

REAL-WORLD CHARACTERIZATION OF HYPERTENSION PATIENTS IN JAPAN: A 1-YEAR OVERVIEWBRUCE CRAWFORD¹*, SIEW HWA ONG², HEATHER FALVEY²¹Adelphi Values, Tokyo Japan, ²Novartis Pharma AG, Basel Switzerland, Email: bruce.crawford@adelphivalues.com*Received: 13 May 2013, Revised and Accepted: 16 July 2013***ABSTRACT**

OBJECTIVE: To characterize the real-world profile of hypertension (HTN) patients in Japan and their treatments, blood pressure (BP) control, and treatment costs with a focus on systolic hypertension (SH) and the elderly population.

METHODS: Data were extracted from insurance claims and annual health checks. Only subjects with blood pressure readings in 2009 and 2010 at 10-14 months apart were included and identified by ICD-10-CM. Treatments and costs were evaluated, focusing on 65+ and <65 year-olds.

RESULTS: 9269 subjects were identified with a HTN diagnosis and BP readings. Subjects mean age was 51.61(9.54) year-old, 73% were male, and they were diagnosed for 3.72(3.95) years. 56% had "controlled" BP (<140/90) and 38.50% had SH. Poly-pharmacy for HTN was common (42 %): The angiotensin receptor blockers (ARBs; 48%) and calcium-channel blockers (CCBs; 28%) were the most frequently prescribed. Subjects with a longer history of HTN received more treatments: 1.23 and 2.45 medications were used within the first year and 10 years, respectively. 22% of subjects controlled at baseline became "uncontrolled" while 40% of SH improved "to-goal" over 1-year. The average treatment costs for controlled subjects and SH were JPY231,626 and JPY202,117 and differed significantly. The treatment cost for subjects aged 65+ (JPY266,771) and <65 (JPY213,091) differed significantly.

CONCLUSION: HTN in Japan is characterized by poly-pharmacy and moderate control. Treatment was dominated by ARBs and CCBs (alone or in poly-pharmacy). The elderly are more expensive to treat, regardless if they are treated to goal or remain hypertensive. HTN remains a significant burden in Japan.

Keywords: hypertension, cost, blood pressure control, treatment

INTRODUCTION

High blood pressure or hypertension (HTN), which approximately 1 billion people worldwide experience, is the leading cause of cardiovascular disease (CVD) and is one of the most treatable risk factors. Scientific evidence shows that people with blood pressure exceeding 140/90 mmHg are two to three times more likely to experience clinical manifestations of coronary heart disease, including heart attack, angina pectoris, and sudden death.¹ With 60% of men and 45% of women aged 30 years old or older in Japan having elevated blood pressure, the Japanese are at great risk of subsequent cardiovascular events. The prevalence of hypertension sharply increases amongst Japanese in their 50s and older. Data from the 2010 National Health and Nutrition Survey in Japan show that prevalence rates for men increase from 34% in their 40s to 58% in their 50s, 64% in their 60s and 81% at 70 years and older. The pattern among female Japanese is similar, starting at 13% in their 40s to 73% at 70 years and older.²

While antihypertensive therapy has been proven to reduce cardiovascular morbidity and mortality, hypertension, especially systolic hypertension (SH; systolic blood pressure \geq 140), continues to be a major risk factor for cardiovascular diseases including stroke and cardiovascular death among Japan's rapidly ageing population.³ The effectiveness of lifestyle modification on the treatment and management of HTN, in combination with antihypertensive therapy, has been shown in clinical trials in Japan.⁴ The Japanese Society of HTN guideline indicates the importance of recognizing the lifestyle problems of hypertensive individuals and advocates comprehensive lifestyle modifications which include salt restriction, dietary choices, weight maintenance, exercise, restriction of alcohol intake, and quitting smoking.⁵ In the recent study investigating the relationship between blood pressure (BP) control status and lifestyle in hypertensive outpatients in Japan, about 60% of the patients achieved strict BP control when they were treated with lifestyle modification and combination antihypertensive therapy.⁶

