Table 1 Mean of each variable at baseline and during the follow-up period in 3900 men aged 20–59 years

Variable	*n*	Mean	Standard deviation
Age (years)			
Year 1994 (baseline)	3900	38.3	9.6
Year 2001	2929	43.9	8.9
Height (cm)			
Year 1994 (baseline)	3900	168.9	6.2
Weight (kg)			
Year 1994 (baseline)	3900	65.0	9.1
Year 2001	2929	66.9	9.7
Body mass index (kg/m^2)			
Year 1994 (baseline)	3900	22.8	2.8
Year 2001	2929	23.3	2.9
Current smokers (%)		58.5	
No. of cigarettes per day — all	3900	11.6	11.6
No. of cigarettes per day — smokers	2282	29.8	8.1
Status of current alcohol consumption (%)			
Non-drinker		19.6	
Ex-drinker		1.4	
less than 100 g/week		32.6	
100–199 g/week		21.0	
200–299 g/week		19.0	
300 g/week or more		6.4	
Current alcohol consumption: all (g/week)	3900	120.1	122.9
Current alcohol consumption: drinker (g/week)	3081	152.0	119.4
Systolic blood pressure (mmHg)			
Year 1994 (baseline)	3900	121.3	14.5
Year 1995	3619	120.7	13.7
Year 1996	3586	123.7	13.8
Year 1997	3446	123.0	14.0
Year 1998	3292	122.9	14.7
Year 1999	3093	123.8	14.0
Year 2000	3046	124.4	13.5
Year 2001	2929	122.4	13.7
Diastolic blood pressure (mmHg)			
Year 1994 (baseline)	3900	73.7	11.4
Year 1995	3619	73.2	10.9
Year 1996	3586	75.3	10.5
Year 1997	3446	75.4	10.5
Year 1998	3292	75.8	11.2
Year 1999	3093	76.7	10.8
Year 2000	3046	76.6	10.3
Year 2001	2929	73.8	10.6

Results

Table 1 presents the mean of each variable at baseline and during the follow-up period. The mean age of the study population was 38.3 years at baseline, but was 43.9 years at the end of the follow-up period, after 7 years. The mean weight increased by 1.9 kg from baseline. At baseline, 19.6% of the subjects were non-drinkers, 1.4% were ex-drinkers who were not currently drinking, and 6.4% were drinkers of $\geq$ 300 g/week. Between baseline and the end of the follow-up period, the average annual increase in systolic BP (SBP) was 0.31 mmHg, and the average annual increase in diastolic BP (DBP) was 0.30 mmHg in the entire subject population (Table 1).

Table 2 presents the association of alcohol consumption with baseline SBP and annual increase in SBP as determined by the GEE method. After adjustment for age only, baseline SBP was significantly higher in drinkers of $\geq$ 100 g/week than in non-drinkers, and the difference increased with increasing alcohol consumption. The difference between drinkers of $\geq$ 300 g/week and non-drinkers was as large as 5.68 mmHg. The results were similar when adjusted for age and weight at each year (Model 1), and even when adjusted for age and weight, plus other lifestyle-related factors (Model 2). Even in Model 3, with additional adjustment for the frequency of intake of various foods, baseline SBP was still significantly higher in drinkers of $\geq$ 200 g/week.

Regarding the association between alcohol consumption and annual change in SBP, after adjustment for age only, ex-drinkers showed a 0.52 mmHg greater annual increase in SBP than non-drinkers. Drinkers of $\geq$ 300 g/week showed a 0.41 mmHg greater annual increase in SBP than non-drinkers, and this was statistically significant. Models 1 and 2 provided similar results. In Model 1, ex-drinkers showed a 0.49 mmHg greater annual increase in SBP, and drinkers of $\geq$ 300 g/week showed a 0.44 mmHg greater annual increase in SBP, when compared with non-drinkers. Drinkers of $\geq$ 300 g/week have an estimated 3.08 mmHg greater SBP rise 7 years later compared with non-drinkers (model 1). In Model 3, with adjustment for the intake of various food groups, the difference in SBP increase was smaller, but drinkers of $\geq$ 300 g/week still showed a significantly greater SBP increase. Results were similar for baseline SBP and annual SBP change in the unadjusted model (data not shown).

Table 3 presents the results of analysis of DBP. Baseline DBP, adjusted for age only, was significantly higher in drinkers of $\geq$ 100 g/week than in non-drinkers, and increased with increasing alcohol consumption. It was 4.58 mmHg higher in drinkers of $\geq$ 300 g/week than in non-drinkers. These results remained unchanged even after multivariate adjustments in Models 1, 2, and 3. Regarding the association between alcohol consumption and the annual change in DBP, ex-drinkers showed a 0.29–0.38 mmHg greater increase, and drinkers of $\geq$ 300 g showed a 0.11–0.19 mmHg greater increase, when compared with non-drinkers in each model, but these differences were not statistically significant. Results were almost similar in the unadjusted model (data not shown).

Discussion

Previous interventional studies of alcohol consumption and BP demonstrated that BP was decreased by moderating or stopping alcohol intake, but the intervention periods were short, ranging from several weeks to several months [10–13]. Many longitudinal observational studies have used the onset of hypertension as their endpoint, and were therefore greatly influenced by baseline BP levels. These studies also ignored BP increases within the normal range. Very few long-term studies have been conducted on the annual increase in BP in relation to alcohol consumption, or have taken into account dietary

Table 2 Relationship of baseline alcohol consumption to adjusted baseline value and adjusted average annual change in systolic blood pressure over 7 years

	Adjusted for age		Model 1[a]		Model 2[b]		Model 3[c]	
Baseline alcohol consumption (g/week)	Differences in blood pressure (mmHg)	P	Differences in blood pressure (mmHg)	P	Differences in blood pressure (mmHg)	P	Differences in blood pressure (mmHg)	P
Differences in baseline systolic blood pressure of drinkers compared with non-drinkers								
Non-drinkers[d]								
Ex-drinkers	−0.57	0.769	−0.87	0.640	−0.96	0.608	−1.07	0.600
< 100	0.51	0.371	0.52	0.353	0.36	0.527	0.25	0.676
100–199	1.37	0.037	1.28	0.044	1.45	0.024	1.01	0.158
200–299	3.72	< 0.001	3.46	< 0.001	3.66	< 0.001	3.87	< 0.001
300 or more	5.68	< 0.001	5.21	< 0.001	5.70	< 0.001	4.97	< 0.001
Differences in average annual change of systolic blood pressure of drinkers compared with non-drinkers								
Non-drinkers[d]								
Ex-drinkers	0.52	0.079	0.49	0.086	0.51	0.077	0.60	0.056
< 100	0.08	0.329	0.07	0.359	0.06	0.441	0.03	0.728
100–199	0.14	0.122	0.13	0.132	0.11	0.232	0.08	0.398
200–299	0.13	0.154	0.15	0.098	0.13	0.128	−0.02	0.874
300 or more	0.41	0.002	0.44	< 0.001	0.41	0.002	0.33	0.022

[a]Model 1 is adjusted for baseline age and weight at each year. [b]Model 2 is adjusted for baseline age, weight at each year, cigarettes per day, exercise, physical and mental work-related stress, and preference for salty and fatty foods. [c]Model 3 is adjusted for Model 2 covariates plus frequency of food intake (beef, pork, chicken, egg, fresh fish, milk, yogurt, cheese, spinach, carrot and pumpkin, tomato, cabbage, lettuce, Chinese cabbage, mushroom, potato, pickle, beans, tofu (bean curd), citrus fruit, other fruits and sweets). [d]Reference level.

habits associated with alcohol intake. The present study revealed that, when adjusted for age and weight change, average annual increases in SBP were greater in drinkers of ≥ 300 g/week than in non-drinkers. This association remained significant even after adjustment for the frequency of intake of various food groups, including vegetables and fruits. These results demonstrated that high alcohol intake itself leads to a long-term increase in BP, independently of other confounding factors.

The association between excessive alcohol intake and hypertension attracted attention after reports by Klatsky *et al.* [4], and it has been shown that alcohol intake ≥ 3–5 drinks/day (approximately 210–350 g/week) is associated with hypertension in both men and women. In an investigation of alcohol and BP in the international cooperative INTERSALT study [9], the SBP was significantly higher in men drinking ≥ 300 ml alcohol/week (approximately 238 g) than in non-drinking men. A 6-year longitudinal study of men in the Chicago Western Electric Study [14] indicated that the incidence rate of hypertension was higher in drinkers consuming ≥ 6 drinks/day (approximately 420 g/week). The US Hypertension Guidelines (JNC7) [3], in their recommended lifestyle modifications for hypertension management, recommend that alcohol intake in men should be limited to ≤ 30 ml

Table 3 Relationship of baseline alcohol consumption to adjusted baseline value and adjusted average annual change in diastolic blood pressure over 7 years

