Original Article

Efficacy and Safety of Long-Term Losartan Therapy Demonstrated by a Prospective Observational Study in Japanese Patients with Hypertension: The Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) Study

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The Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) study is a nationwide, prospective, multicentered, observational study that was designed to enroll 30,000 hypertensive Japanese patients from more than 3,000 private practitioners. It is the first large-scale observational study to assess the efficacy and safety of losartan, an angiotensin II receptor antagonist, in Japan. Patients were enrolled between June 2000 and May 2002, and followed up to June 2005. The data from 29,850 patients were used for the analysis of safety and efficacy. These patients were treated with losartan mostly at a daily dose of 25–50 mg. The mean follow-up period was 2.9 years. The patients were aged 62.4±12.1 years (mean±SD) and their mean systolic/diastolic blood pressure was 165.3±17.2/94.3±11.7 mmHg (mean±SD). Mean blood pressure in patients who were evaluated for efficacy decreased from 165.8/94.8 mmHg (*n*=26,512) at baseline to 145.5/84.4 mmHg after 3 months (*n*=21,269) and 138.6/80.0 mmHg after 36 months of treatment (*n*=13,879). Blood pressure was well controlled during the study period by losartan alone or losartan-based combination therapy. In nearly half of the patients, blood pressure was reduced to less than 140/90 mmHg during the study period. In addition to its antihypertensive effect, losartan reduced the uric acid level in patients whose baseline uric acid level was ≥7 mg/dL. Losartan also prevented acceleration of proteinuria. Adverse drug reactions occurred in 1,081 of the 29,850 patients. Long-term losartan therapy was effective and well tolerated in Japanese clinical practice. (*Hypertens Res* 2008; 31: 295–304)

***Key Words*: hypertension, losartan, Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH), efficacy, safety**

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Introduction

The number of persons with hypertension in Japan has been reported to be as high as 30 million (*1*). Therefore, management of hypertension is one of the major public health measures for preventing cardiovascular disease in this country. Although tight blood pressure (BP) control is recommended by the guidelines produced in Western countries and Japan to prevent cardiovascular disease in hypertensive patients (*2–5*), less than 50% of patients actually achieve good BP control (*6–11*).

Losartan potassium (losartan) is a subtype 1 (AT1)–selective angiotensin II (AII) receptor antagonist (ARB) that is widely prescribed as an antihypertensive agent throughout the world. Several large-scale clinical trials have already demonstrated the benefits of antihypertensive therapy with losartan (*12–17*). Losartan not only lowers the BP, but also has a protective effect on target organs. The Losartan Intervention For Endpoint reduction (LIFE) study demonstrated a more favorable effect of this drug on cardiovascular events than atenolol (*12*), while the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study demonstrated a renoprotective effect of losartan (*13*). In this RENAAL study, Japanese patients were included, and a renoprotective effect of losartan was demonstrated (*14*).

Various beneficial effects of losartan have been reported mainly in Western countries (*12*, *13*, *15–17*). However, these results may not be directly applicable to Japanese hypertensive patients, since the hypertensive patients enrolled in these studies usually have more risk factors than ordinary Japanese hypertensive patients. In addition, the percentage of elderly patients in Japan is different from that in Western countries, and genetic and environmental factors may differ between Japanese and Western patients (*18*, *19*).

Several studies in Japanese hypertensive patients have already been conducted, but these studies have mainly assessed small cohorts in specific rural areas. There have been few large-scale studies on the effects of losartan in daily clinical practice, and losartan's therapeutic benefits for Japanese patients have not been well demonstrated.

To investigate the efficacy and safety of losartan-based antihypertensive therapy and to understand the current status of antihypertensive therapy in ordinary clinical practice, a large scale study of losartan-based antihypertensive treatment in Japanese hypertensive patients would be meaningful.

The Japan Hypertension Evaluation with AIIA Losartan Therapy (J-HEALTH) study is a nationwide, prospective, multicentered observational study that was designed to enroll hypertensive Japanese patients (>30,000 subjects) from more than 3,000 private practitioners. This observational study was designed to investigate the efficacy and safety of long-term losartan therapy in ordinary clinical practice as a post-marketing surveillance study.

