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Clinical characteristics of patients with alcohol dependence comorbid with hypertension among regular drinkers: An internet-based, cross-sectional study in Japan

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ABSTRACT

While evidence suggests a strong association between alcohol and hypertension, little is known about the profile of patients with alcohol dependence comorbid with hypertension. This study aimed to clarify the clinical characteristics and health problems of this population through a web-based questionnaire survey using a research company's panel of adults in Japan. Of 20 000 regular drinkers, 176 on treatment for hypertension and with alcohol dependence (confirmed and/or an Alcohol Use Disorders Identification Test score ≥15 points) were included. Participants were asked about their health-related quality of life, work productivity, blood pressure (BP) control, receipt of brief interventions, and awareness of their alcohol dependence. Results were compared between the BP-controlled and BP-uncontrolled groups. The mean EQ-5D utility score was 0.838 in the entire population, and 0.786 vs. 0.892 in the groups ($p < 0.0001$). When 133 'employed' participants were compared, productivity loss was more apparent in the BP-uncontrolled group (presenteeism, 27.3% vs. 6.1%, $p < 0.0001$; absenteeism, 10.7% vs. 1.0%, $p = 0.0003$). The rate of dissatisfaction with BP control was 55.1% in the entire population (most [76.3%] of those dissatisfied considered alcohol a cause of inadequate BP control), ~78% in the uncontrolled group, and ~34% in the controlled group. Of those previously advised to reduce drinking or abstain from alcohol (60.2% of all participants), 63% (BP-uncontrolled group) and 55% (BP-controlled group) decreased their drinking. Though more than twice as many participants thought themselves to be alcohol-dependent in the BP-uncontrolled group than in the controlled group (41% vs. 15%), most (59% vs. 85%) showed no self-awareness of alcohol dependence. Patients with alcohol dependence comorbid with hypertension had impaired health status and reduced work productivity. They thought alcohol was the most common cause of inadequate BP control. Treatment beyond brief interventions is needed to enhance their awareness of alcohol dependence and their motivation to reduce drinking.

Introduction

According to an epidemiological study conducted in 2013, 1.07 million Japanese individuals were estimated to previously or currently have alcohol dependence, including 0.57 million people with current alcohol dependence (Osaki et al., 2016). Of those currently having alcohol dependence, 82.6% had sought medical advice for any reason in the previous years, but only 17.4% had been treated for alcohol dependence (Osaki et al., 2016). These data suggest that alcohol dependence may remain undiagnosed during screening for various comorbid conditions. A meta-analysis has shown increased mortality associated with excessive alcohol consumption in both men and women (Di Castelnuovo et al., 2006), raising global concerns about health loss and public health burden due to alcohol abuse and dependence.

A systematic review identified more than 200 reports that provide evidence of a causal impact of alcohol consumption on the risk of major conditions such as stroke, as well as hypertensive and ischemic heart disease (Rehm et al., 2010). In one study, alcohol

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intake ≥100 g per week was found to be a significant risk factor for stroke, coronary artery disease (excluding myocardial infarction), heart failure, fatal hypertensive disease, and fatal aortic aneurysm (Wood et al., 2018). Therefore, a substantial proportion of patients treated for various medical conditions probably have concomitant alcohol use disorders.

In Japan, patients who consult physicians are most often treated for hypertension (Japanese Ministry of Health, Labour and Welfare, 2014). Many of those treated for hypertension may be regular drinkers, because several Japanese cohort studies have also observed a significant positive relationship between alcohol consumption and hypertension (Okubo et al., 2014; Ueshima et al., 1984). Based on definitive evidence for a relationship between excessive alcohol intake and hypertension, the recent international guidelines recommend that alcohol consumption be reduced in hypertensive patients (Unger et al., 2020). Some studies have demonstrated that reduced drinking results in an improvement of hypertensive disorders (Minami et al., 2002; Ueshima et al., 1993). Other studies have shown that heavy drinking increases the risk of hypertensive stroke and the level of stroke-specific impairments in quality of life (QOL). Although light-to-moderate drinking could be protective for stroke, as well as coronary artery disease (Higashiyama et al., 2013; Ikehara & Iso, 2010), there is an abundance of evidence that alcohol is a risk factor for aggravation of hypertension (Criqui, Langer, & Reed, 1989; Kastarinen et al., 2007; Klatsky, Koplik, Gunderson, Kipp, & Friedman, 2006; Roerecke et al., 2017; Sesso, Cook, Buring, Manson, & Gaziano, 2008). In the European Union, screening and appropriate interventions have recently been recommended to prevent the aggravation of hypertension that results from hazardous and harmful alcohol use (Rehm et al., 2017).

Thus, previous studies have clearly indicated the significant negative impacts of excessive alcohol use on QOL and survival of hypertensive patients. To eliminate these impacts, it is essential to increase the awareness of hypertensive patients of the harms of heavy drinking and to ensure early diagnosis and treatment of alcohol dependence in hypertensive patients. Since little is known about the profile of hypertensive patients with alcohol dependence, a questionnaire survey of a panel of adult regular drinkers in Japan who had alcohol dependence and were on treatment for hypertension at the time of the survey was conducted to clarify the clinical characteristics and health problems of this population, including a *post hoc* analysis comparing the blood pressure (BP)-controlled and BP-uncontrolled groups.

