True and Apparent Hypertension That is Resistant: Definition, Incidence and Effects

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Abstract

With increased efforts to improve BP control rates and the emergence of device-based therapies for hypertension, resistive hypertension; defined as blood pressure (BP) remaining above goal despite the use of three or more antihypertensive medications at maximally tolerated doses (one of which should ideally be a diuretic) has received more attention. Patients with true resistant hypertension, controlled resistant hypertension, and pseudo-resistant hypertension make up this classically defined resistant group. The term "apparent" resistant hypertension has been used to identify "apparent" lack of control on 3 medications in studies where pseudo-resistant hypertension cannot be excluded (for example, 24-hour ambulatory BP was not obtained).The prevalence of resistant hypertension has recently been reported in large, well-designed studies. The prevalence of resistant hypertension is 14.8% of treated hypertensive patients and 12.5% of all hypertensives, based on prevalence data from these studies and others in North America and Europe with a combined sample size of more than 600,000 hypertensive participants. However, in terms of identifying risk and estimating benefit from newer therapies like renal denervation, the prevalence of true resistant hypertension; defined as uncontrolled by office and 24-hour ambulatory BP monitoring with confirmed medication adherence; may be more significant. In patients with resistant hypertension, rates of cardiovascular events and mortality follow mean 24-hour ambulatory BPs, with true resistant hypertension representing the highest risk. In large trials, the prevalence of true resistant hypertension has not been directly measured; however, the combined results of a number of smaller studies suggest that true resistant hypertension is present in half of the office-controlled resistant hypertensive patients. Uncontrolled resistant hypertension is prevalent in 10.1% of treated hypertensive patients and 7.9% of all hypertensive patients, according to our pooled analysis.

Keywords: Control • Prevalence • Resistance • Hypertension • Epidemiology • Blood pressure

Introduction

According to survey data from various industrialized nations, the prevalence of hypertension in the 1990s ranged from 22% in Canada to 55% in Germany. There are few survey results from after 2006;in any case, information from the US and Britain report comparative commonness rates 10 years after the fact (29% in 2007 and 30% in 2006, separately).The focus has shifted from hypertension awareness to blood pressure (BP) control with relatively stable prevalence rates. The cardiovascular and mortality benefits of BP reduction have been well established through hypertension outcome trials, although the definition of BP control is still up for debate, particularly in certain hypertensive subpopulations. Early data indicated poor BP control overall, particularly in Europe, where less than 10% of people with hypertension had a BP of 140/90 mmHg or higher in the 1990s.Since then, control rates have increased throughout Europe, with recent statistics indicating 19% control in Germany in 2001, 28% control in England in 2006, and 37% control in Italy in 2009. With the rise of device-based therapies for hypertension (such as catheter-based renal denervation and carotid sinus stimulation), there has been renewed interest in the hypertension population that is resistant to medical treatment. As of not long ago, the predominance of this populace was not known. Clinical trials investigating hard outcomes in resistant hypertension and studies designed

to define the epidemiology of resistant hypertension have emerged in recent years. A pooled estimate of resistant hypertensive prevalence in North America and Europe will be presented alongside a review of the most recent data on the prevalence and outcomes of resistant hypertension.

Literature Review

In the beginning, the term "resistant hypertension" was used to identify a group of high-risk patients who might benefit from specialized care, such as the examination and treatment of secondary hypertension causes. An American Heart Association (AHA) scientific statement established the definition as a BP that remains above target despite optimal doses of three different classes of antihypertensive medication, one of which should ideally be a diuretic. By extension, a patient remains resistant if a fourth antihypertensive medication is added to maintain BP control. As a result, people with hypertension who are both controlled and uncontrolled by office measurements make up the resistant hypertensive population [1].