The present report deals with the efficacy, safety, and other effects of losartan as demonstrated by the J-HEALTH study. The incidence of cardiovascular events and mortality will be discussed in another paper in this series.

Methods

Patient Selection

The design of the J-HEALTH and the patient characteristics were described in detail previously (*20*). Patients were screened between June 2000 and May 2002 in all 47 prefectures of Japan. A total of 31,048 patients were enrolled in the study in proportion to the population of each prefecture. Among the patients thus enrolled, 1,198 patients were excluded from the analysis of safety, mainly due to violations of consent, previous treatment history with losartan, or other regulatory infractions. Consequently, 29,850 patients were eligible for safety evaluation. Among those 29,850 patients, 3,338 patients were ineligible for the analysis of efficacy mainly because of protocol violations or a lack of available BP data. Thus a total of 26,512 patients were eligible for the analysis of efficacy.

Study Design

The J-HEALTH is a nationwide prospective observational study that evaluates the efficacy and safety of long-term losartan therapy in the daily clinical setting. The effects of losartan on serum uric acid, urinary protein, and serum creatinine were also evaluated. The J-HEALTH study was designed to enroll a large number of Japanese hypertensive patients (>30,000 subjects) and was initiated as a post-marketing surveillance study in June 2000. The study period was 5 years in total, including a 2-year enrollment period. Patients were followed up to June 2005. The patients received open-label treatment with losartan for a maximum of 5 years.

The eligible patients were men or women aged ≥20 years with untreated or treated hypertension diagnosed by their personal physicians. Only patients who were not receiving antihypertensive drugs for at least 1 month prior to the study were registered. Patients with a history of losartan treatment at any period were excluded from the study. Each patient was informed of the purpose and methods of the study, as well as the effects and possible risks of losartan therapy, their right to withdraw from the study at any time, and the measures taken for privacy protection before the enrollment. Patients gave verbal informed consent and then underwent a medical history review, physical examination, and laboratory evaluation.

Treatment with losartan was started at a dose of 25–50 mg once daily (usually in the morning), which is the approved dosage in Japan. The dose could be increased up to a maximum of 100 mg once daily, if necessary. Addition of other antihypertensive agents was allowed from 3 months after the start of losartan treatment, if required. No restrictions were placed on the treatment of complications. Patients were fol-

Table 1. Patients' Characteristics at Baseline ($n=29,850$)

Male, %	44.1	
Age, years*	62.4±12.1	
BMI, kg/m^2*	24.1±3.6	
Mean clinic SBP, mmHg*	165.3±17.2	
Mean clinic DBP, mmHg*	94.3±11.7	
Grade of HT, %		
<130 and <85 mmHg	0.8	
130–139 or 85–89 mmHg	1.9	
140–159 or 90–99 mmHg	25.1	
160–179 or 100–109 mmHg	45.0	
≥180 or ≥110 mmHg	22.5	
Missing data	4.7	
HT history, months*	33.8±58.0	
HT treatment history, %†	15.4	
Clinic heart rate, bpm*	74.6±10.5	
Smoking habit, %	25.1	
Alcohol consumption, %‡	38.3	
Hyperlipidemia, %	38.8	
Diabetes mellitus, %	13.1	
Hyperuricemia/Gout, %	10.7	
Cardiovascular disease, %	8.0	
Cerebrovascular disease, %	4.4	
Hepatic disease, %	9.6	
Renal disease, %	3.2	
ECG abnormality, %	14.4	
Laboratory test (*n*)		
Creatinine, mg/dL*	0.9±0.3	(19,031)
Uric acid, mg/dL*	5.3±1.5	(17,202)
Urinary protein >"–", %§	19.1	(15,291)
Potassium, mEq/L*	4.2±0.5	(12,344)

*Mean±SD. †HT treatment history: patients who had a treatment history with antihypertensive drugs 1 month or more before the registration. ‡Alcohol consumption: ≥3 times/week and ≥200 mL/time (1 middle-sized bottle of beer or 2 glasses of diluted whiskey with water). §Urinary protein >"–": result of dipstick test for proteinuria more than negative (–). BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HT, hypertension.