Participants and methods

Study design

This was a questionnaire-based, cross-sectional study involving adult regular drinkers in Japan who had alcohol dependence and were being treated for hypertension by physicians. This study aimed to determine the clinical characteristics of this specific population and to uncover their health problems. Prior to the initiation of the study, the protocol for the study was approved by the Ethics Committee of the Japan Physicians Association. The study was conducted in accordance with the Declaration of Helsinki, the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects (Ministry of Health, Labour and Welfare/ Ministry of Education, Culture, Sports, Science and Technology, 2017), and the Japanese Guidelines for Pharmacoepidemiological Study for Drug Safety Assessment based on Medical Information Database (Pharmaceuticals and Medical Devices Agency in Japan, 2014). On an Internet website, all participants were informed of the protocol for the study, and they provided their consent to participate by clicking the "I agree" button. This study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000027639).

Participants

During the period from June 6 to June 18, 2017, a panel of about 900 000 adults registered in Japan at Macromill, Inc (Tokyo, Japan) was invited to participate in this web-based questionnaire survey if they met the following inclusion criteria: 1) drinking ≥2 or ≥3 times a week; 2) aged ≥20 years at the time of informed consent; 3) having alcohol dependence, defined as an established diagnosis of alcohol dependence and/or an Alcohol Use Disorders Identification Test (AUDIT) score ≥15 points; 4) currently on treatment for hypertension by physicians; and 5) informed consent to the study. There were no exclusion criteria.

According to an epidemiological study in Japan in 2013 (Osaki et al., 2016), the proportion of lifetime alcohol dependence diagnosed by ICD-10 was 1.1%, and the proportion of current potential alcohol dependence (AUDIT score ≥15 points) was 2.7%. Medical advice had been sought for any reason in the previous years by 84.1% of those with current/previous alcohol dependence and 64.6% of those with potential alcohol dependence. The 2014 Patient Survey conducted by the Japanese Ministry of Health, Labour and Welfare (2014) estimated that hypertension was the main reason for consultation in about 10% of those who consulted a physician. Considering the feasibility of the study, the target sample size was set at ≥50. Based on the above-mentioned estimates, in order to enroll at least 50 eligible patients, it was thought necessary to have 20 000 panel members with regular alcohol use available for screening. Hence, response collection was stopped when valid responses were received from 20 000 regular drinkers.

Study variables and assessments

Details of the questionnaire used in this study are provided in the Supplementary Table.

Health-related QOL (HR-QOL) was assessed using a validated Japanese version of the EQ-5D-5L (Ikeda et al., 2015). Participants were asked to grade their health status in 5 dimensions at 5 levels. The 5-digit figures generated were converted to HR-QOL scores on a scale from 1 (completely healthy state) to 0 (death).

A validated Japanese version of the Work Productivity and Activity Impairment Questionnaire – General Health (WPAI-GH) v2.2 (Reilly Associates, 2019b) was used to assess the impacts of participants' health problems on their abilities to work and perform regular daily activities. This instrument consists of 6 questions, and all but the first question generated values. From the Q2–Q6 values, presenteeism (impairment at work) and absenteeism (work time missed) scores were calculated as Q5/10 and Q2/(Q2+Q4), respectively, and expressed as percentages (Reilly Associates, 2019a).

Participants were also asked about antihypertensive treatments they received, control of BP, and their liver function status (γ-GTP value). The latter half of the questionnaire focused on participants' satisfaction with current BP control, receipt of brief interventions, motivation to reduce drinking, and awareness of alcohol dependence. The impacts of brief interventions on their alcohol-drinking behavior were also investigated.

Data analyses

Continuous data are summarized by descriptive statistics (*N*, mean, SD, minimum, median, and maximum), and nominal and ordinal variables are summarized as frequencies and proportions. Since patients with alcohol dependence comorbid with hypertension are considered to be heterogeneous with regard to current BP

control, a *post hoc* analysis was performed to determine whether BP control affected the results of this study. Participants were divided into 2 groups: controlled BP (office or clinic systolic BP [SBP] <140 mmHg and diastolic BP [DBP] <90 mmHg; Unger et al., 2020) and uncontrolled BP (office or clinic SBP ≥140 mmHg or DBP ≥90 mmHg) groups. The demographic and clinical characteristics, as well as health problems, of the two groups were compared using Student's *t* test, Fisher's exact test, or the Wilcoxon rank-sum test, as appropriate.

Results

Participants

Of the 20 000 adults reporting regular alcohol use, 3261 (2859 men and 402 women) were being treated for hypertension. Of those being treated for hypertension, 734 (22.5%; 676 [/2859; 23.6%] male and 58 [/402; 14.4%] female) participants were found to have an AUDIT score ≥15 points at screening. Including 168 (5.2%) participants with an established diagnosis of alcohol dependence (some of whom had an AUDIT score ≥15 points), a total of 808 (24.8%) participants treated for hypertension had alcohol dependence. Of the 808 eligible participants, the first 176 who were confirmed to have given informed consent to the study were included, considering the sample size (n = 150) that took account of the feasibility of the study. A flowchart of patient enrollment is shown in Fig. 1.

The demographic and baseline characteristics of the 176 participants are shown in Table 1. Of the 176 participants, 19 (10.8%) currently had an established diagnosis of alcohol dependence, and of the 157 participants who did not currently have an established diagnosis of alcohol dependence, 8 (5.1%) had previously had a diagnosis of alcohol dependence. Similar percentages of those with uncontrolled and controlled BP (9.6% vs. 10.6%) currently had an established diagnosis of alcohol dependence ($p = 1.0000$), and there was a trend toward a higher frequency of a previous diagnosis of alcohol dependence among those with uncontrolled BP (8.0% vs. 1.3%, $p = 0.0631$). The mean (SD) AUDIT score was 21.2 (5.9) points for all participants, and it was not different between those with uncontrolled and controlled BP (22.0 [5.8] vs. 20.5 [6.0] points, $p = 0.0963$).

