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Imai E, Haneda M, Yamasaki T, Kobayashi F, Harada A, Ito S, Chan JC, Makino H	Effects of dual blockade of the renin-angiotensin system on renal and cardiovascular outcomes in type 2 diabetes with overt nephropathy and hypertension in the ORIENT: a post-hoc analysis (ORIENT-Hypertension)	Hypertens Res	36(12)	1051-1059	2013
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Iwakura Y, Morimoto R, Kudo M, Ono Y, Takase K, Seiji K, Arai Y, Nakamura Y, Sasano H, Ito S, Satoh F	Predictors of decreasing glomerular filtration rate and prevalence of chronic kidney disease after treatment of primary aldosteronism: Renal outcome of 213 cases	J Clin Endocrinol Metab			2013(InPress)

糖尿病患者の冠動脈疾患二次予防における脂質管理目標に関する検討

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研究要旨

メタボリックシンドロームは糖尿病や心血管疾患のハイリスクであることから適切な診断と予防・治療が必要とされる。病状が進み脂質異常症や糖尿病を合併すると心血管疾患の超ハイリスク状態となるためその管理は重要な課題である。我が国の動脈硬化性疾患予防ガイドラインでは、一次予防患者の LDL コレステロール (LDL-C) 管理目標値は糖尿病を有する場合より厳しく設定されるが、二次予防患者では糖尿病の有無によらず 100 mg/dL 未満が基本管理目標値となっている。このような背景のもと、糖尿病患者での二次予防における適正な LDL-C 値について検討するために、冠動脈形成術（以下 PCI）を行った患者（一次予防失敗患者および二次予防失敗患者）における LDL-C 値コントロールの現状を解析した。その結果、LDL-C 100mg/dL 未満を達成していたにも関わらず PCI となった例も多いことが明らかとなった。特に二次予防に失敗した糖尿病患者では、LDL-C 100mg/dL 未満にコントロールされていても冠動脈病変の進行を防ぐことができなかった患者の割合が半数以上に上っていた。これらの結果より、糖尿病患者での心血管イベント二次予防における LDL-C 値は、より低値を目標とすべきである可能性があると考えられた。

A. 研究目的

　メタボリックシンドロームは糖尿病や心血管疾患のハイリスクであることから適切な診断と予防・治療が必要となる。そしてさらに病状が進み、脂質異常症や糖尿病が合併すると心血管疾患の超ハイリスク状態となり、その管理は重要な課題である。我が国の動脈硬化性疾患予防ガイドラインでは、一次予防患者の LDL-C 管理目標値は糖尿病を有する場合より厳しく設定されるが、二次予防患者では糖尿病の有無によらず 100 mg/dL 未満が基本管理目標値となっている。そこで、冠動脈形成術（以下 PCI）を行った患者（一次予防および二次予防失敗患者）における LDL-C 値コントロールの現状を把握し、その解析を通して糖尿病患者での二次予防における適正な LDL-C 値について検討することがこの研究の目的である。

B & C. 研究方法と結果

1. 方法と倫理面への配慮

2012 年 4 月から 2013 年 3 月までの間に千葉大学医学部付属病院冠動脈疾患治療部で PCI を施行した患者 132 名のうち、PCI 前に LDL-C 値（直接法）を測定していた BMI 15 kg/㎡ 以上 35 kg/㎡ 未満の 116 例について、LDL-C 値の分布と 100 mg/dL 未満の達

成状況、PCI 歴の有無および糖尿病合併の有無による管理状況の違いなどについて後方視的に解析・検討した。

なお、本研究は千葉大学大学院医学研究院倫理審査委員会の許可を得て行った。

2. 患者背景

全体 116 例の背景は、平均年齢 68.0±9.3 歳、性別は 81.0%が男性、BMI は 24.0±3.19 kg/m² であった。合併症として、脂質異常症 68.1%、糖尿病 74.1%、高血圧症 75.9%を認めた（table 1）。

Table 1

年齢	68.0±9.3（M 67.2±9.5、F 71.6±7.7）
性別	M 94 : F 22（M 81.0%）
身長	162.8±9.0 ㎝
体重	64.1±11.7 kg
BMI	24.0±3.2 kg/㎡
タバコ	68.1%
DLあり	68.1%
スタチン内服	49.1%
DMあり	74.1%
HTあり	75.9%
T-Cho	179.8±35.5 mg/dl
TG	139.5±73.5 mg/dl
HDL-C	49.5±13.4 mg/dl
LDL-C	110.3±31.3 mg/dl
随時血糖	164.1±79.9 mg/dl
HbA1c	6.7±1.2%
Cre	1.33±1.72 mg/dl