Table 2. Antihypertensive Treatment during the Study Period ($n=26,512$)

Losartan	
Mean dose	47 mg/day
Initial dose	
≤25 mg/day	24%
≤50 mg/day	75%
>50 mg/day	1%
Losartan monotherapy	59%
Combination with other antihypertensive drugs	41%
No. of the drugs (including losartan)	
2-drug	29%
3-drug	9%
≥4-drug	3%
Major antihypertensive drugs	
CCB	32%
Diuretics	7%
β-Blockers	6%
α-Blockers	5%

CCB, calcium channel blockers.

lowed up for a maximum of 5 years.

The demographic data, physical data (height and body weight), history of hypertension, past treatment history of hypertension, BP values, pulse rate, complications, and medical history at enrollment were recorded. To assess complications and the medical history, physicians judged the existence of all disease indicated in the registration form before the start of treatment with losartan at their discretion. In addition, the patients who were on drug treatment for hyperlipidemia or diabetes mellitus (DM) and met the definition of either disease indicated in the relevant guidelines were defined as having hyperlipidemia or diabetes. Laboratory test results, ECG findings, and details of lifestyle modification, such as smoking and/or alcohol cessation/restriction, physical activity and weight loss, were also recorded, if available.

The clinic systolic BP (SBP) and diastolic BP (DBP) were measured by the usual methods at each institution. At each time of measurement, one clinic BP value was reported at the discretion of the physician. The clinic BP data were measured at baseline. During the follow-up period, the clinic BP value was measured every 3 months. The clinic BP data thus obtained were used for analysis of the clinic BP values at baseline and during treatment. Standard laboratory tests were reported every 6 months (if performed) during the study period. The investigators evaluated all adverse events and classified these as definitely related to the test drug, possibly related, definitely not related, or unknown. All losartan-related adverse events were pooled and classified as adverse drug reactions (ADRs). The following patient information was recorded in the case report forms and collected every year: adverse events, clinic BP values, pulse rate, heart rate, body weight, daily dose of losartan, concomitant drugs, laboratory test findings (if performed), and ECG findings (if performed).

Statistical Analysis

Variables were compared using the *t*-test, the χ^2 test, or analysis of variance (ANOVA), as appropriate. Results were expressed as the means±SD, and differences were considered statistically significant at $p<0.05$. Statistical analysis was conducted with the SAS software package (Version 8.02; SAS Institute Inc., Cary, USA).

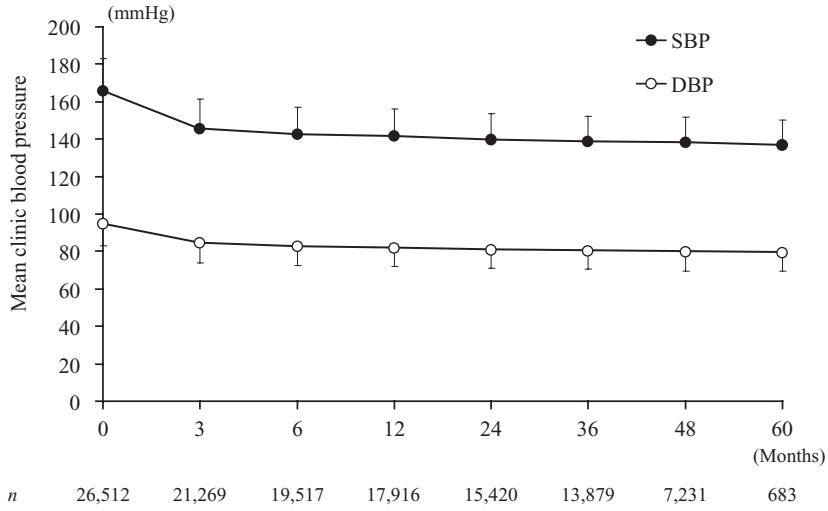


Fig. 1. *Change in mean clinic blood pressure during study period. SBP, systolic blood pressure; DBP, diastolic blood pressure.*

Study Organization

The Monitoring Committee assessed the advisability of continuing the study based on the safety and effectiveness of losartan therapy. The Safety Assessment Committee investigated the causal relationship between each ADR and the drugs administered during the study. The Medical Expert Advisory and Publication Committee were responsible for reviewing the results and writing reports.