Main findings

Table 2 summarizes the data on HR-QOL, work productivity, antihypertensive treatments, BP control, and liver function for the

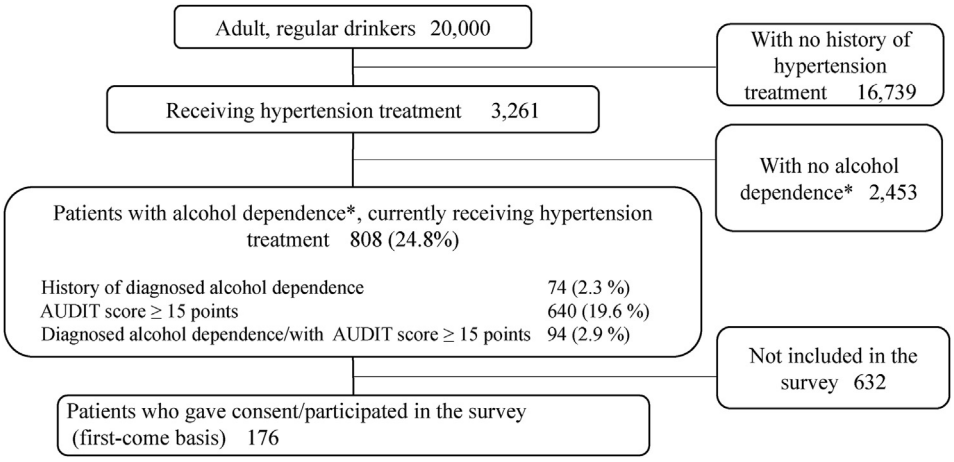

Fig. 1. Flowchart of participant enrollment AUDIT: Alcohol Use Disorders Identification Test. *Alcohol dependence was defined as an established diagnosis of alcohol dependence and/or an AUDIT score ≥15 points.

Table 1
Demographic and clinical characteristics of 176 participants with alcohol dependence comorbid with hypertension.

Variable	All	Blood pressure control[a]		
		Uncontrolled[b]	Controlled[c]	*p* values
	N = 176	N = 83	N = 85	
Age [years], mean (SD)	56.7 (9.3)	55.8 (9.8)	58.0 (8.5)	0.1230[e]
Male, n (%)	164 (93.2)	73 (88.0)	83 (97.7)	0.0171[f]
Currently confirmed alcohol dependence, n (%)	19 (10.8)	8 (9.6)	9 (10.6)	1.0000[f]
Previously confirmed alcohol dependence, n (%)[d]	8 (5.1) (N = 157)	6 (8.0) (N = 75)	1 (1.3) (N = 76)	0.0631[f]
AUDIT score, mean (SD)	21.2 (5.9)	22.0 (5.8)	20.5 (6.0)	0.0963[e]
Any treated condition other than hypertension, n (%)	121 (68.8)	56 (67.5)	63 (74.1)	0.3973[f]

AUDIT Alcohol Use Disorders Identification Test.
[a] Eight participants missing latest data on systolic or diastolic blood pressure were excluded from both subgroups.
[b] Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.
[c] Systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg.
[d] Relative to the number of participants without currently confirmed alcohol dependence, indicated in parentheses.
[e] Student's *t* test.
[f] Fisher's exact test.

Table 2
Results of survey of all participants and by group.

Parameter	All	Blood pressure control[a]		
		Uncontrolled[b]	Controlled[c]	*p* value
Health-related QOL				
EQ-5D utility score, mean (SD)	0.838 (0.155) (N = 176)	0.786 (0.169) (n = 83)	0.892 (0.116) (n = 85)	<0.0001[j]
Work productivity				
Currently employed, n (%)	133 (75.6) (N = 176)	60 (72.3) (n = 83)	67 (78.8) (n = 85)	0.3712[k]
Hours missed from work due to health problems, mean (SD)[d]	1.77 (5.67) (N = 133)	3.25 (7.70) (n = 60)	0.43 (2.51) (n = 67)	<0.0001[l]
Hours missed from work due to non-health problems, mean (SD)[d]	10.24 (21.63) (N = 133)	8.22 (15.13) (n = 60)	12.94 (26.67) (n = 67)	0.6236[l]
Hours spent in actual work, mean (SD)[d]	33.94 (21.31) (N = 133)	33.13 (21.54) (n = 60)	35.58 (20.48) (n = 67)	0.5127[j]
Extent of productivity affected by health problems, mean (SD)[d]	2.62 (2.17) (N = 133)	3.73 (2.48) (n = 60)	1.61 (1.23) (n = 67)	<0.0001[j]
Extent of non-work daily activities affected by health problems, mean (SD)[d]	2.91 (2.28) (N = 176)	3.78 (2.55) (n = 83)	2.04 (1.61) (n = 85)	<0.0001[j]
Presenteeism [%],[e] mean (SD)	16.2 (21.7) (N = 133)	27.3 (24.8) (n = 60)	6.1 (12.3) (n = 67)	<0.0001[l]
Absenteeism [%],[f] mean (SD)	6.1 (14.8) (N = 114)	10.7 (19.0) (n = 52)	1.0 (4.8) (n = 58)	<0.0001[l]
Medical treatment of hypertension				
Any antihypertensive drug prescribed, n (%)	152 (86.4) (N = 176)	73 (88.0) (n = 83)	76 (89.4) (n = 85)	0.2899[k]
≥2 antihypertensive drugs prescribed, n (%)[g]	60 (39.5) (N = 152)	31 (42.5) (n = 73)	29 (38.2) (n = 76)	–
Latest blood pressure				
SBP ≥140 mmHg, n (%)[h]	70 (41.7) (N = 168)	70 (84.3) (n = 83)	— (n = 85)	–
DBP ≥90 mmHg, n (%)[h]	67 (39.9) (N = 168)	67 (80.7) (n = 83)	— (n = 85)	–
Liver function				
γ-GTP ≥100 IU/L, n (%)[i]	61 (72.6) (N = 84)	39 (83.0) (n = 47)	20 (57.1) (n = 35)	0.0134[k]