全体のうち、PCI 既往のない一次予防失敗群（以下 PCI(-)群）は 53.4%（62 例）、PCI 既往のある二次予防失敗群（以下 PCI(+)群）は 46.6%（54 例）であった。PCI(+)群のうち糖尿病合併あり（以下 PCI(+)DM(+)群）は 44.4%（24 例）であった。PCI(-)群では糖尿病合併あり（以下 PCI(-)DM(+)群）が 100%（62 例）にのぼった（Figure 1）。

Figure 1
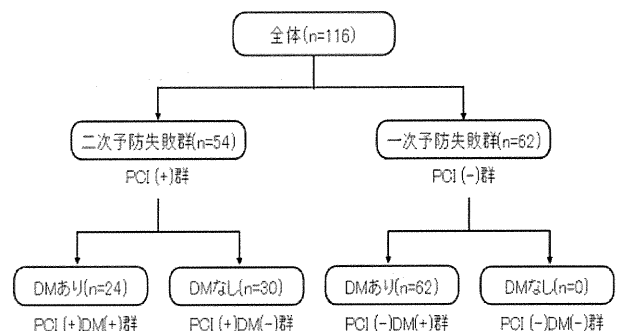
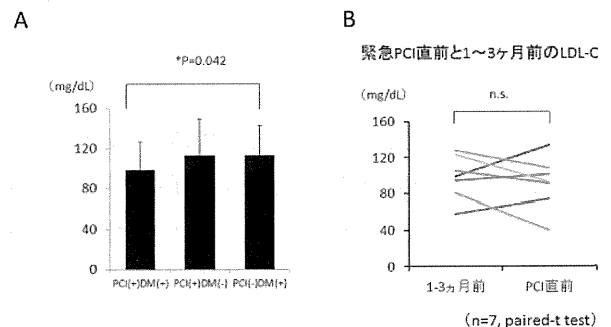## 3. LDL-C 値

全体 116 例の平均 LDL-C は 110.3 ± 31.3 mg/dL であった。また、緊急 PCI を除いた 76 例では 108.6 ± 31.9 mg/dL とほぼ同様であった。

PCI(+)DM(+)群で 98.8 ± 28.2 mg/dL、PCI(+)DM(-)群で 113.5 ± 35.9 mg/dL、PCI(-)DM(+)群 113.2 ± 29.5 mg/dL と、PCI(+)DM(+)群では PCI(-)DM(+)群よりも有意に低かった（p=0.042, paired-t test）（Figure 2A）。

なお、緊急 PCI 40 例のうち、当院で 1〜3 ヶ月前の LDLC 値が確認できた 7 例について検討を行ったところ、1〜3 ヶ月前が 98.1 ± 22.4 mg/dL、PCI 直前が 91.6 ± 27.4 mg/dL とやや低下していたが、有意な変化ではなかった（Figure 2B）。
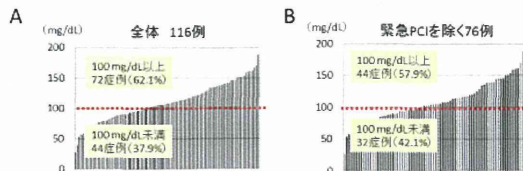
Figure 2

4. LDL-C 100 mg/dL 未満達成率

100 mg/dL 未満達成率は、全体 116 例において 37.9%、緊急 PCI を除いた場合でも 42.1%と大きな差は無く、むしろ後者で割合が高かった（Figure 3A-B）。

Figure 3

PCI（−）群での 100 mg/dL 未満達成率は 33.9%、PCI（+）群では 42.6%と後者で割合が高かった。PCI（+）群で LDL-C が 80 mg/dL 未満であったものに限定すると 22.2%（12 例）とほぼ半減した。