The Ministry of Health, Labor, and Welfare reports that the medical

costs for HTN and related conditions such as cardiovascular disease and ischemic heart disease account for 28% of the total medical costs for the Japanese population and for 33%, the largest of all healthcare costs, for elderly (65 years old and above) in Japan.⁷ Costs of hypertensive disease in 2010 were JPY 13,786 billion. Given the rapidly ageing population and increasing healthcare costs in Japan, there is an urgent need to better understand the characteristics of people with HTN and their treatments, management, and health care resource consumption in Japan, particularly the hypertensive elderly. Therefore the authors set out to characterize the real-world profile of HTN patients in Japan and their treatments, blood pressure (BP) control, and treatment costs with a focus on systolic hypertension (SH) and the elderly population.

Materials and Methods

Data were extracted from the Japan Medical Data Center (JMDC) database, an insurance claims database that contains detailed electronic medical records for more than one million insured people across all prefectures submitted to health insurance societies for reimbursement.⁸ Data were extracted on HTN subjects between January 2010 and December 2011. HTN subjects were defined as using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes I10 - I15. Following the identification of HTN subjects, subjects were required to have 2 consecutive annual health checks which included the measurement of BP. BP results were required in order to evaluate the change in HTN status following one year of treatment. Using these BP data, subjects were classified as "controlled" if their BP was <140/90. SH was defined as systolic BP \geq 140.

Comorbidities were also identified by subjects' claims using ICD-10 codes. Comorbidities included are mental health, musculoskeletal, respiratory, circulatory, diabetes, metabolic disease, chronic kidney disease, heart failure, and myocardial infarction. Comorbidities thought to be more relevant to HTN included diabetes, metabolic

disease, chronic kidney disease, heart failure, myocardial infarction, and stroke.

Direct costs were calculated from the societal perspective, i.e., no attempt was made to remove the patient co-payment for services. Costs associated with each procedure/visit were calculated by the points associated with each service valued at JPY 10 per point. Costs for pharmaceutical treatments were calculated as following: the cost per unit times the number of units times the number of days that supply dispensed.

The primary objective of the study was to describe the current situation of HTN in Japan. Therefore, descriptive statistics on HTN type (controlled, SH) and age group (less than 65 versus 65+ years of age) were the primary means of evaluation. The secondary objective was to evaluate the total cost associated with HTN type and associated sub-populations. Total costs consisted of pharmacy and medical treatment charges and does not include over-the-counter treatments. Total costs between HTN type and age groups were evaluated using a γ -distributed generalized linear model (GLM) with a log-link function. The γ -distributed functional form is particularly useful because it avoids the issues with retransformation of skewed data. Untransformed costs were evaluated by t-tests/Analysis of Variance (ANOVA), and median differences were tested by Mann-Whitney U/Wilcoxon rank-sum test.

RESULTS

A total of 9,269 HTN subjects with 2 consecutive BP readings separated by 10-14 months were included in our study. The majority of subjects were male (73%) and only 5% (n=423) of them were 65 years or older. Among hypertensive men, SH comprised approximately 40% of subjects. Among women, older women had a higher percentage of SH compared to younger women (Table 1). Almost 24% of subjects under the age of 65 had both elevated systolic BP and diastolic BP, compared to 12% among elderly subjects (data not shown).

Table 1: Number of patients by HTN subgroup

| Baseline HTN type | < 65 yrs old (%) | | | 65+ yrs old (%) | | |
|-------------------|------------------|----------------|----------------|-----------------|---------------|---------------|
| | Female (n=2355) | Male (n=6491) | Total (n=8846) | Female (n=187) | Male (n=236) | Total (n=423) |
| Controlled | 1484 63.01% | 3472 53.49% | 4956 56.03% | 116 62.03% | 141 59.75% | 257 60.76% |
| SH | 776 32.95% | 2631 40.53% | 3407 38.51% | 68 36.36% | 94 39.83% | 162 38.30% |

Subjects with controlled HTN at baseline had a greater number of cardiovascular disease (CVD) related comorbidities. Among SH subjects, older subjects had more CVD comorbidities and have, on average, been diagnosed with HTN twice as long compared with younger subjects (Table 2).