	Adjusted for age		Model 1[a]		Model 2[b]		Model 3[c]	
Baseline alcohol consumption (g/week)	Differences in blood pressure (mmHg)	P	Differences in blood pressure (mmHg)	P	Differences in blood pressure (mmHg)	P	Differences in blood pressure (mmHg)	P
Differences in baseline diastolic blood pressure of drinkers compared with non-drinkers								
Non-drinkers[d]								
Ex-drinkers	0.67	0.600	0.40	0.738	0.52	0.667	0.12	0.923
< 100	0.57	0.159	0.58	0.142	0.51	0.198	0.50	0.238
100–199	1.06	0.021	0.99	0.024	1.28	0.005	1.18	0.018
200–299	3.09	< 0.001	2.86	< 0.001	3.10	< 0.001	3.23	< 0.001
300 or more	4.58	< 0.001	4.16	< 0.001	4.85	< 0.001	4.58	< 0.001
Differences in average annual change of diastolic blood pressure of drinkers compared with non-drinkers								
Non-drinkers[d]								
Ex-drinkers	0.32	0.173	0.30	0.187	0.29	0.204	0.38	0.110
< 100	0.00	0.952	0.00	0.993	−0.01	0.862	−0.05	0.454
100–199	0.10	0.142	0.10	0.159	0.06	0.393	0.05	0.572
200–299	0.10	0.187	0.12	0.114	0.09	0.208	0.00	0.993
300 or more	0.17	0.112	0.19	0.067	0.14	0.188	0.11	0.361

[a]Model 1 is adjusted for baseline age and weight at each year. [b]Model 2 is adjusted for baseline age, weight at each year, cigarettes per day, exercise, physical and mental work-related stress, and preference for salty and fatty foods. [c]Model 3 is adjusted for Model 2 covariates plus frequency of food intake (beef, pork, chicken, egg, fresh fish, milk, yogurt, cheese, spinach, carrot and pumpkin, tomato, cabbage, lettuce, Chinese cabbage, mushroom, potato, pickle, beans, tofu (bean curd), citrus fruit, other fruits and sweets). [d]Reference level.

ethanol/day (approximately 167 g/week), and the hypertension guidelines of the European Society of Hypertension and European Society of Cardiology [2] recommend that alcohol intake in men should be limited to less than 20–30 g ethanol/day (140–210 g/week).

Studies in Japanese men [7,28] have shown that the SBP was approximately 7–10 mmHg higher, and the DBP was approximately 2–7 mmHg higher, in drinkers of 3–6 drinks/day (approximately 210–420 g/week) than in non-drinkers. Studies in European men [4,30] indicated that the SBP was approximately 6 mmHg higher, and the DBP was approximately 2 mmHg higher, in drinkers of 3–5 drinks/day (approximately 210–350 g/week) than in non-drinkers. These results and our results on baseline BP suggest that the magnitude of the cross-sectional association between alcohol consumption and blood pressure in Japanese men is similar to that in men in Western countries.

Our results show a significantly higher baseline BP in drinkers of $\geq$ 200 g/week, even after multivariate adjustments. These results suggest that alcohol consumption should be limited to less than 200 g/week in order to prevent hypertension, and are consistent with cut-off points in previous reports and guidelines. However, even stricter limitations will be needed for drinkers of $\geq$ 300 g/week because they showed even greater long-term increases in BP.

Recent studies [19,20] have demonstrated that BP was lowered by the Dietary Approaches to Stop Hypertension diet (increased intake of fruits, vegetables, fish, low-fat dairy products, and reduced intake of red meats, fats, and sweets), drawing attention to the relationship between the intake of food groups and BP. A 7-year longitudinal study in the Chicago Western Electric Study [23] also showed that a higher intake of fruits and vegetables and a lower intake of meat (except fish) suppressed long-term increase in BP. Therefore, studies of the association between alcohol consumption and BP also require analysis with adjustment for the effects of intake of various food groups. There have been almost no reports taking into account the intake of food groups, and the present report may be the first to include adjustment for the intake of food groups.

We noted that the BP increase tended to be greater in ex-drinkers than in non-drinkers in our study. Although the number of ex-drinkers was small in our study, and was not statistically significant, we hope that further detailed longitudinal studies will be made on BP changes in ex-drinkers because very few studies were made on this aspect.

Although some studies have pointed out the relationship between stress and an increase in BP [31,32], it is possible that increased alcohol consumption is due to stress, thereby confounding the association between alcohol consumption and BP. Therefore, the present study also made statistical adjustment for the intensity of work-related stress, but the association between alcohol consumption and BP was not affected by the adjustment.

The present study has the following limitations. First, it did not consider the presence or absence of anti-hypertensive treatment at baseline, or during the study. If anti-hypertensive treatment was initiated during the follow-up period, the association between alcohol consumption and BP increase may have been underestimated. Second, although the frequency of intake of major food groups was taken into account, no adjustment was made for quantities of nutrients or the actual energy intake. Adjustment for salt intake and mental stress would also be insufficient. Third, because alcohol consumption and food intake were evaluated only at baseline, the results are based on an assumption that they did not change during the follow-up period. Finally, these results may not be valid for women, because all our subjects were men. Studies of women need to be performed in the future.

It is believed that primary prevention of cardiovascular diseases can be accomplished through interventions conducted widely within the general population (population strategy), with the objective of achieving a downward shift in the distribution of BP [33,34]. Our study revealed that BP increases within the normal range with high alcohol intake, suggesting the possibility of suppressing the age-related increase in BP in the general population by taking measures against heavy alcohol consumption in the general population, including normotensive individuals. We believe that our results provide important evidence for planning measures for the primary prevention of hypertension in the future.

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References

1 The Guidelines Subcommittee of the World Health Organization–International Society of Hypertension (WHO–ISH) Mild Hypertension Liaison Committee. 1999 World Health Organization–International Society of Hypertension Guidelines for the Management of Hypertension. *J Hypertens* 1999; **17**:151–183.

2 Zanchetti A, Cifkova R, Fagard R, Kjeldsen S, Mancia G, Poulter N, *et al.* 2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; **21**:1011–1053.

3 Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, *et al.* National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 Report. *JAMA* 2003; **289**:2560–2572.

4 Klatsky AL, Friedman GD, Siegelaub AB, Gerard MJ. Alcohol consumption and blood pressure Kaiser-Permanente Multiphasic Health Examination data. *N Engl J Med* 1977; **296**:1194–1200.

5 Arkwright PD, Beilin LJ, Rouse I, Armstrong BK, Vandongen R. Effects of alcohol use and other aspects of lifestyle on blood pressure levels and prevalence of hypertension in a working population. *Circulation* 1982; **66**:60–66.

6 Salonen JT, Tuomilehto J, Tanskanen A. Relation of blood pressure to reported intake of salt, saturated fats, and alcohol in healthy middle-aged population. *J Epidemiol Community Health* 1983; **37**:32–37.

7 Ueshima H, Shimamoto T, Iida M, Konishi M, Tanigaki M, Doi M, *et al.* Alcohol intake and hypertension among urban and rural Japanese populations. *J Chron Dis* 1984; **37**:585–592.

8 Hashimoto T, Fujita Y, Ueshima H, Kagamimori S, Kasamatsu T, Morioka S, *et al.* Sodium and potassium excretion, body mass index, alcohol intake and blood pressure in three Japanese populations. *J Hum Hypertens* 1989; **3**:315–321.

9 Marmot MG, Elliott P, Shipley MJ, Dyer AR, Ueshima H, Beevers DG, *et al.* Alcohol and blood pressure: the INTERSALT study. *BMJ* 1994; **308**:1263–1267.

10 Puddey IB, Beilin LJ, Vandongen R, Rouse IL, Rogers P. Evidence for a direct effect of alcohol consumption on blood pressure in normotensive men. A randomized controlled trial. *Hypertension* 1985; **7**:707–713.

11 Malhotra H, Mehta SR, Mathur D, Khandelwal PD. Pressor effects of alcohol in normotensive and hypertensive subjects. *Lancet* 1985; **14**:584–586.

12 Puddey IB, Parker M, Beilin LJ, Vandongen R, Masarei JR. Effects of alcohol and caloric restrictions on blood pressure and serum lipids in overweight men. *Hypertension* 1992; **20**:533–541.

13 Ueshima H, Mikawa K, Baba S, Sasaki S, Ozawa H, Tsushima M, *et al.* Effect of reduced alcohol consumption on blood pressure in untreated hypertensive men. *Hypertension* 1993; **21**:248–252.

14 Dyer AR, Stamler J, Paul O, Berkson DM, Shekelle RB, Lepper MH, *et al.* Alcohol, cardiovascular risk factors and mortality: the Chicago experience. *Circulation* 1981; **64**:III 20–III 27.

15 Reed D, McGee D, Yano K. Biological and social correlates of blood pressure among Japanese men in Hawaii. *Hypertension* 1982; **4**:406–414.

16 Witteman JC, Willett WC, Stampfer MJ, Colditz GA, Kok FJ, Sacks FM, *et al.* Relation of moderate alcohol consumption and risk of systemic hypertension in women. *Am J Cardiol* 1990; **65**:633–637.

17 Dwyer JH, Li L, Dwyer KM, Curtin LR, Feinleib M. Dietary calcium, alcohol, and incidence of treated hypertension in the NHANES I epidemiologic follow-up study. *Am J Epidemiol* 1996; **144**:828–838.

18 Tsuruta M, Adachi H, Hirai Y, Fujiura Y, Imaizumi T. Association between alcohol intake and development of hypertension in Japanese normotensive men: 12-year follow-up study. *Am J Hypertens* 2000; **13**:482–487.

19 Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, *et al.* A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 1997; **336**:1117–1124.

20 Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, *et al.* Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH–Sodium Collaborative Research Group. *N Engl J Med* 2001; **344**:3–10.