PCI（+）群を詳細に検討すると、PCI （+）DM（−）群で LDL-C 100 mg/dL 未満を達成していたのにもかかわらず再 PCI になったのは 10 例（33.3%）、80 mg/dL 未満では 6 例（20.0%）であった。一方、PCI（+）DM（+）群では LDL-C100 mg/dL 未満を達成していたのにもかかわらず再 PCI になったのは 13 例（54.1%）であったが、80 mg/dL 未満は 6 例（25.0%）と半分以下となった（Figure 3C-E）
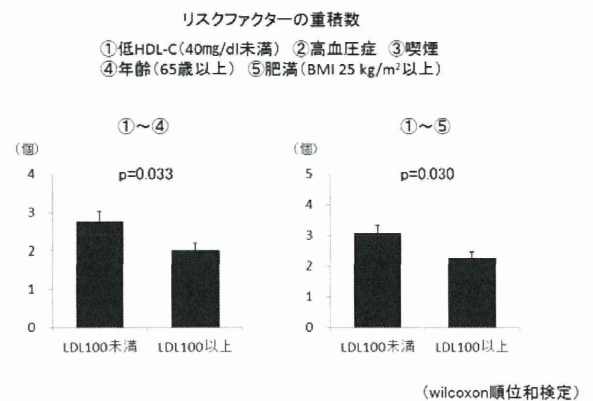
Figure 3
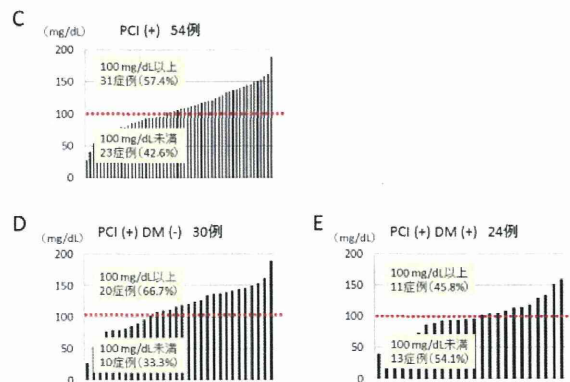
5. 「超ハイリスク糖尿病患者」の特徴

LDL-C100 未満にコントロールされていたにも関わらず再 PCI となった「超ハイリスク糖尿病患者」の特徴を明らかにするために、冠動脈疾患の危険因子として糖尿病と LDL-C 値以外に ①低 HDL-C（40 mg/dL 未満）、②高血圧症、③喫煙、④年齢（65歳以上）、⑤肥満（BMI 25 kg/m² 以上）の 5 つの有無を調べ、LDL-C 100mg/dL 以上群と比較を行った。肥満を除く①～④の危険因子の重積を検討したところ、LDL-C 100mg/dL 未満では 2.8 個、100 以上では 2.0 個（p=0.033）と有意に前者で危険因子が多いと分かった。また肥満を含めた①～⑤の危険因子で重積を検討したところ同様に LDL-C100 未満では 3.1 個、100 以上では 2.3 個（p=0.030）と有意に LDL-C 100mg/dL 未満で危険因子が多かった。（Figure 4）
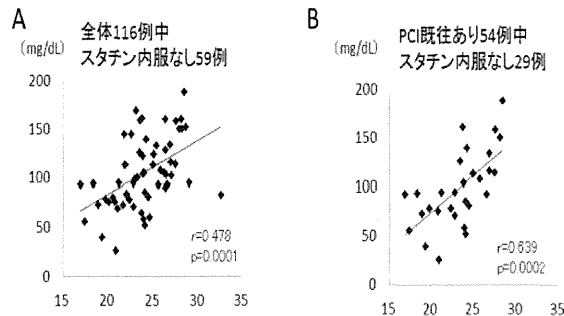
Figure 4

6. 肥満と LDL-C

全体 116 例のうち、スタチンによる LDL-C 低下療法を受けていなかった 59 例について検討してみると、LDL-C と BMI は正の相関を認めた（r =0.478、p=0.0001）。さらに、PCI 既往のある 54 例中 29 例のスタチン内服をしていない患者では、LDL-C と BMI はより強い正の相関を認め、（Fig3B: r =0.693、p=0.0002）。（Figure 5A, B）

Figure 5

A (mg/dL) 全体116例中 スタチン内服なし59例
r=0.478
p=0.0001

B (mg/dL) PCI既往あり54例中 スタチン内服なし29例
r=0.639
p=0.0002

D & E. 考察と結論

今回の研究は後ろ向きの観察研究であるが、LDL-C 100mg/dL 未満を達成していたにも関わらずPCI となった例も多いことが明らかとなった。この傾向は、コレステロール値が低下するとされる緊急 PCI の症例を除いても同様であった。