Results

Baseline Characteristics

The baseline characteristics of the 29,850 patients (13,163 men [44.1%] and 16,687 women [55.9%]) eligible for analysis of safety are summarized in Table 1. The mean follow-up duration was 2.9 years. The mean age of the patients was 62.4±12.1 years, while the mean SBP and DBP were 165.3±17.2/94.3±11.7 mmHg. The prevalences of hyperlipidemia, DM, hyperuricemia/gout, cardiovascular disease, cerebrovascular disease, and ECG abnormalities were 38.8%, 13.1%, 10.7%, 8.0%, 4.4%, and 14.4%, respectively. Young patients (20–39 years) accounted for 2.9%, middle-aged patients (40–59 years) accounted for 38.4%, and elderly patients (60–79 years) made up 51.3% of the study population. It is worth noting that 2,209 patients (7.4%) were very elderly (≥80 years old). According to the Japanese Society of Hypertension (JSH) 2004/World Health Organization (WHO) classifications of hypertension, Moderate/Grade 2 hypertensive patients were predominant (n=13,429, 45.0%), while the percentages of Mild/Grade 1 and Severe/Grade 3 patients were almost equal (n=7,490, 25.1% *vs*. n=6,721, 22.5%, respectively).

Efficacy of Losartan

Follow-Up of Patients

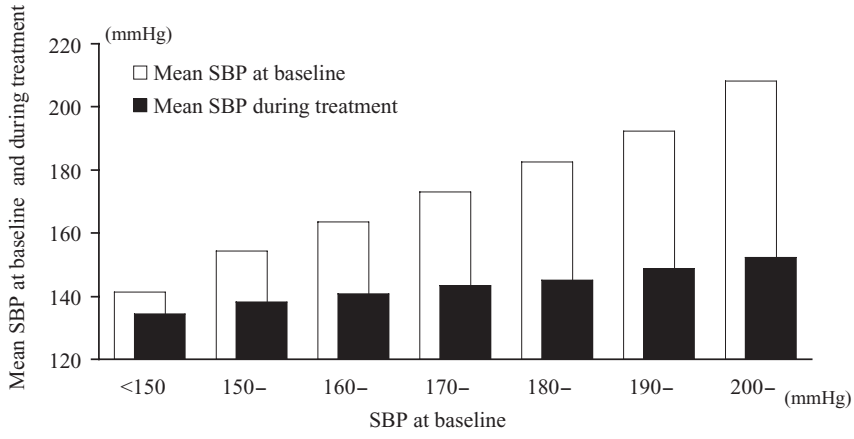
The 26,512 patients eligible for analysis of efficacy were followed up for a maximum of 5 years. However, approximately 45% (11,845 patients) of these patients were not followed up until June 2005, the end of the study period. The main reason for drop-out was failure to visit the clinic (65%).

Clinic Blood Pressure

Table 2 summarizes the antihypertensive therapy provided during the study period. The 26,512 patients were treated with losartan at a mean dose of 47 mg/day, with 59% receiving losartan monotherapy and 41% being treated with losartan-based combination therapy. Calcium channel blockers (CCBs) were the most frequently used concomitant drugs, being combined with losartan in 32% of the patients. Diuretics were prescribed in 7% of the patients. The number of antihypertensive drugs was two in 29%, three in 9%, and four or more in 3% of the patients.

The changes in BP are shown in Fig. 1. The mean BP decreased from 165.8/94.8 mmHg at baseline (n=26,512) to 145.5/84.4 mmHg after 3 months (n=21,269), 138.6/80.0 mmHg after 36 months (n=13,879), and 136.9/79.2 mmHg after 60 months (n=683) of losartan-based treatment. The mean BP during the entire follow-up period was 141.6/82.0 mmHg.