DBP: diastolic blood pressure; *EQ-5D*: Euro QOL Five Dimensions Questionnaire; *γ-GTP*: γ-glutamyl transferase; *SBP*: systolic blood pressure.
[a] Eight participants missing latest data on SBP or DBP were excluded from both subgroups.
[b] SBP ≥140 mmHg or DBP ≥90 mmHg.
[c] SBP <140 mmHg and DBP <90 mmHg.
[d] Values calculated for the most recent 7 days.
[e] Evaluated in participants currently employed (*N* indicated in parentheses).
[f] Evaluated in participants currently employed and with data on absenteeism available (*N* indicated in parentheses).
[g] Relative to the number of participants currently treated for hypertension, indicated in parentheses.
[h] Relative to the number of participants having latest data on blood pressure, indicated in parentheses.
[i] Relative to the number of participants previously diagnosed with elevated γ-GTP and having current data on this parameter, indicated in parentheses.
[j] Student's *t* test.
[k] Fisher's exact test.
[l] Wilcoxon rank-sum test.

entire population, as well as the subgroups of patients with controlled and uncontrolled BP. The entire population had a mean (SD) EQ-5D utility score of 0.838 (0.155); the score was lower in the BP-uncontrolled group than in the BP-controlled group (0.786 vs. 0.892; $p < 0.0001$). Of the 176 participants, 133 were currently employed, and those in the BP-uncontrolled group lost more working hours due to health problems than those in the BP-controlled group (3.25 vs. 0.43 h; $p < 0.0001$). The health problems also affected work productivity and non-work daily activities more in BP-uncontrolled patients ($p < 0.0001$). The mean (SD) presenteeism and absenteeism scores of all participants were 16.2% (21.7) and 6.1% (14.8), respectively. Presenteeism and absenteeism were higher in the BP-uncontrolled group (27.3% vs. 6.1%, $p < 0.0001$; 10.7% vs. 1.0%, $p < 0.0001$). A total of 152 participants (86.4%) were on any antihypertensive drug, with 60 of them (39.5%) receiving 2 or more drugs. Of the 168 participants with current BP data available, 70 (41.7%) had SBP ≥140 mmHg and 67 (39.9%) had DBP ≥90 mmHg. Of 84 participants with current γ-GTP data available, 61 (72.6%) had a value ≥ 100 IU/L, including 39 (83.0%) BP-uncontrolled patients and 20 (57.1%) BP-controlled patients, with a significant difference between the two groups ($p = 0.0134$).

Of the 176 participants, 97 (55.1%) were not satisfied with current BP control. About 66% (23.5% 'very satisfied'+ 42.4% 'fairly satisfied') of the 85 BP-controlled participants were satisfied, whereas a lower percentage (ca. 2.4 + 19.3 = 21.7%) of satisfaction was observed in the BP-uncontrolled participants (Fig. 2A). Of the 97 participants not satisfied with BP control, 76.3% considered alcohol a factor contributing to the unsatisfactory BP control. Other lifestyle-associated factors such as obesity, smoking, salt intake, and stress were considered of secondary importance (Fig. 2B).

A total of 106 participants (60.2%) had been advised by a physician or public health nurse to reduce alcohol intake (52.8%) or abstain from alcohol (7.4%; Fig. 3A). The difference in the percentages of participants receiving any brief intervention was not large between the BP-uncontrolled group and the BP-controlled group (65% vs. ~55%, respectively). Of these 106 participants, 63 (59.4%) reported reduced drinking either 'reduced to the target level as advised' (2.8%), 'reduced but not to the level as advised' (28.3%), or