Table 2: The mean length of diagnosis and number of CVD comorbidities among HTN subjects

| HTN status at baseline by Age Group (Years) | Controlled | | Systolic HTN | |
|---|---------------|---------------|---------------|---------------|
| | < 65 | 65+ | < 65 | 65+ |
| Length of diagnosis (years), Mean (S.D.) | 3.9 (3.76) | 5.2 (4.47) | 3.2 (3.98) | 6.8 (6.67) |
| Number of CVD comorbidities, Mean (S.D.) | 1.1 (1.01) | 1.4 (1.14) | 1.0 (0.96) | 1.3 (1.09) |

Over 42% of subjects received multiple treatments for their HTN (poly-pharmacy), which is more common among subjects younger than 65 years old compared to elderly subjects (43% and 36%, respectively). Angiotensin receptor blockers (ARBs; 48%) and calcium channel blockers (CCBs; 28 %) were the most commonly prescribed treatments. CCB monotherapy is more common among older subjects. Angiotensin converting enzyme inhibitors (ACEi) only comprised 2% of treatments while 12% of subjects did not receive any treatment for their HTN (

Table 3).

Table 3: Drug utilization at baseline

| HTN Treatment | < 65 yrs old | 65+ yrs old | Total |
|--------------------------|--------------|-------------|-------|
| No HTN treatment | 12.4% | 14.4% | 12.5% |
| CCB Alone | 20.5% | 24.9% | 20.7% |
| Beta Blocker Alone | 2.4% | 2.1% | 2.4% |
| Beta Blocker + CCB | 3.0% | <2% | 2.9% |
| ARB Alone | 17.4% | 17.7% | 17.4% |
| ARB + CCB | 19.3% | 16.9% | 19.0% |
| ARB + Beta Blocker + CCB | 2.5% | <2% | 2.4% |
| ACEi Alone | 2.4% | 3.0% | 2.4% |
| ACEi + CCB | 3.2% | 2.5% | 3.1% |

Percent of patients receiving HTN pharmaceuticals within the first month of annual health exam blood pressure reading. Not all combinations displayed.

Upon study inclusion, 44% of subjects were not controlled; 88% of the uncontrolled were SH subjects (39% of the overall subjects; n=3,569) and the remaining were isolated diastolic HTN subjects. The improvements in BP following one year of observation or treatment were seen SH subjects with 40% improving to goal. However, 22% of controlled subjects lost control of their HTN (Table 4).

Table 4: Change in HTN status after 1 year among all subjects

| Baseline HTN status | Unchanged | Improved to goal (140/90) | Worsened |
|---------------------|----------------|---------------------------|----------------|
| Controlled | 4086 78.38% | — | 1127 21.62% |
| Systolic HTN | 2145 60.10% | 1424 39.90% | — |

The overall annual costs for hypertension differed significantly among the controlled and SH populations, with average costs ranging from JPY 202,117 for SH to JPY 231,626 for controlled HTN (Table 5). Due to the interest in SH, isolated systolic HTN (ISH) and HTN consisting of both systolic and diastolic elevations are presented. ISH and controlled patients were the most costly while ISH patients aged 65 and above were the most costly overall.

Table 5: Costs of treatment (JPY) for 1 year by HTN status, subtype and age

| Baseline HTN type | Mean | STD | Median |
|---------------------------------|---------|---------|---------|
| Controlled | | | |
| Total | 231,626 | 594,105 | 137,240 |
| Less than 65 | 230,543 | 604,037 | 136,120 |
| 65+ | 252,516 | 351,506 | 172,860 |
| Systolic HTN | | | |
| Total | 202,117 | 559,605 | 115,220 |
| Less than 65 | 197,785 | 553,911 | 113,430 |
| 65+ | 293,214 | 663,698 | 171,335 |
| Subsets of Systolic HTN | | | |
| Isolated Systolic HTN | | | |
| Total | 230,989 | 640,464 | 126,060 |
| Less than 65 | 222,336 | 628,784 | 121,100 |
| 65+ | 333,202 | 760,928 | 198,935 |
| Hypertension (both SBP and DBP) | | | |
| Total | 182,702 | 497,122 | 108,100 |
| Less than 65 | 182,200 | 500,138 | 107,635 |
| 65+ | 203,643 | 351,940 | 129,405 |