Patients who were treated with losartan alone throughout the study period were defined as the losartan monotherapy group. In the losartan monotherapy group, the mean BP decreased from 163.7/93.9 mmHg at baseline to 143.1/83.4 mmHg after 3 months of treatment and then decreased to 135.9/78.8 mmHg after 60 months of treatment. With combination therapy, the mean BP decreased from 169.0/95.9 mmHg at baseline to 149.1/86.0 mmHg after 3 months and



n	2,259	3,653	4,514	2,866	1,439	544	354
SBP changes							
mmHg	−6.77	−16.03	−22.70	−29.82	−37.41	−43.62	−55.89
%	−5	−10	−14	−17	−20	−23	−27

Fig. 2. *Reduction of mean SBP level by baseline SBP in patients treated with losartan monotherapy. The horizontal axis indicates the range of mean SBP at baseline. The vertical axis indicates the mean SBPs at baseline and during treatment. SBP, systolic blood pressure.*

then decreased to 138.1/79.6 mmHg after 60 months. The mean BP profile was similar between losartan monotherapy and combination therapy. On the whole, the mean BP during treatment was well controlled (<140/90 mmHg) in 46% of all the patients, and the mean follow-up period of these patients was 3.0 years. Furthermore, the BP was well controlled in approximately 50% of the patients receiving losartan monotherapy and 40% of those on combination therapy (data not shown). As shown in Fig. 2, the reduction of clinic BP by losartan monotherapy was more pronounced among the patients with higher baseline BP values than among those with lower baseline values.

The percentages of patients whose mean BP was controlled to less than 140/90 mmHg during treatment are shown in Fig. 3 after classifying into three age ranges and three grades of hypertension at baseline. The BP was well controlled (BP <140/90 mmHg) in more than 50% of Grade 1 patients, but in less than 50% of Grade 2 or Grade 3 patients. The percentage of patients with a well-controlled BP was similar among age groups for each grade of hypertension.

Proteinuria

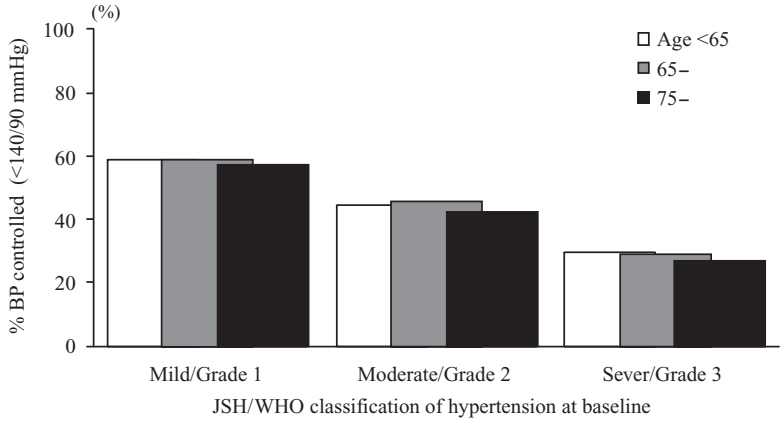
The prevalences of proteinuria in DM and non-DM patients are shown in Fig. 4. The percentage of patients with proteinuria decreased significantly following treatment in both the DM and non-DM groups.

Serum Uric Acid

In patients with baseline serum uric acid ≥7 mg/dL, the mean serum uric acid level decreased without uric acid–lowering drugs from 7.6 mg/dL (baseline) to 6.3 mg/dL (after 60 months), for a mean decrease of 1.3 mg/dL (Fig. 5). In patients whose baseline level was ≥7 mg/dL with uric acid–lowering drugs, there was a decrease from 7.3 mg/dL (baseline) to 6.3 mg/dL (after 60 months), for a mean decrease of 1.0 mg/dL. Thus, the change of uric acid levels was the same whether patients were administered uric acid–lowering drugs or not. The mean serum uric acid level of the patients with a baseline level <7 mg/dL was 4.9–5.0 mg/dL, and showed no clinically significant change throughout the study period.