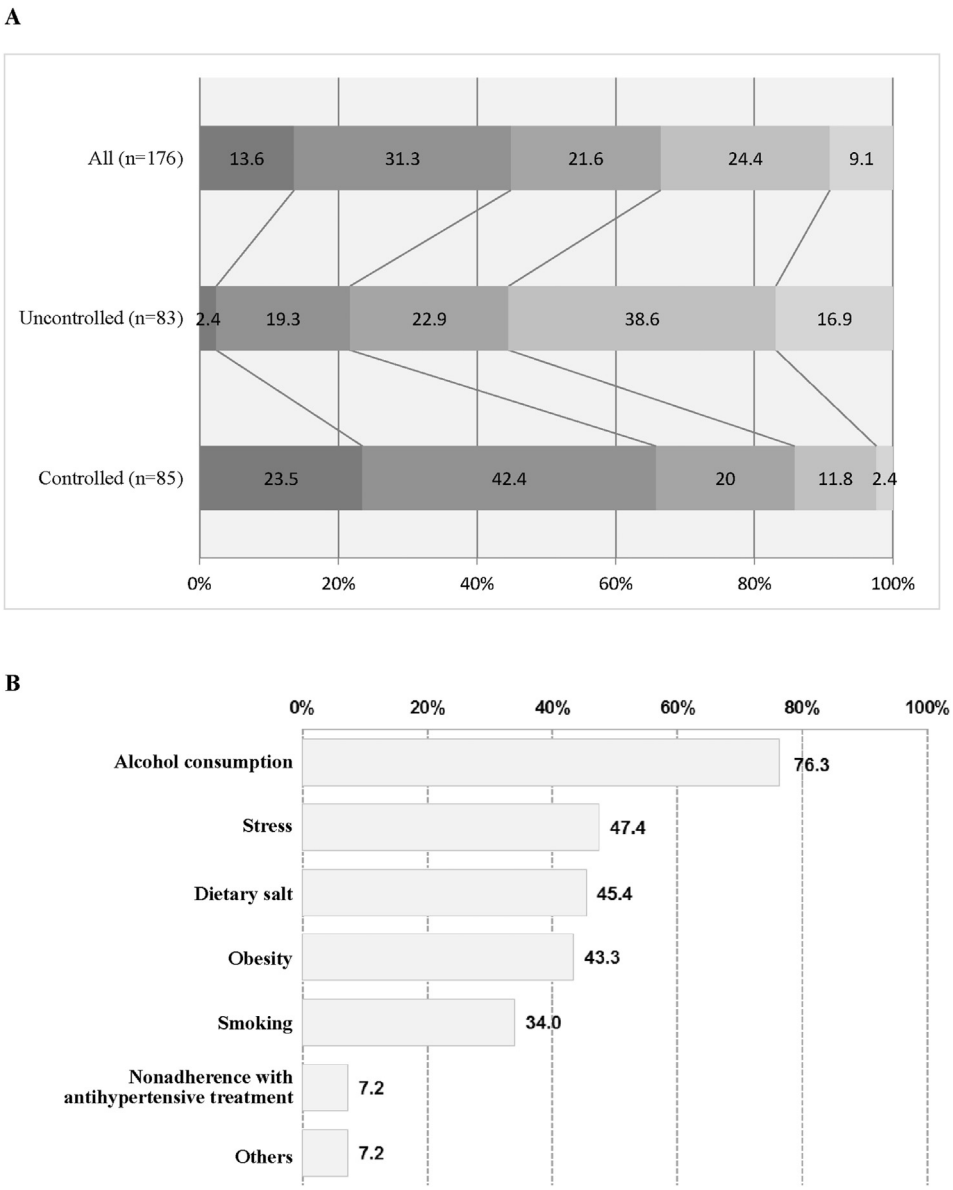

Fig. 2. Satisfaction of participants with blood pressure control (**A**) Satisfaction of the participants with their blood pressure control (N = 176) ■ Very satisfied; ■ Fairly satisfied; ■ Neither satisfied nor unsatisfied; ■ Somewhat unsatisfied; ■ Very unsatisfied (**B**) Lifestyle factors that likely contributed to insufficient blood pressure control (N = 97) Participants not satisfied with their BP control selected likely factors out of the listed choices.

'reduced but no target was set' (28.3%), as seen in Fig. 3B. The percentage of participants with reduced alcohol consumption was somewhat higher in the BP-uncontrolled group than in the BP-controlled group (63.0% vs. 55.3%), and a higher percentage (37% vs. ~45%) of 'not considerably changed' plus 'increased' participants was concomitantly observed in the BP-controlled group.

With respect to the question about motivation to reduce alcohol consumption, 61 (34.7%) participants answered that they had no intention to reduce their drinking, and 81 (46.0%) answered that they were weak-willed (i.e., willing but unable to reduce), as seen in Fig. 4A. Eighteen (10.2%) reported that they were going to reduce drinking before long (in a month), and 16 (9.1%) had reduced drinking for <6 months or longer. There were fewer participants who had no motivation to reduce alcohol consumption in the BP-uncontrolled group than in the BP-controlled group (21 (25.3%) vs. 35 (41.2%)), whereas there were slightly more weak-willed participants in the BP-uncontrolled group (42 [50.6%] vs. 36 [42.4%]). More participants in the BP-uncontrolled group showed motivation for early reduction or had already initiated reduction than in the BP-controlled group (Fig. 4A). Fifty (28.4%) of the entire participant group thought that they might currently have alcohol dependence, whereas 126 (71.6%) did not think that they currently had alcohol dependence (Fig. 4B). More than twice as many participants in the BP-uncontrolled group were aware of their alcohol dependence compared to those in the BP-controlled group (41.0% vs. 15.3%), but it should be noted that the majority (59.0% and 84.7%, respectively) were still unaware of the disorder.

Discussion

In regular drinkers, alcohol dependence may be comorbid with hypertension and often remains undiagnosed, despite its significant association with various risks. Using self-administered questionnaires, a web-based survey of a panel of adults with regular