21 Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986; **73**:13–22.

22 Stamler J, Liu K, Ruth KJ, Pryer J, Greenland P. Eight-year blood pressure change in middle-aged men: relationship to multiple nutrients. *Hypertension* 2002; **39**:1000–1006.

23 Miura K, Greenland P, Stamler J, Liu K, Daviglus ML, Nakagawa H. Relation of vegetable, fruit, and meat intake to 7-year blood pressure change in middle-aged men: the Chicago Western Electric Study. *Am J Epidemiol* 2004; **159**:572–580.

24 Morikawa Y, Nakagawa H, Miura K, Ishizaki M, Tabata M, Nishijo M, *et al.* Relationship between shift work and onset of hypertension in a cohort of manual workers. *Scand J Environ Health* 1999; **25**:100–104.

25 Ishizaki M, Martikainen P, Nakagawa H, Marmot M. The relationship between employment grade and plasma fibrinogen level among Japanese male employees. *Atherosclerosis* 2000; **151**:415–421.

26 Okamura T, Tanaka T, Yoshita K, Chiba N, Takebayashi T, Kikuchi Y, *et al.* Specific alcoholic beverage and blood pressure in a middle-aged Japanese population: the High-risk and Population Strategy for Occupational Health Promotion (HIPOP-OHP) Study. *J Hum Hypertens* 2004; **18**:9–16.

27 Choudhury SR, Ueshima H, Kita Y, Kobayashi KM, Okayama A, Yamakawa M, *et al.* Alcohol intake and serum lipids in a Japanese population. *Int J Epidemiol* 1994; **23**:940–947.

28 Iso H, Kitamura A, Shimamoto T, Sankai T, Naito Y, Sato S, *et al.* Alcohol intake and the risk of cardiovascular disease in middle-aged Japanese men. *Stroke* 1995; **26**:767–773.

29 Diggle PJ, Liang K-Y, Zeger SL. *Analysis of longitudinal data*. New York: Oxford University Press; 1994.

30 Marmot MG, Rose G, Shipley MJ, Thomas BJ. Alcohol and mortality: a U-shaped curve. *Lancet* 1981; **14**:580–583.

31 Markovitz JH, Matthews KA, Kannel WB, Cobb JL, D'Agostino RB. Psychological predictors of hypertension in Framingham Study. Is there tension in hypertension? *JAMA* 1993; **270**:2439–2443.

32 Schnall PL, Schwartz JE, Landsbergis PA, Warren K, Pickering TG. A longitudinal study of job strain and ambulatory blood pressure: results from a three-year follow-up. *Psychosom Med* 1998; **60**:697–706.

33 Rose G. Some implications of population change. In: *The strategy of preventive medicine*. New York: Oxford University Press; 1992, pp. 64–94.

34 Cook NR, Cohen J, Hebert PR, Taylor JO, Hennekens CH. Implications of small reduction in diastolic blood pressure for primary prevention. *Arch Intern Med* 1995; **155**:701–709.

2）日本人男性従業員における交代勤務と糖尿病発症との関連（富山職域コホート）

（Morikawa Y, Nakagawa H, Miura K, Soyama Y, Ishizaki M, Kido T, Naruse Y, Suwazono Y, Nogawa K. Shift work and the risk of diabetes mellitus among Japanese male factory workers. *Scand J Work Environ Health* 2005;31:179-183.）

【目的】

交代勤務が糖尿病発症と関連するのかどうかを前向きコホート研究で明らかにする。

【方法】

富山県のアルミ製品製造企業従業員男性2,860人を8年間追跡し、追跡期間中の糖尿病発症を把握した。コホートには常日勤現場作業者、交代勤務現場作業者、および事務職従事者が含まれる。毎年の検診におけるHbA1c 6.1以上の出現または医師による糖尿病診断をもって糖尿病発症と定義した。相対危険度をCox比例ハザードモデルで算出した。

【結果】

追跡期間中に87人が糖尿病を発症し、罹患率は1000人年対4.41であった。年齢調整罹患率は2交代勤務者で最も高く、事務作業者で最も低かった。常日勤作業者と比べた糖尿発症相対危険度（多変量調整後）は、2交代勤務者で1.73、3交代勤務者で1.33であったが、統計学的には有意ではなかった。事務職を比較群とすると、2交代勤務者の多変量調整相対危険度は2.01と有意にリスクを上昇させたが、3交代勤務者および常日勤作業者では有意な上昇はなかった。

【結論】

交代勤務は糖尿病発症危険因子と考えられたが、異なる交代スケジュールによりリスクが異なると考えられた。

Original article

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Shift work and the risk of diabetes mellitus among Japanese male factory workers

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Objectives This study investigated whether shift work is a risk factor for the development of diabetes mellitus.
Methods The workers, 2860 men in a sash and zipper factory in the Toyama prefecture of Japan, were followed for 8 years, and the incidence rate of diabetes mellitus was determined. The cohort contained fixed daytime blue-collar workers, shift blue-collar workers, and white-collar workers. The workers were considered to have diabetes mellitus if, in their annual health examination, they had a glycated hemoglobin level of ≥6.1 or if the diagnosis had been made by a hospital physician. The relative risks were estimated by Cox's proportional hazards regression model.
Results Among the 2860 workers, there were 87 cases of new-onset diabetes mellitus, resulting in an incidence rate of 4.41 per 1000 person-years. The age-adjusted incidence was highest for the two-shift workers and lowest for the white-collar workers. The relative risk of diabetes mellitus for the two-shift workers and the three-shift workers compared with the fixed daytime workers was 1.73 and 1.33, respectively, after adjustment for all the confounding factors, but these values were not statistically significant. When the white-collar workers were used as a reference group, a significantly increased risk of diabetes mellitus was found for the two-shift workers (relative risk was 2.01 after adjustment for all confounding factors), but not for the three-shift workers or the fixed daytime blue-collar workers.
Conclusions The study suggests that shift work is a risk factor for the onset of diabetes mellitus and that there is a different risk associated with different shift schedules.

Key terms cohort study; glucose tolerance; glycated hemoglobin.

Shift work has been associated with an increased risk of cardiovascular disease (1–3). Four pathways (ie, the mismatch of circadian rhythms, social disruption, behavioral changes, and changes in biomarkers) are considered factors that predispose shift workers to this disease (1). Changes in the biomarkers may be related to a mismatch of the circadian rhythm and behavioral changes (4). Some studies have shown that obesity, high triglyceride levels, and low concentrations of high-density lipoprotein (HDL) cholesterol seem to cluster together more often in shift workers than in day workers. This trend may indicate an association between shift work and the metabolic syndrome (5–10). In the metabolic syndrome, the effects of shift work on glucose tolerance are not understood, although there have been several cohort studies examining this issue. Insulin sensitivity is known to be lower during the night than during the day (11, 12). Furthermore, sleep debt has a harmful impact on carbohydrate metabolism and endocrine function (13). Some experimental studies that were carried out to investigate postprandial hormone and metabolic responses during simulated shift work (14, 15) found decreased glucose tolerance during the night. Therefore, it is legitimate to presume that shift work may have some effect on glucose tolerance. The objective of this cohort study was to investigate whether shift work is a risk factor for the onset of diabetes mellitus and whether there are different risks associated with different shift schedules.

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Study population and methods

Study population

The study population included male blue- and white-collar workers who were between 19 and 49 years of age, worked in a sash and zipper factory in the Toyama prefecture of Japan, and underwent health check-ups in 1993 (participation rate of 95%). The target population consisted of 3106 workers, and the 246 workers with a history of diabetes mellitus or glucose intolerance or a glycated hemoglobin (HbA1c) level of ≥5.6% at baseline (over the normal range) were excluded. Therefore, the cohort consisted of 2860 men who were followed annually until they were diagnosed as having diabetes mellitus or until the end of 2001. From 1994 to 2001, annual screening tests were carried out, including HbA1c, blood glucose measurement, and the administration of medical history questionnaires. The questionnaire in 1993 contained questions regarding the workers' history of diabetes mellitus and family history of diabetes mellitus, as well as health-related behavior, such as smoking, drinking, dietary habit, and leisure-time physical activities.

Occupations

Information on the occupational category and the shift work schedule at baseline was obtained from a questionnaire. Jobs were classified into two types (blue-collar and white-collar). All white-collar workers were engaged in fixed daytime work. The blue-collar workers were engaged in mainly the following three types of work schedules: fixed daytime work, rotating two-shift work, and rotating three-shift work. The three-shift workers' schedule rotated counterclockwise with two-thirds of them engaged in a noncontinuous shift system (5 day shifts, 5 night shifts, and 5 evening shifts) and one-third of them working a continuous-shift system (3 or 4 day shifts, 3 or 4 night shifts, and 3 or 4 evening shifts, with one rest day between successive shifts). Both rotating three-shift systems changed shifts at 0800, 1630, and 0015 or at 0630, 1300, and 2130. Most of the rotating two-shift workers did day shifts and evening shifts with a noncontinuous shift system. There were 1099 fixed daytime blue-collar workers, 228 two-shift workers, 492 three-shift workers, and 1041 white-collar workers. Certain jobs, such as those involving the operation of machines that melt, heat, mix, or cast, are routinely performed by three-shift workers, while jobs involving processing or the construction of aluminum products are done by fixed daytime workers or two-shift workers.