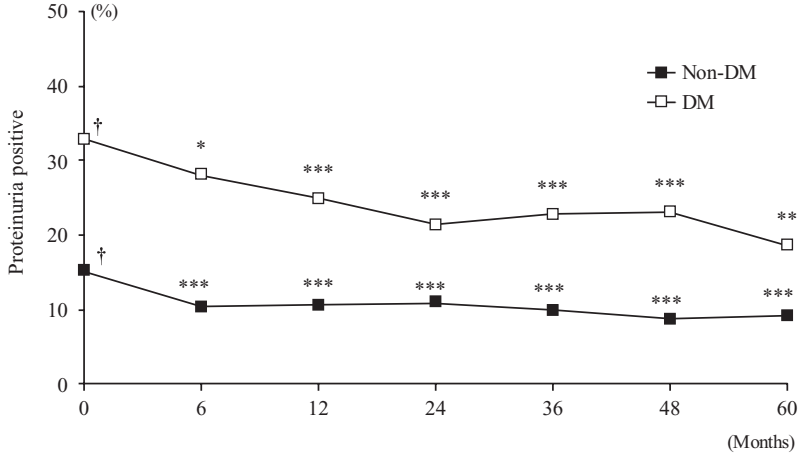
Safety of Losartan

Twenty-nine thousand, eight hundred and fifty subjects were eligible for analysis of ADRs, which were reported in 1,081 of the patients (Table 3). Unfortunately, the incidence of laboratory ADRs could not be determined definitively because laboratory examination was not mandatory for this survey protocol. However, no clinically significant or unknown ADRs were reported by the attending physicians during this study. The most frequent ADRs were dizziness, hepatic dysfunction, headache, anemia, and cough. The most frequently reported ADR of angiotensin converting enzyme inhibitors (ACEIs), cough, was detected in only 46 patients. Although renal dysfunction and hyperkalemia are known to be side effects of ARBs, renal dysfunction, including an increase of serum creatinine levels, was found in 46 patients, and hyperkalemia was found in 26 patients in the present study. Mean creatinine level stratified by sex and the baseline renal function are shown in Fig. 6. Renal dysfunction was defined by baseline serum creatinine ≥1.3 mg/dL for men and 1.2 mg/dL for women according to the JSH 2004 guidelines (5). No sus-



Age <65 years	(*n*)	3,849	7,415	4,082
65–	(*n*)	2,458	3,992	1,739
75–	(*n*)	1,318	2,222	995

Fig. 3. *Control rate of BP (< 140/90 mmHg) by grade of hypertension and age at baseline. JSH/WHO classification of hypertension: Mild/Grade 1, SBP 140–159 mmHg or DBP 90–99 mmHg; Moderate/Grade 2, SBP 160–179 mmHg or DBP 100–109 mmHg; Severe/Grade 3, SBP ≥180 mmHg or DBP ≥110 mmHg. BP, blood pressure; JSH, Japanese Society of Hypertension; WHO, World Health Organization; SBP, systolic blood pressure; DBP, diastolic blood pressure.*



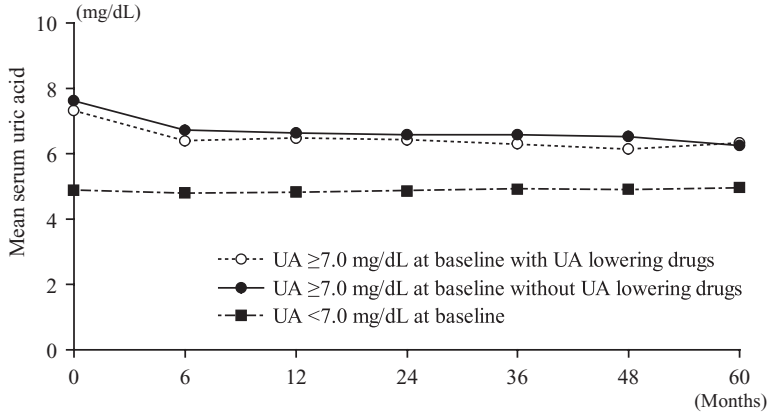
DM	1,576	892	887	730	693	414	102
Non-DM	7,357	3,003	3,720	3,337	3,076	1,977	490

Fig. 4. *Time courses of the proportion of proteinuria-positive in non-DM and DM patients during the study period. Proteinuria positive includes trace ±, +, ++ or +++ on urine dipstick test. DM, diabetes mellitus. **p < 0.01, ***p < 0.001 vs. †reference category, proportion of proteinuria positive at baseline.*

tained increase in the mean serum creatinine levels was observed in the patients, regardless of their baseline renal function, although the number of the patients decreased with time, especially after 48 months of treatment.