In its definition of resistant hypertension, the American Heart Association (AHA) makes no attempt to differentiate between resistant and pseudo-resistant hypertension. The term "pseudo-resistant hypertension" refers to individuals who do not actually have true resistant hypertension but do have elevated office blood pressures as a result of white-coat hypertension, improper BP measurement, or medication no adherence. Epidemiological studies used the term "apparently resistant hypertension" when referring to the group of patients who were taking three antihypertensive medications and had an office BP greater than 140/90 mmHg. This was done to make it clear that pseudo-resistance had not been ruled out. The distinction between true and apparent resistance can be made after pseudo-resistance has been excluded through proper office BP measurement technique, 24-hour ambulatory BP monitoring, and confirmation of medication adherence [2]. As a result, true resistant hypertension is defined as a properly measured office BP greater than 140/90 mmHg and a mean ambulatory BP greater than 130/80 mmHg over the course of 24 hours in a patient who has been confirmed to be taking

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three antihypertensive medications. Excluding participants with pseudo-resistant hypertension from the test population makes it difficult to determine the prevalence of true resistant hypertension.

Resistant hypertension prevalence

A prospective cohort study in a large hypertensive population with forced titration up to full doses of three different classes of antihypertensive medications, including a diuretic, would be ideal for estimating the prevalence of true resistant hypertension. Additionally, 24-hour ambulatory BP monitoring, standardized BP measurement, and an established method for establishing adequate medication adherence (such as electronic pill bottle monitoring, pill counts, or toxicology) would need to be used to rule out pseudo-resistant hypertension. This study has not yet been conducted, but the prevalence of resistant hypertension is estimated from: 1) BP control data from population studies; 2) outcome-based clinical trial subpopulations; 3) retrospective analyses of registry data; and 4) population studies that specifically identify resistant hypertension. Indirect estimates of the prevalence of resistant hypertension are provided by population studies on the prevalence, treatment, and control of hypertension [3]. The number of patients taking fewer than three antihypertensive medications and overall BP control rates are frequently reported in these studies. One can estimate the proportion of patients uncontrolled on fewer than three medications and the prevalence of apparent resistant hypertension by assuming comparable control rates among the population taking at least three medications [4].

1856 of the 8299 patients in a 2009 Italian study who were receiving treatment for hypertension from a general practitioner received at least three medications. Although the most common two-drug combination was an angiotensin-converting enzyme inhibitor and a diuretic, the percentage of diuretics used and optimal medication dosing were not reported. The European Society of Hypertension and European Society of Cardiology guidelines stated that the group taking fewer than three medications had a BP control rate of 22.3%.In this treated hypertensive populace, 17.4% are uncontrolled on three prescriptions [5]. Thirty percent of the more than 7000 participants in a 2006 survey of the English population were found to have hypertension.1375 (54%) of those with hypertension received treatment.60 of the treated patients were taking four medications, while 222 of the treated patients were taking three medications.76% of people taking three antihypertensive medications reported using diuretics.52% of the hypertensive patients in this study had their blood pressure under control (140/90 mmHg). This study included 12.0% of the treated hypertensive population who were taking four medications, making the prevalence of resistant hypertension estimated. Assuming an expected 31 people who were controlled on ≥4 drugs were avoided, then 9.8% of the treated populace comprised of people with uncontrolled safe hypertension [6].

Discussion

Although the ideal study to estimate the prevalence of true resistant hypertension has not been conducted, prevalence rates of resistant hypertension can be estimated from a number of well-designed trials. Among those who were being treated for hypertension, prevalence rates of resistant hypertension that met the AHA criteria ranged from 8.4% to 17.4%, with a pooled average of 14.8%.The prevalence rates of resistant hypertension among all hypertensive individuals estimated in the four studies ranged from 8.9% to 12.8%, with an average prevalence rate of 12.6%.Reporting the prevalence of uncontrolled resistant hypertension may be more important for risk assessment and estimating the benefit of device-based hypertension therapies due to the direct relationship between adverse cardiovascular outcomes and mean 24-hour ambulatory blood pressure. Uncontrolled resistant hypertension has a pooled prevalence rate of 10.1% among treated patients and 7.9% among all hypertensive patients, respectively.