特に糖尿病患者に注目すると、PCI の既往がある群の LDL-C 値は既往のない群よりも有意に低く、100mg/dL 未満の症例が実に半分以上を占めていた。すなわち、PCI の既往があり糖尿病を合併している場合、LDL-C 100mg/dL 未満にコントロールされていても冠動脈病変の進行を防ぐことができない患者がおり、心血管イベント再発の半数以上はLDL-C100mg/dL 未満で起きていることが明らかとなった。

現在の我が国における糖尿病患者のLDL-C管理目標値は冠動脈疾患の既往がない場合は120mg/dL 未満、ある場合は 100mg/dL 未満である。一方、欧米ではそれぞれ 100mg/dL 未満、70mg/dL 未満である。本研究の結果も踏まえると、糖尿病患者での心血管イベント二次予防における LDL-C 値はより低値を目標とすべきである可能性があるが、同時にLDL-C 以外の要因が寄与する可能性もある。

一方、本研究では、PCI 既往のない群の全例（62例）で糖尿病を合併しており、さらに PCI 既往あり群の中でLDL-Cが 100mg/dL 未満であったにも関わらず再度PCI を行った患者の割合はDMなしでは33.8%、ありでは 54.1％と後者で多かった。これらの結果は糖尿病の合併が冠動脈疾患の強いリスクファクターであることを反映していると考えられた。ただし、今回の対象は大学病院通院中の患者であることから、糖尿病患者をより慎重にフォローアップして積極的に PCI を行った結果が反映された可能性もある。2013 年に米国で発表されたAHA/ACC のガイドラインでは、「40-75 才の糖尿病患者」はそれだけで冠動脈疾患のハイリスクでありLDL-C 値によらずスタチンによる LDL-C 低下療法を行うべきであると提言されている。今後、我が国においてもエビデンスが集積されれば、糖尿病患者におけるスタチン投与の基準についての再考が必要となろう。

LDL-C100mg/dL 未満で再 PCI となった「超ハイリスク糖尿病患者」についての解析からは、LDL-C値だけでなく、他のリスクファクターの管理も重要であることが改めて示された。その中で肥満に注目して解析を行ったところ、スタチン投与を行っていない肥満患者では LDL-C の管理が不十分となる傾向が示された。このことから、肥満患者ではより厳密にリスク管理を行う必要があると考えられた。

F. 健康危険情報
特記事項なし

G. 研究発表
1. 論文発表
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Daida H, Dohi S, Egusa G, Hiro T, Hirobe K, Iida M, Kihara S, Kinoshita M, Maruyama C, Ohta T, Okamura T, Yamashita S, Yokode M, Yokote K.(2013) Comprehensive risk management for the prevention of cardiovascular disease. J Atheroscler Thromb 20 (7):603-615.

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2. 学会発表
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「二次予防の観点からみた糖尿病患者の脂質管理目標」横手幸太郎

H.　知的財産権の出願、登録状況
特記事項なし

富山職域コホート研究

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研究要旨

　富山職域コホートは、富山県にある企業の従業員を追跡する職域コホートである。就労中の男女、特に地域ではコホート設定が困難な働き盛りの中高年男性における循環器疾患のリスクの評価や、リスクと就業状態の関連等の検討を行っている。

　今回は、糖尿病発症における家族歴の影響を検討した。対象者を 7 年間追跡し、糖尿病の発症を確認した。家族歴のないものを基準とした家族歴を有する者の性、年齢で調整した糖尿病発症ハザード比は 1.82（95%信頼区間 1.36-2.43）と有意に上昇した。糖尿病のリスク上昇は、特に母親の糖尿病家族歴と強い関連を認めた。肥満やインスリン抵抗性（HOMA-IR）、膵ベータ細胞機能（HOMA-B）の程度、喫煙、飲酒、運動習慣の有無、摂取熱量や職種の違いなどの他の糖尿病危険因子と家族歴の間に交互作用は認めなかった。すなわち、家族歴による糖尿病リスクの上昇は、肥満やインスリン抵抗性、生活習慣などの糖尿病危険因子の有無にかかわらず同等であった。