Discussion

The J-HEALTH study is a large scale observational study designed to evaluate the efficacy and safety of losartan-based antihypertensive therapy. A large number of Japanese hypertensive patients (>30,000 subjects) were enrolled in propor-



≥7.0, drugs	854	533	542	465	417	265	62
≥7.0, no drugs	1,310	711	729	581	514	317	95
<7.0	10,524	5,386	6,015	5,107	4,613	2,941	633

Fig. 5. *Time course of the mean serum uric acid levels in patients who had a baseline uric acid level of 7 mg/dL or higher (with and without uric acid–lowering drugs). UA, uric acid.*

Table 3. Summary of Major Drug-Related Adverse Experiences (*n* = 29,850)

	n
Total drug-related adverse experiences*	1,081
Major drug-related adverse experiences	
Dizziness	90
Hepatic function abnormal	61
Headache	48
Anemia	46
Cough	46
Blood pressure decreased	35
Blood creatinine phosphokinase increased	34

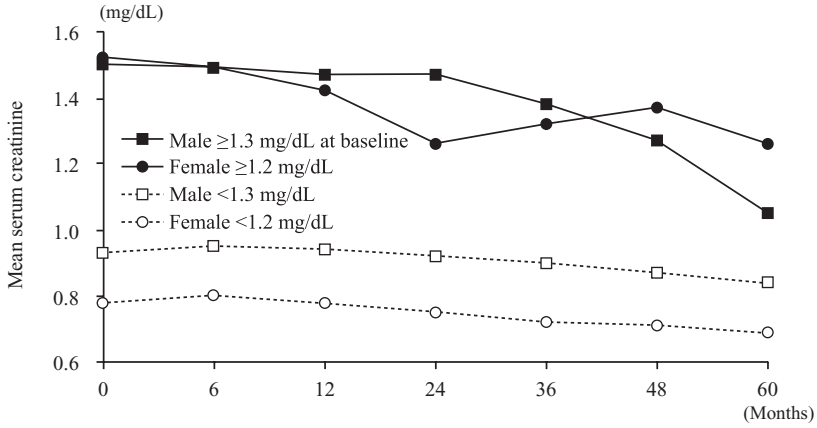
*Determined by the investigator to be possibly, probably or defined drug-related.

tion to the population of each prefecture. There was a broad range of ages and severities of hypertension among the enrolled patients, and thus the data are reasonably representative of the current status of antihypertensive therapy in daily clinical practice in Japan.

In the present study, long-term losartan-based antihypertensive therapy was shown to be effective for controlling the BP and well tolerated in Japanese hypertensive patients in routine clinical practice. The patients were followed for a mean of 3.0 years (5 years at maximum). The mean BP during the entire follow-up period was 141.6/82.0 mmHg. Nearly half of the patients had their BP controlled (< 140/90 mmHg). Sixty percent of the patients were treated with losartan monotherapy. Long-term use of losartan in daily clinical practice was shown to have beneficial effects on both uric acid and proteinuria.

Proteinuria and albuminuria have been well established as prognostic risk factors for cardiovascular and renal outcomes in both non-hypertensive and hypertensive patients (*21–25*). An antiproteinuric effect of losartan, which was independent of its BP-lowering effect, was demonstrated in long-term trials (*13*, *26*). However, few data are available concerning the antiproteinuric effect of losartan when used in daily clinical practice. In our study, losartan was shown to prevent acceleration of proteinuria both in DM and non-DM patients when used in daily clinical practice, although the detailed underlying mechanism remains uncertain because of the study design. Other studies have demonstrated a transient rise in the serum creatinine level soon after initiation of an ARB or ACEI in association with a persistent renal protective effect, particularly in patients with renal insufficiency (*27*, *28*). However, a significant transient increase in serum creatinine was not observed in our study.