Within-group analysis of patients who had SH at baseline revealed that being controlled or being 65 year-olds or older resulted in significantly higher costs (both $p < 0.001$; Figure 1). Overall, attaining control costs approximately JPY54,000 more than remaining uncontrolled, and subjects older than 65 years old spent almost JPY150,000 more than the overall average among controlled subjects. Attaining or maintaining control was consistently more costly than not being controlled. Elderly were also consistently more expensive to treat, regardless of control status.

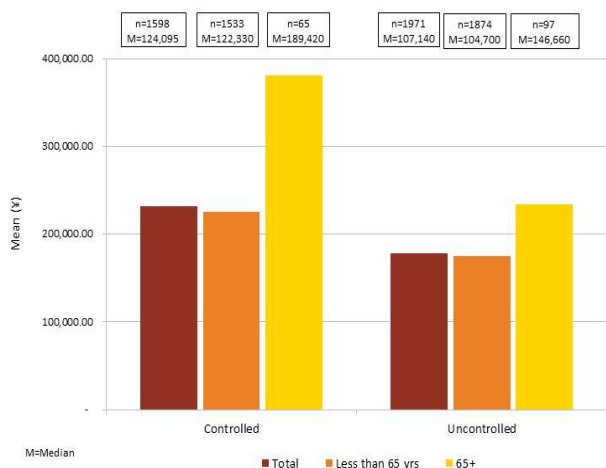


Figure 1. Total costs of SH subjects by control status after 1 year and age (JPY)

Discussion

In the current study, we examined the real-world characteristics of HTN patients in Japan based on insurance claims data and annual health checks. The use of insurance claims data and annual health checks from across the country allow us to compare actual blood pressure results to determine control status and treatments prescribed in a retrospective manner such that physician treatment behavior is not altered (i.e., if physicians know we are looking at their practice patterns, they may pay more attention to their patients). This is the first real world evaluation of HTN in Japan for control rates, cost of care and patient characteristics.

In this evaluation, we found that 44% of subjects were not adequately controlled at baseline. Moreover, only 78% of subjects who were controlled at baseline remained controlled one year later and less than 40% of SH subjects were able to gain control of their HTN one year later.

The use of poly-pharmacy is common with 42% of subjects receiving more than one HTN medication. ARBs and CCBs were the most commonly prescribed treatments, confirming appropriate treatment within Japanese Society for Hypertension guidelines.⁵

Overall, elderly SH patients incurred the highest expenditure with mean annual costs above JPY 290,000. Notably, within the elderly SH population, those with isolated SH incurred more than 1.5 times the expensive of elderly patients with both elevated systolic and diastolic BP. The costs of SH patients in the present study are comparable with prior research. Nakamura et al found that the average cost of treating HTN in Shiga prefecture was between JPY 22,378 – JPY 45,947 per month over a 10-year follow-up. Stage 1 annual HTN costs ranged between JPY 203,976 for women and JPY 268,536 for men which is more costly than found in the current study; however, as this was averaged over 10 years, there was a greater likelihood of capturing cardiac events which will increase the costs. In this study, the authors evaluated the subjects in Shiga who were enrolled in the National Health Insurance scheme for self-employed persons such as farmers and fishermen.

There are several limitations that need to be considered within this analysis. Our population sample was significantly limited by requiring two consecutive BP readings approximately 1 year apart. As the inclusion of these data is relatively new to the JMDC database,

only a portion of HTN subjects could be included. However, using actual BP readings ensured the relevancy of the analysis.