A. 研究目的

　富山県にある企業の従業員を追跡する職域コホートである。就労中の男女、特に地域ではコホート設定が困難な働き盛りの中高年男性における循環器疾患のリスクの評価や、リスクと就業状態の関連等の検討を行っている。

B. 研究方法

コホートの概要
　富山県にあるアルミ製品製造業企業の黒部事業所及び滑川事業所従業員を対象としたコホートである。1980 年以降、研究者が産業医として従業員の健康管理を 25 年にわたり行っている。コホート規模は約 8,000 人で、男女比は約 2 対 1 である。

　本コホートは職域コホートであるため、従業員全体が毎年 95%以上の受診率で健診を受診しており、各種検査値の高い率での経年追跡が可能である。また現業系従業員では転勤が少なく、また、途中退職も比較的少ないため長期の追跡が可能である。

　本コホート研究グループは本事業所での産業医活動を通して、詳細なエンドポイント発

生の把握を実施している。すなわち、在職中の脳卒中、虚血性心疾患、悪性新生物、精神疾患等の発症および死亡の把握、健診データ追跡による在職中の高血圧、糖尿病、高脂血症等の発症の把握である。また、一般に職域コホートでは定年退職後の疾患発症の追跡が困難であるが、本コホートでは退職後も近隣に在住するものがほとんどのため、1990年以降退職者については郵送による退職後健康調査を毎年実施し、生活習慣病の治療状況、脳血管疾患・心疾患の発症および死亡を追跡している。在職中および退職後の脳心事故発症者については同意を得た上で、医療機関での医療記録調査を実施している。

　以上より、本コホートの特色としては、（1）地域ではコホート設定が困難な青壮年期の男性を多く含むコホートであること、（2）青壮年期男性のライフスタイルや危険因子に影響が大きいと考えられる職業面での要因について詳細な情報が収集されていること、（3）各種危険因子の経年推移が高い追跡率で把握されていること、が挙げられる。

C. 研究結果

研究の成果

Sakurai M, Nakamura K, Miura K, Takamura T, Yoshita K, Nagasawa SY, Morikawa Y, Ishizaki M, Kido T, Naruse Y, Suwazono Y, Sasaki S, Nakagawa H. Family history of diabetes, lifestyle factors, and the 7-year incident risk of type 2 diabetes mellitus in middle-aged Japanese men and women. J Diabetes Invest 4(3):261-268, 2013.

【目的】日本人の糖尿病発症における家族歴の影響を検討した。

【方法】北陸の某製造業事業所の従業員3,517名（男性2,037名、女性1,480名）を対象に、健診時に身体計測、血液検査を行った。問診により糖尿病家族歴の有無を調査した。対象者を7年間追跡し、糖尿病の発症を確認した。

【結果】全対象者3,517名のうち、630名（18%）に糖尿病の家族歴を認めた。7年間の追跡で228名の新規糖尿病発症を確認した。家族歴のないものを基準とした家族歴を有する者の性、年齢で調整した糖尿病発症ハザード比は1.82（95%信頼区間 1.36-2.43）と有意に上昇した。これらの関連はbody mass indexや飲酒、喫煙、運動習慣、他の代謝異常の有無で調整しても変わらなかった。糖尿病のリスク上昇は、特に母親の糖尿病家族歴と強い関連を認めた。肥満やベースラインのインスリン抵抗性（HOMA-IR）、膵ベータ細胞機能（HOMA-B）の程度、喫煙、飲酒、運動習慣の有無、摂取熱量や職種の違いなどでの層別解析において、糖尿病家族歴による糖尿病リスク上昇は、いずれの群でも同様であり、家族歴とこれらの糖尿病危険因子とのあいだに交互作用は認めなかった。

【まとめ】日本人において、糖尿病家族歴を有する者は約1.8倍糖尿病発症のリスクが高く、家族歴による糖尿病リスクの上昇は、肥満やインスリン抵抗性、生活習慣などの糖尿病危険因子と独立していた。

D. まとめ

　富山職域コホートでは、職域の特徴を生か

したコホート研究を、引き続き継続して展開していく予定である。現在、働き盛りの中年労働者の生活習慣、職業的要因と循環器疾患危険因子との関連を検討中であり、今後横断研究、縦断研究として肥満・メタボリックシンドロームの疫学に関する研究の成果を発表していく。