Baseline characteristics

The baseline characteristics and information on health-related behavior are shown in table 1. The baseline body mass index (BMI) and HbA1c levels were similar among the occupational groups. The prevalence of unfavorable health-related behavior, such as smoking, habitual drinking, and lack of regular leisure-time physical exercise, was higher for the blue-collar workers than for the white-collar workers. Among the blue-collar workers, the prevalence of regular physical exercise was lower for the shift workers than for the fixed daytime workers.

Endpoint determination

The determination of the presence of diabetes mellitus was based on an HbA1c of ≥6.1 or a diagnosis having been made by hospital physicians. Although blood glucose levels were also measured during the screening, they were not always taken as fasting samples. Therefore, we did not use the blood glucose level as a diagnostic criterion.

Statistics

The incidence rates of diabetes mellitus were expressed per 1000 person-years. Age-adjusted rates were calculated with the indirect method of standardization by using all blue-collar workers as a standard population. The relative risks and their 95% confidence intervals for diabetes mellitus among the shift workers were calculated after adjustment for confounding factors using Cox's proportional hazards regression model. The baseline characteristics used for the analysis were age, BMI, family history of diabetes mellitus (limited to first-degree

Table 1. Baseline characteristics for each occupational category. (BMI = body mass index, HbA1c = glycated hemoglobin)

Occupational category	Age (years)		BMI		HbA1c		Family history[a] (%)	Current smoking (%)	Habitual drinking[b] (%)	No exercise[c] (%)
	Mean	SD	Mean	SD	Mean	SD				
Blue-collar workers										
Fixed-daytime workers (N=1099)	35.3	8.5	22.4	2.7	4.87	0.32	7.3	66.2	41.1	64.5
Two-shift workers (N=228)	33.5	8.6	22.5	3.2	4.83	0.34	8.0	60.0	36.4	71.7
Three-shift workers (N=492)	33.7	8.5	22.6	2.9	4.87	0.30	8.0	67.4	41.4	68.6
White-collar workers (N=1041)	33.7	7.6	22.7	2.7	4.86	0.32	9.2	52.9	39.4	60.2

[a] Limited to first-degree relatives.
[b] Drinking ≥6 times/week.
[c] Participating in leisure-time physical exercise <1/week.

relatives), and health-related behavior. The software package used for the analysis was SPSS 11.0 (SPSS Inc, Chicago, IL, USA).

Results

Table 2 shows the age-adjusted incidence rates of diabetes mellitus by occupational category. Among the 2860 workers, there were 87 cases of new onset diabetes mellitus, for an incidence rate of 4.41/1000 person-years. Among these 87 cases, 51 were diagnosed both with respect to HbA1c level and medical history, 21 were diagnosed according to the HbA1c level alone, and 15 were diagnosed with regard to medical history alone. The age-adjusted incidence rate for blue-collar workers was 5.94/1000 person-years. Among blue-collar workers, the incidence rate was the highest for the two-shift workers (6.84/1000 person-years), followed by the three-shift workers (5.32/1000 person-years) and the fixed daytime workers (4.23/1000 person-years). The incidence of diabetes mellitus among the white-collar workers was 3.53/1000 person-years.

Table 3 shows the relative risks of the demographic factors and health-related behavior for diabetes mellitus using Cox's proportional hazards regression model. Age, BMI, and smoking statistically significantly increased the risk of diabetes mellitus. A family history of diabetes showed a trend towards increasing the risk of diabetes mellitus, although this trend was not statistically significant. Lack of leisure-time physical exercise and habitual drinking (≥5 times/week) were not associated with diabetes mellitus.

Table 4 shows the relative risks of diabetes mellitus for the occupational categories using Cox's proportional hazards regression model. The relative risks of diabetes mellitus for the shift workers were calculated by using the fixed daytime workers as reference. The relative risk of diabetes mellitus for the two-shift workers compared with the fixed daytime workers was 1.70 after adjustment for age alone, 1.80 after adjustment for age, BMI and family history, and 1.73 after adjustment for all the confounding factors, but none of these were statistically significant. Of note, the relative risks of the three-shift workers compared with the fixed daytime workers were smaller than those of the two-shift workers.

When the white-collar workers in the same factory were used as a reference group, a statistically significant increase in the risk of diabetes mellitus was found for the two-shift workers. In fact, adjustment for age, BMI, and family history, as well as for all confounding factors, including health-related behavior (smoking, drinking and leisure-time physical activity), resulted in a statistically significantly increased risk of diabetes mellitus among the two-shift workers when they were compared with the white-collar workers. Finally, when compared with the white-collar workers, the three-shift workers and the fixed daytime workers showed no difference in the risk for diabetes mellitus when the results were adjusted for age, BMI, and family history or for all the confounding factors.

These results suggest that shift work, particularly two-shift work, is a risk factor for diabetes mellitus. An increased risk was apparent when comparisons were made with the white-collar workers, but not with the fixed daytime blue-collar workers. The increased risk

Table 2. Incidence rate[a] of diabetes mellitus by occupational category. (95% CI = 95% confidence interval)

Occupational category	N	Person-years	Cases	Crude incidence rate	Incidence rate[b]	95% CI
Blue-collar workers						
Total	1819	12853	64	4.98	..	..
Fixed daytime	1099	7675	34	4.43	4.23	3.24–6.08
Shift workers	720	5178	30	5.79	6.23	4.60–9.06
Two-shift workers	228	1608	11	6.84	7.04	3.61–11.93
Three-shift workers	492	3570	19	5.32	5.83	3.76–9.00
White-collar workers	1041	6877	23	3.34	3.53	2.53–5.42

[a] Per 1000 person-years.
[b] Adjusted for age, calculated by the indirect method of standardization using all blue-collar workers as a standard population.

Table 3. Relative risks (RR) of the demographic factors[a] and health-related behavior for diabetes mellitus according to Cox's proportional hazard model. (95% CI = 95% confidence interval)

Factor	Category	RR	95% CI
Age	Linear (each 1 year increase)	1.07	1.04–1.10
Body mass index	Linear (each 1 increase)	1.14	1.06–1.23
Family history	+ versus −	1.69	0.92–3.12
Drinking	Almost everyday versus others	0.64	0.40–1.01
Smoking	+ versus −	1.81	1.11–2.94
Physical exercise	<1 time/week versus others	0.96	0.61–1.51

[a] All factors were put into the model together.

Table 4. Relative risks (RR) of diabetes mellitus by the occupational categories according to Cox's proportional hazard model. (95% CI = 95% confidence interval)

	RR[a]	95% CI	RR[b]	95% CI	RR[c]	95% CI
Blue collar workers						
Fixed daytime workers	1	..	1	..	1	..
Two-shift workers	1.70	0.86–3.36	1.80	0.91–3.55	1.73	0.85–3.52
Three-shift workers	1.33	0.76–2.34	1.33	0.75–2.34	1.33	0.74–2.36
White-collar workers	1	..	1	..	1	..
Blue-collar workers						
Fixed daytime workers	1.10	0.65–1.86	1.15	0.69–1.93	1.19	0.66–2.16
Two-shift workers	1.93	0.95–3.91	2.11	1.05–4.22	2.01	1.00–4.34
Three-shift workers	1.51	0.83–2.74	1.53	0.85–2.76	1.61	0.88–2.97

[a] Adjusted for age.
[b] Adjusted for age, body mass index, and family history.
[c] Adjusted for age, body mass index, family history, health-related behavior [current smoking (yes versus no), habitual drinking (yes versus no), lack of physical exercise (0/week versus ≥1/week)].

of diabetes mellitus among the two-shift workers, as compared with the white-collar workers, remained even after adjustment for health-related behavior. This finding suggests that the higher risk of diabetes mellitus for two-shift workers is caused primarily by factors not related to lifestyle.

Discussion

In this 8-year cohort study, we investigated the effects of shift work on the incidence rate of diabetes mellitus. The incidence rate of diabetes mellitus was the highest for the two-shift workers, followed by three-shift workers, fixed daytime workers, and white-collar workers. Although there was a trend towards a higher risk of diabetes mellitus among the shift workers overall, this was not statistically significant when these workers were compared with the fixed daytime workers. However, when compared with the white-collar workers, the two-shift workers had a statistically significant increased risk of diabetes mellitus.

In this study, the onset of diabetes mellitus was diagnosed primarily by documenting an increase in the HbA1c level. HbA1c is widely accepted as a useful index of mean blood glucose in the treatment of patients with diabetes mellitus. However, its use as a screening test for diabetes mellitus has not been widely accepted. On the other hand, fasting blood glucose is accepted as the most sensitive and specific test for diabetes mellitus screening (16). However, we used only HbA1c, because obtaining fasting blood samples from all of the participants during the entire observation period was not feasible. Using both HbA1c and fasting plasma glucose would be the best means of screening for new onset diabetes mellitus. Nevertheless, the sole use of HbA1c has been widely accepted for epidemiologic studies, because epidemiologic studies using HbA1c and fasting plasma glucose as screening tests for undiagnosed diabetes mellitus have found that HbA1c is both highly specific and convenient (17–19). The Japan Diabetes Society acknowledges the utility of HbA1c as a screening test and has announced that a HbA1c level of ≥6.1% can be used to estimate the prevalence of diabetes mellitus in epidemiologic studies (20), since an HbA1c concentration of 6.1% corresponds to both a fasting plasma glucose of 7.0 mmol/l and a 2-hour value of a 75-gram oral glucose tolerance test of 11.1 mmol/l (21).