The JMDC database is the only claims database accessible to all researchers (fee to access) however it is limited by the inclusion of employment based insurers only. Due to the mandatory retirement age of 60 years, there are a limited number of elderly subjects in the database. This limits the generalizability of the data to subjects who are in the employment based insurance system rather than the National Health Insurance system which covers the self-employed, fishermen, farmers, etc.

Additionally, only claims with a HTN diagnosis on it were included. This limited our ability to evaluate the total costs of HTN subjects, accounting for their comorbidities. It also would not allow us to evaluate subjects who may have had prior cardiovascular events or other comorbidities not seen on the same medical claim as the HTN diagnosis. Although this does not affect the costs associated with HTN alone, it does not allow us to fully understand impact of various comorbidities on costs.

Conclusion

These data demonstrate the costs and lack of control associated with SH and the elderly. Given the rapidly aging population in Japan, it is likely that HTN will become a greater burden to the health care system. The lack of ability of SH subjects to gain control of their HTN raises concerns about the unmet need of these subjects, and especially within the elderly. These subjects may need additional education about lifestyle modifications and more aggressive antihypertensive therapy, as evidenced by Ohta et al.⁶

Real world evidence on control rates, cost of care and patient characteristics are critical to understand the value of treatments for HTN. Given the recent discussions within the Central Social Insurance Medical Council regarding the use of health technology assessment, this real world data provide the background for future evaluations on specific HTN therapies. The results of this analysis highlight the significant costs associated with controlling HTN in Japan. Specifically, the costs associated with SH (ISH in particular) and elderly subjects highlights the need for more attention to these subpopulations in an effort to improve control rates in a cost-effective manner.

Acknowledgements

This study was funded by Novartis Pharma AG

Conflict of interest statement: BC is employed by Adelphi Values, a consultant to Novartis. SHO and HF are employees of Novartis Pharma AG and sponsored this investigation. The authors have no other conflicts to declare.

REFERENCES

- Weber M. What is high blood pressure? In: High Blood Pressure and Health Policy. New York: Ruder Finn, Inc.; 2007:11-25.
- Japan Ministry of Health Labour and Welfare. Report on 2010 National Health and Nutrition Survey. <http://www.mhlw.go.jp/bunya/kenkou/eiyou/h22-houkoku.html> 2012.
- Ueshima H, Iida M, Shimamoto T, Konishi M, Tsujioka K, Tanigaki M, et al. Multivariate analysis of risk factors for stroke: Eight-year follow-up study of farming villages in Akita, Japan. *Prev Med* 1980; 9: 722-740.
- Hozawa A, Ohkubo T, Kikuya M, Yamaguchi J, Ohmori K, Fujiwara T, et al. Blood pressure control assessed by home, ambulatory and conventional blood pressure measurements in the Japanese general population: the Ohasama study. *Hypertens Res* 2002; 25, 57-63.
- Ogihara T, Kikuchi K, Matsuoka H, Fujita T, Higaki J, Horiuchi M, et al; on behalf of the Japanese Society of Hypertension Committee for guidelines for the management of hypertension. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2009). *Hypertens Res* 2009; 32, 3-107.

6. Ohta Y, Tsuchihashi T, and Kiyohara K. Relationship between blood pressure control status and lifestyle in hypertensive outpatients. *Intern Med* 2011; 50, 2107-2112.
7. Ministry of Health, Labor and Welfare. <http://www.mhlw.go.jp/topics/bukyoku/kenkou/seikatu/koukētuatu/reason.html>
8. Kimura S, Sato T, Ikeda S, Noda M, Nakayama T. Development of a database of health insurance claims: Standardization of disease classifications and anonymous record linkage. *J Epidemiol* 2010; 20 (5): 413-419.
9. Nakamura K, Okamura T, Kanda H, Hayakawa T, Kadowaki T, Okayama A, et al. Impact of hypertension on medical economics: A 10-year follow-up study of National Health Insurance in Shiga, Japan. *Hypertens Res* 2005; 28: 859-864.