E. 研究発表

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F. 知的財産権の出願・登録状況（予定を含む）
なし

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表雑誌	巻号	ページ	出版年
Sakurai M, Nakamura K, Miura K, Takamura T, Yoshita K, Nagasawa SY, Morikawa Y, Ishizaki M, Kido T, Naruse Y, Suwazono Y, Sasaki S, Nakagawa H.	Family history of diabetes, lifestyle factors, and the 7-year incident risk of type 2 diabetes mellitus in middle-aged Japanese men and women.	Journal of Diabetes Investigation	4	261-268	2013
Morikawa Y, Sakurai M, Nakamura K, Nagasawa SY, Ishizaki M, Kido T, Naruse Y, Nakagawa H.	Correlation between shift-work-related sleep problems and heavy drinking in Japanese male factory workers.	Alcohol Alcohol	48	202-206	2013

Family history of diabetes, lifestyle factors, and the 7-year incident risk of type 2 diabetes mellitus in middle-aged Japanese men and women

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ABSTRACT

Aims/Introduction: This cohort study of middle-aged Japanese participants investigated the relationship between family history of diabetes, the incident risk of type 2 diabetes and the interaction of these variables with other factors.

Materials and Methods: Study participants were 3,517 employees (2,037 men and 1,480 women) of a metal products factory in Japan. Baseline health examinations included questions about medical history, physical examination, anthropometric measurements, questions about lifestyle factors, such as smoking, alcohol consumption and habitual exercise, and a self-administered diet history questionnaire. Family history of diabetes was defined as having at least one-first-degree relative with diabetes. The incidence of diabetes was determined in annual medical examinations over a 7-year period. Hazard ratios (HRs) for type 2 diabetes were estimated by Cox proportional hazards analysis.

Results: Of the 3,517 participants, 630 (18%) had a family history of diabetes mellitus. During the study, 228 participants developed diabetes. The age and sex-adjusted HR for type 2 diabetes in participants with a family history of diabetes was 1.82 (95% confidence interval 1.36–2.43) as compared with those without a family history of diabetes. HRs did not change after adjustment for body mass index and lifestyle factors. We found no interactions with body mass index, insulin resistance, pancreatic β-cell function or lifestyle factors.

Conclusions: Family history of diabetes was associated with the incident risk of diabetes, and these associations were independent of other risk factors, such as obesity, insulin resistance, and lifestyle factors in Japanese men and women. (J Diabetes Invest doi: 10.1111/jdi.12033, 2013)

KEY WORDS: Cohort study, Epidemiology, Family history

INTRODUCTION

The prevalence of type 2 diabetes mellitus is similar in Asian and Western countries, even though the prevalence of obesity is lower in Asia[1]. The high incidence of diabetes in the relatively lean Asian population might be explained, in part, by a difference in fat distribution[2,3] and lower pancreatic β-cell function as compared with Western populations, rather than by insulin resistance[4–8]. One well-known risk factor for diabetes is family history. Family history of diabetes can include environmental in addition to genetic risk factors[9]. Obesity[10–14] and some lifestyle factors, such as alcohol consumption[14–16] and diet[15], were reported to be associated with a family history of diabetes, and these non-genetic factors explain a substantial part of the association between family history and risk of type 2 diabetes[15–17]. However, these reports were from Western countries, and it is not clear whether the association between family history and risk of diabetes involves interactions with obesity, insulin resistance and lifestyle factors in relatively lean Asian people.

In the present cohort study of middle-aged Japanese men and women, we examined the association between family history of diabetes and the 7-year incident risk of type 2 diabetes mellitus. We also evaluated the influence of interactions

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involving obesity, insulin resistance and lifestyle-related risk factors on this relationship.

METHODS

Participants

The study participants were employees of a factory that produces zippers and aluminum sashes in Toyama Prefecture, Japan. Detailed information on the study population has been reported previously[8,18-20]. The Industrial Safety and Health Law in Japan requires employers to provide annual health examinations for all employees. A test for diabetes mellitus was carried out during annual medical examinations between 2003 and 2010. In 2003, 3,776 employees (2,243 men and 1,533 women) aged 35–55 years underwent health examinations and responded to a dietary survey. Of these 3,776 potential participants, 259 (10%) were excluded for the following reasons: 193 had diabetes or high levels of fasting plasma glucose (FPG; ≥126 mg/dL) or glycated hemoglobin (HbA$_{1c}$; ≥6.5%) at the time of the baseline examination; 14 had a total daily energy intake of ≤ 500 kcal or ≥5,000 kcal; and 52 did not participate in consecutive annual follow-up health examinations. The remaining 3,517 participants (2,037 men and 1,480 women) were included in the present study.