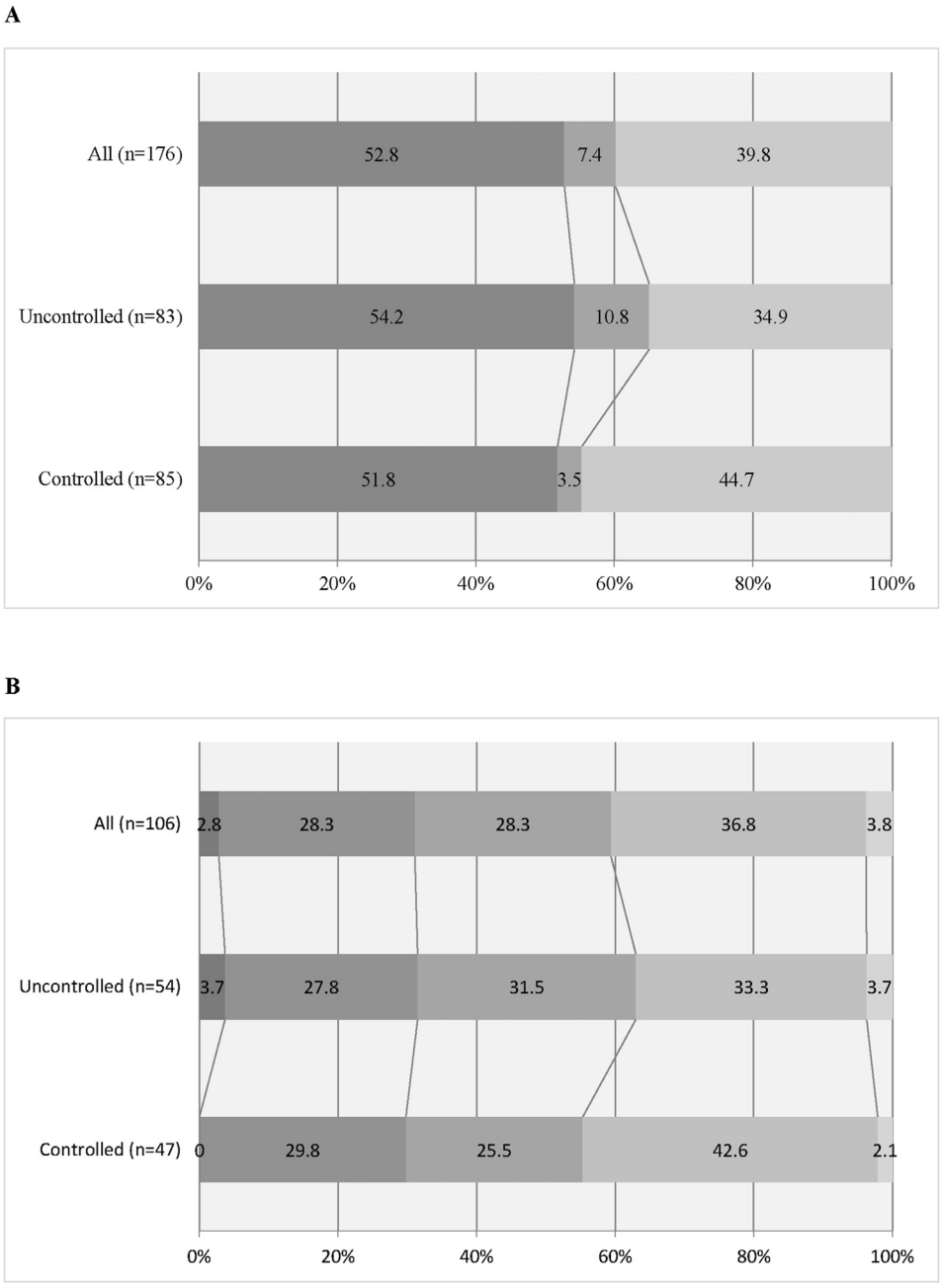

Fig. 3. Brief intervention and subsequent reduction of alcohol consumption (**A**) Participants receiving advice by healthcare providers (physicians or public health nurses) to reduce alcohol consumption (N = 176) ■ Advised to reduce alcohol consumption; ■ Advised to abstain from alcohol consumption; ■ Not previously advised (**B**) Changes in alcohol consumption following advice (N = 106). Participants who received brief interventions judged the changes in their alcohol consumption based on the listed choices that applied best. ■ Reduced to the target level as advised; ■ Reduced, but not to the level as advised; ■ Reduced, but no target was set; ■ Not considerably changed; ■ Increased.

alcohol use who had alcohol dependence and were treated for hypertension was conducted in Japan. The aim of this study was to identify alcohol use disorders and to quantify the impacts of alcohol use on QOL and work productivity in this population. In the study, more impaired health status and reduced work productivity/daily activities were found in the patients with alcohol dependence and uncontrolled BP compared to those with controlled BP. BP-controlled patients were found to have more negative attitudes with respect to alcohol reduction and awareness of alcohol dependence.

In a previous large, multi-center study, alcohol dependence was detected using the Kurihama Alcoholism Screening Test (KAST) in 12.6% of male and 1.9% of female Japanese patients treated at primary care internal medicine clinics (Ban et al., 1999). In another Japanese study, 12.6% of male and 3.9% of female patients who attended an internal medicine department were found to have alcohol dependence defined as an AUDIT score ≥15 points (Fujii et al., 2016). These data collectively suggest that, regardless of screening methodology, about 13% of Japanese men and 2–4% of Japanese women treated by physicians have alcohol dependence. Compared with these general internal medicine patients, a greater percentage (24.8%) of regular drinkers currently treated for hypertension were found to have alcohol dependence in the present study. To detect potential alcohol dependence, the AUDIT, a simple