It is essential to identify the potential underestimation and overestimation of prevalence rates when interpreting the studies mentioned earlier. Retrospective analyses, patient dropout, and patient exclusion would all underestimate the number of resistant patients and, as a result, the prevalence of resistant hypertension. Failure to uptitrate the number of antihypertensive

medications in those uncontrolled on medications. White-coat hypertension pseudo-resistant hypertension, medication no adherence or inaccurate BP measurement, and suboptimal medication regimens consisting of fewer than three medications (duplicate drug classes, medication underdoing, or the absence of a diuretic) would result in an overestimation of the number of resistant patients and, consequently, an overestimation of the prevalence of resistant hypertension.

When interpreting the prevalence rates from outcome-based studies like Allhat, Life, Invest, and Accomplish, for instance, there is uncertainty. It is difficult to determine whether more or fewer people with resistant hypertension were included in these studies. It's possible that including people with resistant hypertension was more likely if participants were chosen specifically based on their cardiovascular risk. Additionally, antihypertensive titration protocols were not developed to maximize three or four drug regimens. By deteriorating BP control, a non-optimal multi-drug regimen would falsely raise the prevalence of resistant hypertension. When compared to hydrochlorothiazide plus benazepril, ACCOMPLISH had the highest control rate of the four outcome trials when it added spironolactone, alpha-blockers, or beta-blockers to amlodipine plus benazepril. As a result, only 8.4% of those treated for hypertension were uncontrolled on fewer than three medications.

White-coat hypertension was present in 35.7% of the uncontrolled resistant population, according to some studies, which provide insight into the degree of underestimation or overestimation associated with each cause. According to pharmacy refill rates, Daugherty discovered that 12.4% of the uncontrolled resistant population was no adherent to their medical regimens. According to Egan data, the prevalence of resistant hypertension rises by up to 12.1% with an increase in the number of antihypertensive medications. In addition, urine toxicology revealed that 53% of uncontrolled individuals were nonadherent in a study aimed at determining the degree of medication adherence among people with resistant hypertension.30% of nonadherents did not take any antihypertensive medication. These studies, taken together, suggest that white-coat hypertension or pseudo-resistant hypertension caused by nonadherence probably account for half of all uncontrolled resistant hypertensive patients. As a result, the estimated prevalence of true resistant hypertension among treated and all hypertensive individuals is 4.0% and 5.0%, respectively.

Conclusion

It is anticipated that this small group of true resistant individuals, who stand to benefit most from aggressive treatment and early identification, will continue to shrink over time. BP control rates are likely to continue rising if concerted efforts to improve BP control are supported by the dissemination of strategies to simplify and optimize multiple medication regimens. The study revealed this effect. In 2006–2007, BP control rates of 67% were achieved using a simplified BP treatment algorithm, exceeding the 50% reported using NHANES data for the same time period. Notably, mineralocorticoid antagonists were added to the Kaiser Permente BP treatment algorithm in 2009, following the study period. Utilizing ideal dosing of an angiotensin-changing over compound inhibitor or angiotensin receptor blocker with a dihydropyridine calcium channel blocker and a diuretic, properly evaluating for optional reasons for hypertension and adding a mineralocorticoid receptor bad guy, BP control rates in people with safe hypertensive can arrive at 91.5%.32 Given that a little extent of hypertensive patients bomb ideal prescription treatment, very much planned viability studies are expected to characterize the job of gadget based treatments for treatment of safe, both controlled and uncontrolled. Device-based treatments are definitely something to think about for patients who don't respond to effective antihypertensive regimens. However, even controlled patients might be a good candidate for these treatments if they can significantly improve their quality of life by taking fewer pills or avoiding medication-related side effects.

Acknowledgement

Conflict of Interest

None.

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