High serum uric acid is an independent risk factor for cardiovascular events (*29–31*). Losartan has been reported to decrease the serum uric acid level in normal volunteers (*32*) and in hypertensive patients (*33*). Losartan inhibits the uric acid transporter (URAT1) and thus decreases the serum uric acid level, while other ARBs only inhibit URAT1 weakly (*34*, *35*). Hoieggen *et al*. (*36*) also indicated that decreased serum uric acid due to losartan was related with the prevention of cardiovascular events. In the present study, losartan was confirmed to decrease the serum uric acid level during the treatment period. Notably, the changes in uric acid were similar in patients with and without concomitant uric acid–lowering drugs, indicating that the serum uric acid level of patients treated with uric acid–lowering drugs was further decreased by losartan therapy. The reduction of uric acid by losartan observed in the present study is also favorable for preventing



n							
Male <1.3 mg/dL	5,748	3,075	3,303	2,812	2,571	1,553	357
Female <1.2 mg/dL	8,124	4,307	4,752	4,089	3,734	2,402	554
Male ≥1.3 mg/dL	437	247	265	220	171	108	19
Female ≥1.2 mg/dL	215	140	129	99	94	48	9

Fig. 6. *Changes in serum creatinine levels by sex and the baseline renal function.*

cardiovascular events in addition to its BP-lowering effect in clinical practice.

The present study demonstrated that losartan was well tolerated in clinical practice. Increases in serum creatinine and hyperkalemia are always a concern when using an ARB or ACEI. A number of studies have reported the necessity of carefully monitoring renal function, such as by measuring creatinine or electrolyte levels, and especially in patients with renal insufficiency (*27*, *37*–*39*). In the present study, the incidence of renal dysfunction and hyperkalemia associated with losartan therapy were relatively rare. In addition, no sustained increase in mean serum creatinine levels was observed regardless of the patient's renal function. Regular monitoring of renal function is, however, still required when ARBs or ACEIs are administered.

Other studies conducted in Japan and Western countries have reported BP control in less than 50% of the treated hypertensives (*6*–*11*). Similarly, BP was maintained at less than 140/90 mmHg in nearly half of the patients in the present study. Patients with severe hypertension were less sufficiently controlled than those with mild-to-moderate hypertension. Therefore, we should treat hypertensive patients more strictly to prevent cardiovascular events and increase the rate of BP control, especially in severe hypertensive patients.

This study was not a randomized controlled trial but a prospective observational study supported by general practitioners in clinical practice. Although a large-scale observational study can provide valuable information about the treatment in ordinary clinical practice that is not available in conventional controlled clinical trials, it has some limitations.

First, a long-term observational study based on daily clinical practice permits a considerable number of patients to drop out during the follow-up period. Those who dropped out within the first 3 months of this study, during which period the use of other hypertensive drugs was prohibited, may have had insufficient BP reduction. This kind of bias may influence the rate of losartan monotherapy as well. Therefore, it should be taken into consideration that the rate of losartan monotherapy and the rate of good BP control could have been evaluated only in patients who were followed up for the long-term. However, our data may indicate that good adherence to therapy leads to good BP control in a daily practice setting. Second, in contrast to clinical trials, the post-marketing surveialnce can not regulate items and timing of laboratory examinations. This means that we may have underestimated the incidence of ADRs, including laboratory examination abnormalities, for the whole study period. Despite such limitations, the results of the J-HEALTH study are still valuable as data reflecting hypertensive treatment performed in daily clinical practice in Japan.

In conclusion, long-term losartan-based antihypertensive therapy was effective and well tolerated in a daily clinical practice setting. The BP was maintained at less than 140/90 mmHg with losartan-based antihypertensive treatment in nearly half of the patients over the study period. With losartan monotherapy, the mean BP decreased from 163.7/93.9 mmHg to 135.9/78.8 mmHg. Antiproteinuric and uric acid–lowering effects were also confirmed. However, the BP control rate was still inadequate for treated Japanese hypertensive patients in daily clinical practice, as reported elsewhere. Therefore, stricter treatments, such as multiple antihypertensive treatments, will be needed to improve the BP control rate in hypertensive patients, and especially for those with severe hypertension.

Based on the results of the J-HEALTH, losartan is favorably recommended as an initial therapy for Japanese patients with hypertension, mainly due to its BP-lowering effects and long-term tolerability. However, it is also recommended that multiple agents be considered in order to improve the BP control of Japanese hypertensives, especially in those with severe hypertension.

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Appendix

J-HEALTH Committees

Monitoring Committee: Takenori Yamaguchi (Chair), Tanenao Eto, Toshiharu Furukawa, and Katsumi Yoshida.
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