In investigating the effects of shift work on the onset of diabetes mellitus, it is more appropriate to use fixed daytime workers as a reference. Since the physical load of the blue-collar workers in the target factory has been lightened during recent decades, we did not need to consider any differences in the physical exertion of the blue-collar workers; one of the most relevant issues for the blue-collar workers was the work schedule. On the other hand, using white-collar workers as a reference group may have introduced factors other than shift work as confounders, including work characteristics, socioeconomic differences, and lifestyle. However, studies dealing with glucose tolerance or related factors have shown higher risks of diabetes mellitus among sedentary workers, such as managerial workers, drivers, or air traffic controllers, even after adjustment for other confounding factors (22–24). Therefore, the finding that there is a higher risk of diabetes mellitus among blue-collar workers as compared with white-collar workers is not in accordance with the literature. Therefore, these results may have been caused by factors unrelated to physical workload. Furthermore, the finding that there was no statistically significant difference between fixed daytime blue-collar workers and white-collar workers with respect to the risk of diabetes mellitus also suggests that shift work affects the onset of diabetes mellitus.

The increased risk of diabetes mellitus among the two-shift workers as compared with the white-collar workers may also have been due to a difference in health-related behavior. Smoking and drinking are considered risk factors for diabetes mellitus (25–27). Our study also confirmed that smoking is a risk factor for diabetes mellitus. In this study, shift workers showed a more unfavorable lifestyle than the fixed daytime workers or white-collar workers did. However, the risks of shift work for diabetes mellitus decreased only slightly after adjustment for health-related behavior, and a large part of the risk remained. Therefore, health-related behavioral factors that we did not deal with, such as nutritional intake or a disturbance of biological and physiological circadian rhythm, may have been responsible for the higher risk of diabetes mellitus among two-shift workers. Moreover, since there are several studies showing that HbA1c concentration is an indicator of job strain (28–30), psychosocial stress related to shift work may have also been responsible. However, the reason for the higher risk of diabetes mellitus among only the two-shift workers (not among the three-shift workers) is not evident. Although there are differences in the prevalence of certain types of health-related behavior, such as smoking and leisure-time physical activity, between two-shift and three-shift workers, adjustment for health-related behavior did not diminish the risk difference between the two types of shift work. Therefore, more information on job strain, dietary habit, and nutritional intake is needed to clarify the difference in the risk of diabetes mellitus between these two types of shift schedules.

Thus far, there have been few prospective studies that have dealt with the effects of shift work on glucose tolerance. Some cross-sectional epidemiologic studies have found an increase in the prevalence of metabolic syndrome among shift workers (5–10). Kawachi et al

(31) found a relationship between the duration of shift work and diabetes mellitus. Mikuni et al (32) also reported a higher prevalence of diabetes mellitus among shift workers. Our result is consistent with these previous reports. In conclusion, our study suggests that shift work is a risk factor for the onset of diabetes mellitus and that there are different risks associated with different types of shift schedule. Furthermore, since the shift system of the employer studied represents a common type of shift system, used in well-organized Japanese factories, the results of this study can be generalized to represent the effects of shift work on glucose tolerance among all Japanese shift workers.

References

1. Bøggild H, Knutsson A. Shift work, risk factors and cardiovascular disease [review]. Scand J Work Environ Health 1999;25(2):85–99.
2. Knutsson A. Health disorders of shift workers. Occup Med 2003;53:103–8.
3. Kristensen TS. Cardiovascular diseases and the work environment: a critical review of the epidemiologic literature on nonchemical factors [review]. Scand J Work Environ Health 1989;15:165–79.
4. Knutsson A, Bøggild H. Shiftwork and cardiovascular disease: review of disease mechanisms. Rev Environ Health 2000;15:359–72.
5. Theorell T, Åkerstedt T. Day and night work: changes in cholesterol, uric acid, glucose and potassium in serum and in circadian patterns. Acta Med Scand 1976;200:47–53.
6. Orth-Gomér K. Intervention on coronary risk factors by adapting a shift work schedule to biologic rhythmicity. Psychosom Med 1983;45:407–15.
7. Knutsson A, Åkerstedt T, Jonsson BG. Prevalence of risk factors for coronary artery disease among day and shift workers. Scand J Work Environ Health 1988;14:317–21.
8. Karlsson B, Knutsson A, Lindahl B. Is there an association between shift work and having a metabolic syndrome? results from a population based study of 27,485 people. Occup Environ Med. 2001;58(11):747–52.
9. Karlsson BH, Knutsson AK, Lindahl BO, Alfredsson LS. Metabolic disturbances in male workers with rotating three-shift work. Results of the WOLF study. Int Arch Occup Environ Health. 2003;76:424–30.
10. Nagaya T, Yoshida H, Takahashi H, Kawai M. Markers of insulin resistance in day and shift workers aged 30–59 years. Int Arch Occup Environ Health. 2002;75:562–8.
11. Carroll KF, Nestel PJ. Diurnal variation in glucose tolerance and in insulin secretion in man. Diabetes 1973;22:333–48.
12. Van Cauter E, Desir D, Decoster C, Fery F, Balosse EO. Nocturnal disease of glucose tolerance during constant glucose infusion. J Clin Endocrinol Metab 1989;69:604–11.
13. Spiegel K, Leproult R, van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet 1999;354:1435–9.
14. Ribeiro DCO, Hampton SM, Morgan L, Deacon S, Arendt J. Altered postprandial hormone and metabolic responses in simulated shift work environment. J Endocrinol 1998;158:305–10.
15. Lund J, Arendt J, Hampton SM, English J, Morgan LM. Postprandial hormone and metabolic responses amongst shift workers in Antarctica. J Endocrinol 2001;171:557–64.
16. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26 suppl 1:S5–20.
17. Rohlfing CL, Harris MI, Little RR, Flegal KM, Wiedmeyer HM, Eberhardt MS, et al. Use of GHb (HbA1c) in screening for undiagnosed diabetes in the U.S. population. Diabetes Care 2000;23:187–91.
18. Takahashi Y, Kuzuya T, Noda M, Ito C, Tsugane S, Kadowaki T. Prevalence of diabetes estimated by plasma glucose criteria combined with standardized measurement of HbA1c among health checkup participants an Miyako Island, Japan. Diabetes Care 2000;23:1092–6.
19. McCance DR, Hanson RL, Charles MA, Jacobsson LT, Pettitt DJ, Bennett PH, et al. Comparison of tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes. BMJ 1994; 308:1323–8.
20. The committee of Japan Diabetes Society for the Diagnostic Criteria of Diabetes Mellitus. Report of the Committee of Japan Diabetes Society on the Classification and Diagnostic Criteria of Diabetes Mellitus [in Japanese]. J Jpn Diabetes Soc 1999:42;385–404.
21. Ito C. Study on correlation among fasting plasma glucose, 2-h plasma glucose at GTT and HbA1c. J Jpn Diabetes Soc 1998:41 suppl 2; A63–4.
22. Morikawa Y, Nakagawa H, Ishizaki M, Tabata M, Nishijo M, Miura K, et al. Ten-year follow-up study on the relation between the development of non-insulin-dependent diabetes mellitus and occupation. Am J Ind Med 1997;31:80–4.
23. Cobb S, Rose RM. Hypertension, peptic ulcer and diabetes in air traffic controllers. JAMA 1973;224:489–92.
24. Ng TP. Occupational mortality in Hong Kong, 1973–1983. Int J Epidemiol 1988;17:105–10.
25. Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Effects of smoking on the incidence of non-insulin dependent diabetes mellitus. Am J Epidemiol 1997;145:103–9.
26. Sairenchi T, Iso H, Nishimura A, Hosoda T, Irie F, Saito Y, et al. Cigarette smoking and risk of type 2 diabetes mellitus among middle-aged and elderly Japanese men and women. Am J Epidemiol 2004;160:158–62.
27. Nakanishi N, Nakamura K, Matsuo Y, Suzuki K, Tatara K. Cigarette smoking and risk for impaired fasting glucose and type 2 diabetes in middle-aged Japanese men. Ann Intern Med 2000;133:183–91.
28. Cesana G, Panza G, Ferrari M, Zanettini R, Arnoldi M, Grieco A. Can glycosylated hemoglobin be a job stress parameter? J Occup Med 1985;27:357–60.
29. Netterstrøm Bo, Sjøl A. Glycated haemoglobin (HbA1c) as an indicator of job strain. Stress Med 1991;7:113–8.
30. Kawakami N, Akachi K, Shimizu H, Haratani T, Kobayashi F, Ishizaki M, et al. Job strain, social support in the workplace, and haemoglobin A1c in Japanese men. Occup Environ Med. 2000; 57:805–9.
31. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Speizer FE, et al. Prospective study of shift work and risk of coronary heart disease in women. Circulation 1995; 92:3178–82.
32. Mikuni E, Ohoshi T, Hayashi K, Miyamura K. Glucose intolerance in an employed population. Tohoku J Exp Med 1983; 141 suppl:251–6.