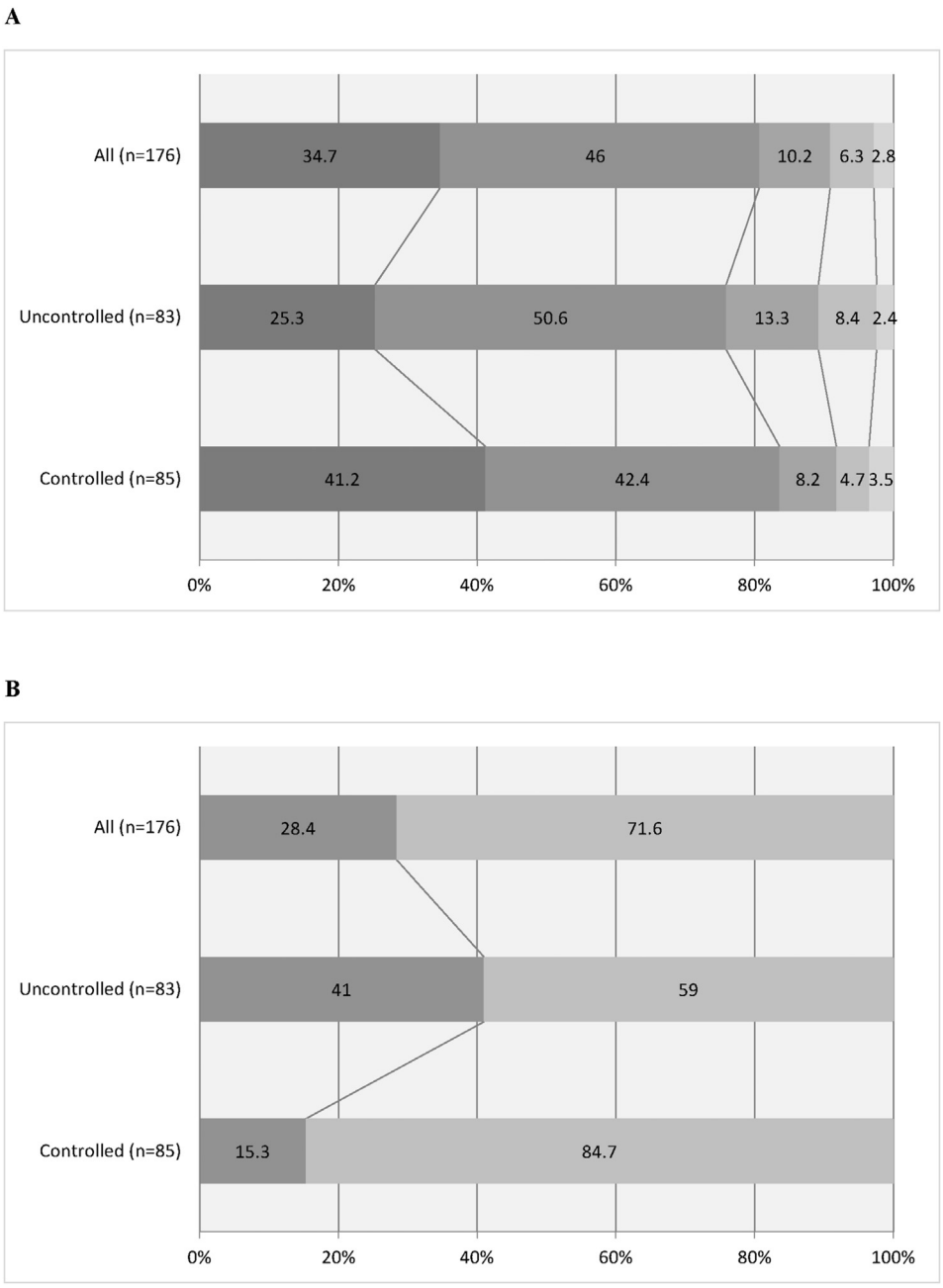

Fig. 4. Awareness of alcohol dependence (**A**) Motivation to reduce alcohol consumption (N = 176) ■ No motivation; ■ Weak-willed to reduce; ■ Will reduce before long (in one month); ■ Reduced <6 months ago; ■ Reduced for ≥6 months (**B**) Self-awareness of alcohol dependence (N = 176) ■ Think myself to be currently alcohol-dependent; ■ Do not think myself to be currently alcohol-dependent.

alcohol-screening test that reliably identifies individuals with alcohol dependence and/or alcohol use disorders, was used. The AUDIT was developed by the World Health Organization (1987) through collaborative research in 6 countries (Norway, Australia, Kenya, Bulgaria, Mexico, and the United States). A study conducted in Japan (Fujii et al., 2016) has established AUDIT scores of 8 and 15 points as cutoff values for detecting hazardous drinking and alcohol dependence, respectively. Of the 19 participants in the present study with an established diagnosis of alcohol dependence, 6 (31.5%) had an AUDIT score <15 points. These patients might have reduced drinking or resolved their alcohol use disorders before participating in the study, or their previous diagnosis of alcohol dependence might have been despite AUDIT scores less than 15 points.

The EQ-5D is a comprehensive system that assesses changes in health status using cardinal values and has been used globally, with translations available for many countries/regions (Ikegami, Fukuhara, Shimozuma, & Ikeda, 2004; Japanese EuroQol Translation Team, 1988). The 176 participants in the present study had a mean EQ-5D utility score of 0.838, which was close to that reported in Japanese diabetic patients with or without complications (0.8486 and 0.8840, respectively) (Ikegami et al., 2004; Sakamaki et al., 2006). These data indicate that hypertensive patients with alcohol dependence in Japan have health impairments as severe as those in Japanese diabetic patients with or without complications. It should be noted that the EQ-5D-based health status of BP-uncontrolled participants was even worse than that of BP-controlled participants (0.786 vs. 0.892; $p < 0.0001$).

