the most common complications of hypertension, which has a complex reciprocal association is chronic kidney disease (CKD) [25]. In the event of CKD, blood pressure control and homeostasis will be severely altered, resulting in a further increase in blood pressure. Another effect of CKD would cause the progression of the atherosclerotic process chronically, and further increase the risk of developing cardiovascular events in patients with a history of IHD [26].

#### 4. Blood Pressure Control in Ischemic Heart Disease

The main goal of blood pressure control in CVD patients including IHD is to prevent further CVD events and reduce the risk of mortality and morbidity. The recommended blood pressure target for patients with a history of IHD is below 140/90 [27]. A lower range of 130/80 or below should be considered to further control the risk of CVD events and mortality as well as morbidity rate. Blood pressure control in general starts with preventive strategies at an early age and throughout the years. One of the most important preventive strategies is to monitor office blood pressure starting from late childhood and adolescence, particularly in populations with genetic predisposition shown by the history of relatives with hypertension or CVD [28]. Further preventive strategies include non-pharmacological interventions, especially routine physical activity with class I recommendation for at least 150 minutes per week of moderate-intensity aerobic training or 75 minutes of vigorous-intensity aerobic training [29]. Another important lifestyle modification is the practice of a sodium intake limitation of 2.5g/day, which lowers the risk of CVD events by 20% accompanied by high potassium intake (30,31). Another is the cessation of alcohol as well as smoking, accompanied by healthy dietary composition [32].

More importantly, blood pressure control in hypertensive patients should utilize the usage of

blood pressure-lowering drugs. The first line of treatment option for hypertension is using angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), dihydropyridine calcium channel blockers (CCBs), and diuretics [33]. Beta-blockers are now uncommon to use in hypertension, due to the evidence of lower efficacy and safety compared to ACEi, ARBs, CCBs, and diuretics in recent studies [34]. Even though the use of beta-blockers has subsided, beta-blockers are a particularly important therapy to reduce blood pressure in the settings of post-angina or post-myocardial infarction [35].

Another class of blood pressure-lowering drugs, the mineralocorticoid receptor antagonists (MRAs) could be useful in several settings, including resistant hypertension and hypertension in IHD. The PATHWAY-2 randomized control trial (RCT) shows that MRA appears as the most effective regiment in comparison with other drugs in resistant hypertension to prevent further CVD events [36]. Even though MRAs could be an alternative to lower blood pressure in this setting, further research must be conducted to further verify this effect.

Newer blood pressure-lowering drug classes have emerged with an emphasis on blood pressure control in CVD patients. One of which is the combination of angiotensin receptor-neprilysin inhibitor (ARNi) with ACEi which shows superior risk reduction of further CVD events compared to ACEi alone [37]. Another novel drug class is the SGLT2 inhibitors, which were initially used in the management of type-2 diabetes mellitus, and have shown favorable outcomes in some heart failure trials to reduce the risk of CVD events and improve renal hemodynamics, even in patients without type-2 diabetes mellitus [38]. Even though it has a blood pressure-lowering profile, the degree to which this drug may be used to treat hypertension still needs further assessment as some of the results show just a modest decrease in blood pressure [39].

Monotherapy may be insufficient in the treatment of hypertension, thus using combination drug therapy is usually the most effective and safe way in comparison to just increasing the dosage of one type of drug alone. For instance, the QUARTET trial has shown that a combination therapy of quadruple blood pressure-lowering drugs type shows a higher reduction in blood pressure compared to the standard monotherapy [40]. Another desired benefit of combination therapy is to lower the dose of each drug to lower the risk of side effects [41]. Thus, utilizing combination therapy is commonly needed in the management of hypertension, especially in strict regimens used in IHD patients.

Any of the major 4 blood pressure-lowering agents mentioned earlier can be used either independently or in combination with others [33]. Exclusion should be aware if the combination of RAS blockers (ACEi and ARBs) together is not recommended, particularly in patients with a high risk of vascular events such as IHD patients [42].

This is due to the interaction between these two classes of drugs, increasing adverse events without further superiority in effectiveness. If the use of a triple combination, with maximally tolerated doses, fails, then patients are considered resistant and the addition of spironolactone should be considered (36). Other MRAs or beta-blockers may be used if the patient cannot tolerate spironolactone. Last option treatment, if the former line has failed, hydralazine as a potassium-sparing diuretic or minoxidil, an alpha blocker, may be indicated with the cautious approach as those are associated with several adverse events (43).

## CONCLUSION

In conclusion, the management of hypertension in IHD should be assessed according to the clinical conditions. Combination therapy is needed and newer therapy may prove excellent in IHD.

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