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3）交代勤務と高血圧発症との関連についてのコホート研究（富山職域コホート）

（Morikawa Y, Nakagawa H, Miura K, Ishizaki M, Tabata M, Nishijo M, Higashiguchi K, Yoshita K, Sagara T, Kido T, Naruse Y, Nogawa K. Relationship between shift work and onset of hypertension in a cohort of manual workers. *Scand J Work Environ Health* 1999;25:100-104.）

【目的】

3交代勤務が高血圧発症と関連するのかを前向きコホート研究にて明らかにする。

【方法】

日本のアルミ製品製造事業所に勤務する18-49歳男性1,551人を5年間追跡し、高血圧発症率を3交代勤務者と日勤作業者とで比較した。ベースラインの年齢、BMI、血圧、飲酒の調整のために多重ロジスティック回帰分析を行った。

【結果】

若年群では多変量調整後の高血圧発症相対危険度は日勤作業者に比べて3交代勤務者では上昇していた。中年群では交代勤務を続けている群では高血圧発症リスクは高くなかったが、交代勤務から日勤に変更になった者では高血圧発症リスクが高くなった。

【結論】

3交代勤務は高血圧発症と関連すると考えられた。

4）職種と糖尿病発症との関連についての10年間の追跡研究（富山職域コホート）

（Morikawa Y, Nakagawa H, Kawano S, Tabata M, Nishijo M, Miura K, Ishizaki M, Kido T, Nogawa K. Ten-year follow-up study on the relation between the development of non-insulin-dependent diabetes mellitus and occupation. *Am J Ind Med* 1997;31:80-84.）

【要約】

職種と糖尿病発症との関連を明らかにするために、アルミ製品製造事業所の男性従業員1,087人を10年間追跡する研究を実施した。対象者は、管理職、技術職、事務職、運輸職、現場作業者の5種に分類した。10年間の糖尿病罹患率は3.1%であった。年齢調整罹患率は運輸職で最も高く、現場作業者で最も低かった。ベースラインの年齢、BMI、空腹時血糖、糖尿病家族歴を調整した相対危険度を多重ロジスティック回帰分析を用いて算出したところ、現場作業者に比べて運輸職では3.95倍となった。職種と糖尿病発症は関連があると考えられた。

5）日本人男女における血清HDLコレステロールと脳卒中発症リスクとの関連（小矢部コホート）

（Soyama Y, Miura K, Morikawa Y, Nishijo M, Nakanishi Y, Naruse Y, Kagamimori S, Nakagawa H. High-density lipoprotein cholesteroland the risk of stroke in Japanese men and women: the Oyabe study. *Stroke* 2003;34:863-868.）

【目的】

近年，脳出血が減少，脳梗塞が増加するなど脳卒中の病型も変化しつつあり，そのリスクファクターも変化してきていると考えられる。脳卒中発症のリスクファクターとしてこれまで高血圧，糖尿病，心房細動等が報告されているが，血清脂質が我が国における脳卒中発症のリスクファクターとなりうるかに関するエビデンスは未だ十分とは言えない。低HDLコレステロール血症は冠動脈疾患発症のリスクファクターであるとするエビデンスが確立しているが，血清HDLコレステロールと脳卒中発症との関連については近年ようやく欧米男性における疫学研究にて関連があるとする結果が報告され始めた段階であり，女性やアジア系民族でも同様の関連があるのかは明らかになっていない。

本研究は，日本人の男女において，血清HDLコレステロール値が将来の脳卒中(特に脳梗塞)罹患を予測しうる指標となるかを，地域住民の大規模かつ長期の前向きコホート研究から明らかにすることを目的とする。

【方法】

1988年に富山県小矢部市住民健診を受診した35歳以上80歳未満の男女をコホートに設定し，1998年末まで約10年間にわたる追跡調査を行った。脳卒中既往のある者(65人)，BMIデータ欠損者(20人)を除外した男1,523人（平均年齢58.2歳），女3,466人（平均年齢55.6歳）の合計4,989人を追跡コホートとした。ベースラインデータとして1988年の住民健診受診者において血圧，血清総コレステロール，血清HDLコレステロール，および喫煙習慣，飲酒習慣を調査した。追跡期間中の脳卒中罹患については旧小矢部保健所(現在の砺波保健所小矢部支所)において実施されている脳卒中登録システムから厳密かつ悉皆的に把握し，また小矢部市外の転出や脳卒中を含む死亡については小矢部市住民基本台帳をもとに把握した。

解析のエンドポイントは全脳卒中罹患および脳梗塞罹患の発生とし、血清HDLコレステロール値のカテゴリー別に年齢調整罹患率を人年法にて算出した。さらに，他の交絡要因とは独立した関連を明らかにするためにCox比例ハザードモデルを用い，性・年齢調整相対危険度および，性・年齢に加え肥満度・収縮期血圧・血清総コレステロール・喫煙習慣・飲酒習慣の多変量を調整した相対危険度を算出した。

【結果】

追跡期間中の全脳卒中罹患(脳梗塞罹患)数は男で63人(46人)，女で69人(35人)であった。全脳卒中の年齢調整罹患率は血清HDLコレステロール値60mg/dl以上の群では男で1万人年対26.4，女で1万人年対15.5であったが，30mg/dl未満の群では男で103.4，女で49.3と3-4倍高い率を示した。エンドポイントを脳梗塞とした時の年齢調整罹患率も血清HDLコレステロール値60mg/dl以上群では男で26.5，女で6.7であったが，30mg/dl未満群では明らかに高く男で79.7，女で31.9であった。Cox比例ハザードモデルにて算出した，血清HDLコレステロール値60mg/dl以上群に対する30mg/dl未満群の全脳卒中罹患に関する性・年齢調整相対危険度は3.10（95%信頼区間1.50-6.39，p=0.002)と有意に高リスクであり，さらに収縮期血圧・BMI・総コレステロール・喫煙習慣・飲酒習慣を調整後の相対危険度も2.89（95%信

頼区間1.35-6.20, p=0.007)と有意に上昇していた。脳梗塞罹患に関しても同様で,60mg/dl以上群に対する30mg/dl未満群の多変量調整相対危険度は2.92 (95%信頼区間1.17-7.32, p=0.022)と有意に高いリスクを示した。血清HDLコレステロール値60mg/dl以上群に対する30-59mg/dl群の脳卒中・脳梗塞罹患リスクの上昇は有意でなかった。

【考察と結論】

大規模な日本人男女の10年間にわたるコホート研究にて以下の結果が得られた。①30mg/dl未満の血清HDLコレステロールの低値は，他の要因と独立して10年間の全脳卒中及び脳梗塞罹患リスクを有意に上昇させた。②血清HDLコレステロール値60mg/dl以上群に対する30mg/dl未満群の全脳卒中罹患に関する多変量調整相対危険度は約3倍にのぼった。③血清HDLコレステロール値60mg/dl以上に対する全脳卒中リスクの上昇は30-59mg/dlでは有意ではなく，30mg/dl未満での上昇が著しいものであった。④血清HDLコレステロールと脳卒中発症との関連は血圧，肥満度，飲酒習慣，喫煙習慣，血清総コレステロール値とは独立したものであった。

血清HDLコレステロールと脳卒中罹患との関連についてはFramingham studyでも検討されているが，脳卒中発症率がアジア系民族に比べ低い欧米では十分なコホート規模でなく有意な関連が示されていない。その他近年の欧米男性を対象としたコホート研究でも未だ十分なエビデンスが得られたとは言えないのが現状であり，アジア系民族であり，かつ女性が研究対象に含まれている本研究において血清HDLコレステロールと脳卒中（脳梗塞）罹患との独立した関連が示されたことは，今後の脳卒中・脳梗塞予防対策における大変重要なエビデンスを提出したものと言える。

以上，本研究では日本人男女における脳卒中，特に脳梗塞の発症には加齢や高血圧に加え血清 HDL コレステロール低値が関連することが示された。日常の健康管理における血清 HDL コレステロールの評価やスクリーニングは脳卒中一次予防のためにも重要であり，また，高血圧・糖尿病等の脳卒中リスクファクター管理における血清 HDL コレステロール評価の重要性も示唆される。

6）中高年男女の 10 年間の脳卒中罹患予測における 4 つの血圧指標の比較（小矢部コホート）

（Miura K, Soyama Y, Morikawa Y, Nishijo M, Nakanishi Y, Naruse Y, Yoshita K, Kagamimori S, Nakagawa H. Comparison of four blood pressure indexes for the prediction of 10-year stroke risk in middle-aged and older Asian. *Hypertension* 2004;44:715-720.）

【目的】

血圧指標の循環器疾患発症予測能については、歴史的には拡張期血圧（DBP）から収縮期血圧（SBP）に重要性がシフトしてきているが、近年は脈圧（PP）の重要性を指摘する報告も見られる。しかしこれまでの多くの報告は虚血性心疾患の多い欧米からもので、アジア系民族の脳卒中発症予測能について、SBP、DBP、PP、および平均血圧（MBP）を長期のコホ