Loss of work productivity due to health problems is a serious concern for all patients and their families. Above all, loss of work productivity due to alcohol-related health problems can pose significant public health burdens. The WPAI-GH is a self-administered questionnaire tool for assessing work productivity and activity impairment that includes questions about work/activities in the past 7 days. The WPAI-GH yields work/activity impairment scores expressed in percentages, with higher numbers indicating greater impairment and less productivity (Reilly, Zbrozek, & Dukes, 1993). Of the four WPAI outcomes, presenteeism and absenteeism were assessed in this study. European/United States occupational health and labor scientists have defined absenteeism as work time missed due to health problems and presenteeism as reduced on-the-job effectiveness due to health problems despite presence at the workplace (Ida, Nakagawa, Miura, Ishikawa, & Yakura, 2012; Kono, Matsushima, & Hosaka, 2009). In Japan, Yamashita and Arakida (2006) proposed that presenteeism be defined as "reduced ability of workers present at workplace to perform their jobs due to health problems". They thought that workers' ability to perform their jobs had impacts on work productivity and that presenteeism could be measured subjectively (Ida et al., 2012; Yamashita & Arakida, 2006). Many reports provided evidence for the negative impacts of excessive alcohol use on work productivity (Aas, Haveraaen, Sagvaag, & Thørrisen, 2017; Bragazzi et al., 2018; Buvik, Moan, & Halkjelsvik, 2018; Roche, Pidd, Berry, & Harrison, 2008). In the present study, those participants who were employed had a mean presenteeism score of 16.2% and a mean absenteeism score of 6.1%. Compared with workers with controlled BP, those with uncontrolled BP had higher mean absenteeism and presenteeism scores, indicating a greater loss of work productivity. This suggests that certain lifestyle factors may contribute to both inadequate BP control and loss of productivity. Together with the fact that the participants in this study had alcohol dependence, this also suggests that alcohol use may contribute as a causal factor to the loss of work productivity.

In the management of hypertension, it is generally accepted that excessive drinking induces resistance to antihypertensive therapy and results in inadequate BP control. The 2020 Guidelines of the International Society of Hypertension Global Hypertension Practice recommend that the volume of alcohol taken per day be restricted to 2 standard drinks for men and 1.5 for women (10 g alcohol/standard drink) (Unger et al., 2020). A meta-analysis of randomized, controlled studies demonstrated that reduction of alcohol intake has a significant BP-lowering effect (Xin et al., 2001).

Excessive drinking also causes liver disorders. In the present study, current γ-GTP data were used to determine the degree of hepatic dysfunction. At least mild hepatic dysfunction (γ-GTP $\geq$100 IU/L) was found in as many as 72.6% of the hypertensive patients with alcohol dependence. The proportion of participants with hepatic disorders was higher in the BP-uncontrolled group than in the controlled group (83.0% vs. 57.1%; $p = 0.0134$). Since multiple factors in addition to alcohol, such as hypertension and antihypertensive medication (Japanese Society of Hypertension, 2019), seem to contribute to the deterioration of hepatic function, careful monitoring of hepatic function is recommended for patients with alcohol dependence comorbid with hypertension.

Based on the results of this study, about one-fourth of hypertensive patients with regular alcohol use seem to have alcohol dependence. In the present study, 65.3% of hypertensive patients with alcohol dependence were willing to reduce drinking, but only 28.4% considered themselves as having alcohol dependence, suggesting their relative unawareness of the degree of their dependence on alcohol. Alcohol dependence may progress in 4 stages to eventually cause serious outcomes, including physical/mental disorders, loss of social opportunities, and economic loss. Patients in the first stage (pre-alcoholism) show no physical tolerance or emotional dependence, and if treated in this stage, they may recover and eliminate the risks of these outcomes. Notably, patients' awareness that they are in the stage of pre-alcoholism is essential for their recovery (Arai, Morita, & Nirasawa, 2013). Care should be provided to both patients and their families while the patients are in this stage (Arai et al., 2013). Patients with alcohol dependence typically do not admit their dependence on alcohol and overestimate their ability to stop drinking (Saito, 1989). Therefore, the initial step of treatment of alcohol dependence is to help patients become aware of their status and to bring them into contact with self-help groups (Iwasaki, 1998; Yasukawa, 2008).

The present study had several limitations. First, the panel of adult regular drinkers screened for eligibility for the study included a smaller percentage of elderly individuals (aged $\geq$60–79 years), as compared with a general population of Japanese regular drinkers studied in 2013 (Japanese Ministry of Health, Labour and Welfare, 2013). This was probably due to the restriction of questionnaire respondents to those who were able to use the Internet, which could cause a sampling bias. Therefore, the results of this study should be interpreted cautiously in the context of alcohol dependence in elderly patients with hypertension. Further studies should be conducted in elderly patients to confirm the study findings in this population. The second limitation was that no analysis of potential differences between males and females was performed. A larger sample size may be needed to address such limitations. In addition, this was a web-based questionnaire survey conducted in Japan. Therefore, it is unknown whether the findings from the study can be extrapolated to other ethnic populations. Furthermore, for most participants, the diagnosis of alcohol dependence was only based on self-reported AUDIT scores. To eliminate the diagnostic uncertainty and to more strictly define the study population, the diagnosis should have been confirmed by direct interview.

In conclusion, patients with alcohol dependence comorbid with hypertension had impaired health status and reduced work productivity. The health impairment and productivity loss were greater in patients with uncontrolled BP than in those with controlled BP. No relationship was found between the level of BP control and the degree of alcohol dependence based on the AUDIT score. Hypertensive patients with alcohol dependence who were not satisfied with current BP control most often thought alcohol was a cause of inadequate BP control. Of those previously receiving brief interventions, more than half had reduced drinking, but the remaining group had not, suggesting some effect of brief interventions and the need for treatment other than brief interventions. Additional interventions are also needed to help them recover loss of productivity and correct impairments in health. In hypertensive patients with regular alcohol use, it is important to detect and treat potential alcohol dependence early and to help them become aware of their dependence on alcohol.

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Declaration of competing interest

Izuru Nakamura and Yoshitsugu Kojima are full-time employees of Otsuka Pharmaceutical Co., Ltd. Hisashi Yoshimoto has no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.alcohol.2020.09.005.

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