Data Collection

The annual health examination included medical history, a physical examination, anthropometric measurements, and measurements of FPG, fasting insulin, HbA$_{1c}$ and serum lipid levels. Height was measured without shoes to the nearest 0.1 cm using a stadiometer. Weight was measured with participants wearing only light clothing and no shoes to the nearest 0.1 kg using a standard scale. Body mass index (BMI) was calculated as weight / height^2 (kg/m^2). Blood pressure was measured twice using an automatic manometer (BP 103i; Nippon Colin, Komaki, Japan) after a 5-min rest in a seated position. All measurements were carried out by trained staff.

Plasma glucose levels were measured enzymatically using a glucose ultraviolet test (Abbott Laboratories, Chicago, IL, USA), and plasma insulin levels were determined by radioimmunoassay (Shionogi, Tokyo, Japan). HbA$_{1c}$ was measured by high-velocity liquid chromatography using a fully automated hemoglobin A1c analyzer (Kyoto Daiichi Kagaku, Kyoto, Japan). Quality control of the HbA$_{1c}$ measurements was carried out using the standard certified by the Japan Diabetes Society (JDS), and HbA$_{1c}$ values were converted to National Glycohemoglobin Standardization Program (NGSP) values using the formula provided by the JDS: HbA$_{1c}$ (NGSP) (%) = 1.02 × HbA$_{1c}$ (JDS) (%) + 0.25[21]. All present analyses used the HbA$_{1c}$ values by the NGSP methods. Total cholesterol and triglycerides were measured using an enzymatic assay. High-density lipoprotein (HDL) cholesterol was measured using direct methods. Insulin resistance was calculated by the homeostasis model assessment (HOMA) method using the following formula: HOMA of insulin resistance (HOMA-IR) = fasting insulin (μU/mL) × FPG (mg/dL) / 405[22]. HOMA of pancreatic β-cell function (HOMA-B)[22] was calculated using the formula: HOMA-B = 20 × fasting insulin (μU/mL) / (FPG [mg/dL] / 18 – 3.5).

A questionnaire was used to collect information about smoking, alcohol consumption, habitual exercise, family history of diabetes, medical history of hypertension, dyslipidemia, diabetes and the use of antidiabetic medication. The presence of high FPG was defined by the JDS criteria[23], and the presence of hypertension and dyslipidemia were defined by the Japanese criteria for the metabolic syndrome[24]. High FPG was defined as FPG levels ≥110 mg/dL; hypertension was defined as systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or use of antihypertensive medications; and dyslipidemia was defined as serum triglycerides ≥150 mg/dL, HDL cholesterol <40 mg/dL, or use of cholesterol-lowering medications. Hypercholesterolemia was defined as a serum total cholesterol ≥220 mg/dL or use of cholesterol-lowering medications. Participants were asked to report in the questionnaire whether any of their first-degree relatives (father, mother and/ or siblings) had ever had diabetes. Total energy intake (kcal/ day) was assessed using a self-administered diet history questionnaire (DHQ)[25]. The DHQ was developed for epidemiological studies in Japan to estimate the dietary intakes of macronutrients and micronutrients. Estimates of dietary intakes of 147 food and beverage items, energy, and nutrients were calculated using an ad hoc computer algorithm developed for the DHQ and based on the Standard Tables of Food Composition in Japan[26]. A detailed description of the methods used to calculate dietary intakes and the validity of the DHQ have been reported previously[25,27,28].

Participants were categorized as non-manual workers or manual workers according to their occupation. Non-manual workers consisted of managers, engineers and clerks, whereas the remaining individuals (laborers, and other workers including guards, gardeners, employees at the shop of the branch factory, and individuals engaged in managing dormitories and catering) were considered manual workers.

Diagnosis of Diabetes

FPG and HbA$_{1c}$ were measured during the annual medical examinations. According to the definition of the American Diabetes Association[29] and the JDS[23], the diagnosis of diabetes was confirmed by at least one of the following observations: (i) a FPG concentration ≥126 mg/dL; (ii) a HbA$_{1c}$ value ≥ 6.5%; and (iii) treatment with insulin or an oral hypoglycemic agent.