ート研究で比較した報告はほとんどない。本研究では日本人成人集団の10年間のコホート研究からこれを明らかにすることを目的とする。

【方法】

1988年に富山県小矢部市住民健診を受診した35歳以上80歳未満の男女をコホートに設定し，1998年末まで約10年間にわたる追跡調査を行った。脳卒中既往のある者(65人)，BMIデータ欠損者(20人)を除外した男1,523人（平均年齢58.2歳），女3,466人（平均年齢55.6歳）の合計4,989人を追跡コホートとした。血圧は1988年ベースラインにおいて、5分間の座位安静後、ランダムゼロ血圧計で測定された。そのほか、血清総コレステロール，血清HDLコレステロール，および喫煙習慣，飲酒習慣を調査した。追跡期間中の脳卒中罹患については旧小矢部保健所(現在の砺波保健所小矢部支所)において実施されている脳卒中登録システムから厳密かつ悉皆的に把握し，また小矢部市外の転出や脳卒中を含む死亡については小矢部市住民基本台帳をもとに把握した。

解析のエンドポイントは全脳卒中罹患、およびこのうち脳梗塞罹患、出血性脳卒中（脳出血およびくも膜下出血)罹患とした。各血圧指標の1標準偏差上昇あたりハザード比をCox比例ハザードモデルにて多変量を調整して算出した。関連の強さはWaldのχ自乗値で比較した。分析は男女別、年齢別（35-64歳、65-79歳）の４つの性年齢群別にも行った。

【結果】

追跡期間中の全脳卒中罹患数は男で63人，女で69人あった。全脳卒中罹患に対する調整ハザード比はSBPで1.68、DBPで1.72、MBPで1.80であり、PPの1.34にくらべていずれも高かった。SBPとDBPは互いに調整したあとも、ともに正に脳卒中罹患リスクに関連した。PPはいずれの性年齢群においても４つの血圧指標の中で最強の予測因子となることはなかった。65-79歳男性ではSBPが全脳卒中罹患に最も強く関連した（ハザード比 1.62)。65-79歳女性では、全脳卒中罹患のハザード比はMBPで2.48、DBPで2.46、SBPで2.25、PPで1.57であった。

【結論】

アジア系民族の長期の脳卒中罹患リスクの予測は、SBP、DBPの両方を用いるか、MBPを用いるべきであり、PPは重要な指標ではないことが明らかとなった。

３．今後の研究計画

１）富山職域コホート

本コホートでは引き続き血圧、血清脂質、血糖値等、検査データの経年追跡が続けられるとともに、脳卒中、虚血性心疾患の在職中および退職後の発症、在職中の悪性新生物、精神疾患等各種疾患の発症についても追跡が続けられる。これまで調査が行われた各種の要因と各種エンドポイント発生との関連について、多様な解析が行われる予定である。主なものを以下に示す。

① 青壮年男女における各種危険因子（血圧、血清脂質、血糖値、肥満、喫煙）と長期の循環器発症リスクとの関連についての検討

特に青壮年男性集団の長期循環器リスクに関する検討はわが国では少ない。比較的若年期における危険因子の状態がその後の循環器疾患発症とどの程度関連するかを明らかにするためには大規模な集団をかなり長期に追跡する必要があるため、本コホートは重要な知見を提出する可能性がある。

② 職業要因と循環器疾患発症との関連についての検討

本コホートでは折に触れて職業関連要因、特に、交代勤務、職種、職業ストレスなどについての詳細な調査がなされており、これらの要因と長期の循環器疾患発症リスクとの関連についての検討が可能である。わが国の産業衛生分野において重要な知見を提出する可能性がある。

③ 各種の新たな危険因子と循環器疾患発症との関連の検討

近年新たに注目されている危険因子として、高感度 CRP、ウエスト／ヒップ、フィブリノーゲン、LDL コレステロール、インスリン抵抗性などについての測定も最近なされており、今後の長期の追跡により循環器疾患発症との関連の検討が可能となる。

④ 各種栄養素および食品摂取と高血圧、高脂血症、糖尿病、循環器疾患発症との関連についての検討

2003 年に詳細な食事調査が従業員全員を対象として実施された。本調査から明らかとなった各種栄養素摂取量および食品群摂取量と各種循環器危険因子との関連についての横断的検討、さらに、今後の追跡継続により、高血圧発症、高脂血症発症、糖尿病発症、さらには脳卒中および虚血性心疾患発症との関連についての様々な栄養疫学的研究の展開が可能である。

⑤ 身体活動と高血圧、高脂血症、糖尿病、循環器疾患発症との関連についての検討

2003 年に詳細な身体活動量調査が従業員全員を対象として実施された。本調査から明らかとなった身体活動量と各種循環器危険因子との関連についての横断的検討、さらに、今後の追跡継続により、高血圧発症、高脂血症発症、糖尿病発症、さらには脳卒中および虚血性心疾患発症との関連についての様々な運動疫学的研究の展開が可能である。

⑥ 睡眠と高血圧、糖尿病、循環器疾患発症との関連についての検討

2004 年に詳細な睡眠に関する調査が従業員全員を対象として実施された。本調査から明らかとなった睡眠に関する要因と各種循環器危険因子との関連についての横断的検討、さらに、今後の追跡継続により、高血圧発症、糖尿病発症、さらには脳卒中および虚血性心疾患発症との関連についての様々な検討が可能である。

⑦ 在職中の悪性新生物、精神疾患などの発症要因に関する検討

在職中の悪性新生物、精神疾患などの発症については産業医活動の中で把握されており、これらの疾患の発症要因に関する検討が可能である。

2）小矢部コホート

小矢部コホートについては脳卒中登録の富山県全域への移行によってコホートの脳卒中エンドポイントの追跡が困難となったため、従来のデータセットをもって追跡が終了とな

った。今後は、他の循環器疾患コホート研究とのデータ統合によるメタアナリシスなどにデータを活用してゆく予定である。

１０．診療ガイドラインとの整合性の検討：国内外の診療ガイドラインの現状と動向

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研究要旨：根拠に基づく医療（EBM）の手法を用いた診療ガイドラインに対する関心が医療者のみならず、一般の人々の間でも高まっている。診療ガイドラインの定義は「特定の臨床状況のもとで、医療者と患者の意思決定を支援する目的で、系統的に作成された文書」である。本課題では国内における診療ガイドラインの現状、疫学的成果の反映のあり方について検討を行った。

1.　はじめに

診療ガイドラインは米国の Institute of Medicine により「特定の臨床状況のもとで、臨床医や患者が、適切な判断や決断を下せるように支援する目的で体系的に作成された文書」と定義されている　1）。また英国・スコットランドで診療ガイドライン作成・普及の責任を担っている SIGN(The Scottish Intercollegiate Guidelines Network)は、「私たちの目的は、現在のエビデンスに基づく治療の有効性に関する推奨を含む国レベルの診療ガイドラインの作成、普及を通じて、診療とアウトカムのばらつきを減じ、スコットランドにおける患者ケアの質を向上させることである」として、診療ガイドラインに求められる特性とその役割を簡潔に表現している。

国内では厚生省（当時）は 1999 年度の厚生科学研究から、EBM の手法を用いた診療ガイドライン作成を開始した　2）。それまでは診療ガイドラインの作成において、従来は根拠とする文献の選択・入手法、評価法、勧告（推奨）の決定法などが明示されず、何人かの主導的立場にある臨床医のコンセンサスによって作られることが一般的であった。厚生（労働）科学研究によるプロジェクトでは（臨床）疫学者や生物統計学者のような研究方法論の専門家や、適切な文献を検索するために医学図書館員の参加が強く求められた　3）。現在は公的研究費の枠外でも多くの学会が独自に診療ガイドライン作成を進めている。

2.　診療ガイドラインの構造と作成手順

ガイドラインを作成するテーマを設定したら，その問題の関係者を集めて作成グループを組織する。日本では学会の主導でガイドライン作成が進められることが多く，当該学会の主導的立場にある関係者という、「仲間うち」で作業が進められることが多いが、欧米では幅広い専門家により作成グループを組織し、また stakeholders（利害関係者）にも発言の機会が提供されていることが多い。

EBM の手法による診療ガイドライン作成は、まず推奨を示すべき臨床的課題(clinical questions) を挙げ（scoping)、それに対してシステマティック・レビューの方法に準じて、関連文献の系統的検索と吟味を行なう　4）。

推奨度の決定は、診療ガイドラインの核心である。あるテーマの文献が収集され、その内容が抽出された「診療エビデンス（clinical evidence）集」は、方向性を示す推奨を含まない点で診療ガイドラインと決定的に異なる。推奨度は得られたエビデンスの質（レベル）に大きく影響されるが、それだけではなく表１の各要素を勘案して総合的に判断されるものである　5）。

推奨度の表示形式を表２に示す。国内では１９９０年代前半に米国の AHCPR（Agency for Health Care Policy and Research、現 Agency for Healthcare Research and Quality：AHRQ）方式が多くのガイドラインで用いられたが、判定・解釈が困難な場合も少なくない。特に「推奨度 C：根拠が無いので推奨できない」の解釈については混乱が多い。

日本脳卒中学会の合同ガイドライン（2001 年）では C 判定を「C1：行うことを考慮してもよいが、十分な科学的根拠はない」と「C2：科学的根拠がないので勧められない」に区別している。棚橋は、同ガイドラインにおける急性期治療の推奨７１のうち、A が０件、B が６件、C1 が５３件、C2 が８件、D が４件であり、C1 が７５％を占めていることを報告している６）。これは、必ずしも「日本の臨床医学は、高いレベルのエビデンスに基づいて行われていない」という否定的な意味ではなく、「実際に臨床で行われていることの多くは高いレベルのエビデンスで裏付けられていないものである」という臨床の現実を意味していると捉えることもできる。

臨床における予防医学的テーマの包括的ガイドラインである米国 Preventive Services Task Force（USPSTF）の第 3 版では、ABCD の 4 段階の推奨度に新たに I 判定を加えている。推奨度 C、I とも明確な推奨が難しい課題であるが、C は複数の信頼し得る研究報告が存在するが、利益と害が拮抗しているため一定の推奨が困難であるのに対し、I はエビデンスが無いか、その質が低いために推奨が決定できないケースがあたるとしている。国内でも厚生労働科学特別研究「最新の科学的知見に基づいた保健事業に係わる調査研究」のグループによる推奨度決定（2005 年度）や、厚生労働省がん研究助成金「がん検診の適切な方法とその評価法の確立に関する研究」班による有効性評価に基づくがん検診ガイドライン７）において、USPSTF の 5 段階の推奨度表記が採用されている。

カナダの予防医学に関するタスクフォースも米国に類似した、しかし独自の推奨度分類を提案している。これは医療の非専門家も含め関係者の誤解・齟齬を減らす意味で有益な視点と思われる。同タスクフォースは、推奨度 C のようにエビデンスが明確でない場合の意思決定・行動の基準の提案も行っている（表 3）。

３．　診療ガイドラインの評価

有効な診療ガイドラインの要件として、Grimshaw は　①　内容が妥当か？　②　普及し利用可能か？　③　実際に利用されているか？　④　患者アウトカムの改善　を挙げ、診療ガイドラインの臨床行為への影響・患者アウトカムの改善の視点からレビューを行なった８）。その結果、59 の診療ガイドラインのうち 55 で臨床行為の改善が見られたこと、患者アウトカムへの影響を検討した 11 論文では 2 論文を除いてアウトカムが改善したことを報告している。小山らは 1991 年から 2000 年にかけて発表された、学会または国家機関レベルで作成された治療に関する診療ガイドラインが患者アウトカムに与えた効果を、ランダム化比較試験または準実験的研究デザインにより検討した研究のシステマティック・レビューを行った９）。17 篇の論文が同定され、うち 10 篇(59%)で患者アウトカムの改善が示されていた。また、患者アウトカムの改善が示されなかった研究のうち、2 篇ではガイドライン遵守率が低く、3 篇ではガイドライン遵守率が報告されていなかった。本研究の結果は、診療ガイドラインを診療上用いることにより患者アウトカムが改善される可能性を強く示唆している。

1997 年から 2001 年にかけて国内で公表された 48 診療ガイドラインを Shaneyfelt らの方法で評価した結果、平均値は 25 点満点で 8.49 点（標準偏差 4.28 点．　範囲：0

～18.5点）であった 10)。1985～97年に発表された米国の279診療ガイドラインは25点満点で10．77点であり、それと比べると国内で作成された診療ガイドラインの内容はまだ十分ではないことがうかがわれた。２５項目の評価ポイントの中で80%以上の遵守率が５項目、遵守率が10%未満であったのは８項目であり、内容別に見ると「ガイドラインの作成方法と様式について」の10項目は平均遵守率が60．0%、「エビデンスの検索・要約について」の10項目は平均遵守率が13．0%、「勧告の作成方法について」の５項目は平均遵守率が23．8%であった。

診療ガイドラインの評価に関する国際的な取り組みとして、European Union (EU)を中心に発足したAGREE共同計画（"Appraisal of Guidelines Research and Evaluation"がある。AGREEのグループは発表された診療ガイドラインの質を調べるため、次に示す6領域23項目と総合評価から成る評価手法を提示している 11,12)。

範囲と目的（項目1-3）：ガイドラインの全体的な目的、具体的な臨床問題と対象とする患者集団に関する項目。

利害関係者の関与（項目4-7）：ガイドラインがそのユーザーとして意図された者の見方をどれほど代表するものであるかに関する項目。

開発の厳密さ（項目8-14）：根拠を集め集約するのに用いられた過程と、推奨を導き出す方法、その更新に関する項目。

明快さと提示（項目15-18）：ガイドラインの言葉と形式に関する項目。

適用性（項目19-21）：考えられるガイドライン適用、組織的、行動的、経済的影響に関する項目。

編集の独立性（項目22-23）：ガイドライン作成グループが利害の衝突を生じる影響力から独立していることに関する項目。

AGREEによる診療ガイドラインの評価は臨床医の行動や患者アウトカムの変化ではなく、診療ガイドライン作成の「枠組み」の評価に焦点を当てている。2003年9月には米国が中心となって行なわれたThe Conference on Guideline Standardization (COGS)の成果が報告された 13)。COGSの提案は作成された診療ガイドラインを報告する際のチェック項目であり、既に発表された診療ガイドラインの評価法としてのAGREEの提案と表裏一体である。表４にCOGSの提案とAGREEの方法の対応を示す 14)。COGSの提案は推奨が導き出された過程の透明性を確保するだけでなく、作成者、目的、資金提供者に始まり、可能な場合は有効期限を示すことを求めるなど、その診療ガイドラインの作られた枠組みに関する情報を重視している。これは情報学でいうメタデータ、すなわち「データに関するデータ」の一種であり、個々の情報の持つ意味を利用者が判断する際の有益な手がかりとなる。このような国際的な標準様式に沿った形で診療ガイドラインを作成し、報告することが、今後、質の高い診療ガイドラインを世に出すための必須要件となるであろう。

４．　診療ガイドラインにおける疫学的知見の活用

診療ガイドラインにおいてリスク情報を医療者と患者の間で効果的に共有する手法は検討を進めるべき課題の一つである。特に臨床医学と公衆衛生が協調して生活習慣病対策を進めていくためには、地域住民を対象としたコホート研究の成果を、診療ガイドラインに適切に反映していくことが大きな意義を持つ。

ニュージーランドはEBMの手法によって開発された診療ガイドラインが一般臨床に

広く取り入れられている国の一つである。2005年6月にNew Zealand Guidelines Groupによって刊行された　“New Zealand Cardiovascular Guidelines Handbook”では、性・糖尿病合併の有無・年代・血圧レベル・総コレステロール値：HDLコレステロール値比の5軸で対象者を分類し、各サブカテゴリーの5年間循環器疾患リスク（絶対リスク）を8段階に色分けして視覚的に理解しやすく図表化している。この方法は臨床医と患者のコミュニケーションを促進し、患者の関心を高めるのに有用であったとされている。

疫学研究の知見を活用して、絶対リスクを対象者に提示する類似の取り組みとして、萬有製薬によるシンバスタチン服用者の6年間追跡を行った“Japan Lipid Intervention Trial（J-LIT）”　の結果に基づくJ-LITチャート（http://www.medical-tribune.co.jp/mtbackno5/3507/07hp/M3507281.htm）や健康・体力づくり事業財団の健康ネット内で提供されている“HEALTH WATCHING 21（http://www.health-net.or.jp/kenko_check/health-check/）”がある。“HEALTH WATCHING 21”はいわゆる「健康危険度評価（Health Risk Appraisal：HRA）」の一種であり、Websiteで各人のリスクファクター保有状況を入力することで、絶対リスクから余命を計算し、現時点の「健康年齢」を推測する形を取っている。Website上でのインタラクティブなシステムは、インターネットに慣れていれば使いやすく馴染みやすいが、様々なリスクファクター保有パターンの絶対リスクが図表で一覧されるのも手軽であり、また相応のインパクトがあると思われる。今後、診療ガイドラインは紙媒体とインターネットでの普及が進んでいくことを予想すると、このような絶対リスクの提示について、その媒体の特性を考慮して、より効果的な方法を検討すべきであろう。

国内でも高血圧、高脂血症、糖尿病などの主要な生活習慣病について、その診療ガイドライン整備や医療者と患者の情報共有に際して、整備されつつある国内の疫学研究の成果を活用していく視点は不可欠であろう。大規模な統合コホートの構築により、詳細なサブグループごとに妥当性の高い絶対リスクが得られるようになれば、循環器疾患を中心とする診療ガイドラインに大きく寄与するエビデンスが提示できるものと思われる。

5．　臨床研究・疫学研究・診療ガイドライン

1999年以降、国内ではEBMによる診療ガイドライン作成がさまざまな学会を中心に行なわれ、その成果が発表された。その作業過程で明らかにされた多くの課題の中で、最も大きなものの一つは「日本人を対象としたレベルの高いエビデンスがきわめて乏しい」事実の確認であった。基礎的な医学研究が偏重され、臨床現場の意思決定を支援する臨床研究や疫学研究が立ち遅れていた日本の研究風土の特性が、期せずして明らかにされたと言える。近年、インパクトファクターに象徴される研究業績の得点主義は、国内において臨床医を含む医学研究者の志向に少なくない影響を与えている。インパクトファクターによる学術誌やその研究領域のランク付けと、診療ガイドラインに引用される文献（臨床の問題解決に貢献する研究と考えられる）を多く掲載している学術誌の評価は一致していない15)。EBMと診療ガイドラインの認知が高まると共に、実際の患者の役に立つエビデンスを作るという問題意識と適切な研究方法論が普及することで、真に意味ある臨床研究や疫学研究が活性化されることが期待される。

診療ガイドラインは医療の質を向上させるための特効薬ではない。使い方を誤れば瞬時に両刃の剣に転じる。その意義、役割、そして限界を医療者と社会一般の人々がど