Statistical Analysis

Mean baseline values were compared between the participants with and without a family history of diabetes using Student's *t*-tests. Because fasting insulin, HOMA-IR and HOMA-B were log-normally distributed, log-transformed values were used for analyses. We calculated crude incidence rates and hazard ratios (HRs) for diabetes according to the family history of diabetes. The Cox proportional hazards model was used to calculate

adjusted HRs. Adjustment for possible confounders was carried out sequentially as follows: (i) for age and sex (model 1); (ii) for age, sex and BMI (model 2); (iii) for family history of diabetes (no, yes), smoking status (never smoker, ex-smoker or current smoker), alcohol consumption determined by the DHQ (non-drinker, occasional drinker, consumption <20 g/day, consumption ≥20 g/day), habitual exercise (no, yes), occupational class (non-manual worker, manual worker), and presence of hypertension (no, yes), dyslipidemia (no, yes), and hypercholesterolemia (no, yes; model 3); (iv) for total energy intake (kcal/day; model 4); and (v) for HOMA-IR (model 5). Using the HR from model 5, the diabetes incidence fraction attributable to family history in this population was estimated. HRs for diabetes according to family history were calculated separately for males and females, different BMI categories (<22, 22–25 and ≥25 kg/m^2), different HOMA-IR and HOMA-B categories (ter-

tiles), and other lifestyle factors. Interactions between family history and variables associated with obesity and lifestyle factors were also evaluated. Statistical analyses were carried out using the Japanese version of the Statistical Package for the Social Sciences (SPSS version 17.0; SPSS Japan Inc., Tokyo, Japan). A P-value of <0.05 was deemed to show statistical significance.

The present study was approved by the Institutional Review Committee for Ethical Issues of Kanazawa Medical University.

RESULTS

The mean age at baseline was 46.2 years and mean BMI was 23.0 kg/m^2. Of the 3,517 participants, 630 (18%) had a family history of diabetes mellitus. The participants' baseline characteristics according to family history of diabetes are shown in Table 1. The degree of obesity, variables for glucose metabolism and insulin resistance, pancreatic β-cell function, and lifestyle

Table 1 | Baseline characteristics of the 3,517 participants according to family history of diabetes

	No family history	Family history	P-value†
n	2,887	630	
Women (%)	41.7	43.9	0.303
Age (years)	46.3 ± 6.1	45.8 ± 6.0	0.051
Body mass index (kg/m^2)	23.0 ± 3.1	22.9 ± 3.1	0.634
Fasting plasma glucose (mg/dL)	91.1 ± 9.2	91.7 ± 9.4	0.121
Hemoglobin A1c (%)	5.3 ± 0.3	5.4 ± 0.4	0.078
Fasting insulin (μU/mL)	4.9 (3.0–7.0)	4.9 (3.3–7.0)	0.915
HOMA-IR	1.05 (0.70–1.60)	1.06 (0.70–1.60)	0.688
HOMA-B	66.6 (46.5–94.7)	65.0 (45.0–94.7)	0.344
Total cholesterol (mg/dL)	207.9 ± 33.4	207.1 ± 33.3	0.592
Triglycerides (mg/dL)	85.9 (56.0–126.0)	88.5 (58.0–128.0)	0.248
HDL-cholesterol (mg/dL)	62.4 ± 15.1	62.4 ± 16.5	0.993
Systolic blood pressure (mm Hg)	117.7 ± 18.8	116.3 ± 17.0	0.087
Diastolic blood pressure (mm Hg)	74.8 ± 13.4	73.9 ± 12.2	0.135
Total energy intake (kcal/day)	2,048 ± 600	2,036 ± 613	0.632
Smoking status (%)			0.084
Never smoker	56.8	52.0	
Ex-smoker	8.6	9.5	
Current smoker	34.6	38.5	
Alcohol consumption			0.340
Never	31.9	35.1	
Occasional	14.9	15.3	
Consumption <20 g/day	26.9	26.1	
Consumption ≥20 g/day	26.3	23.5	
Habitual exercise – yes (%)	24.0	27.0	0.113
Presence of metabolic abnormalities (%)			
High fasting plasma glucose	3.9	4.6	0.451
Hypertension	29.3	26.2	0.118
Dyslipidemia	24.4	25.3	0.666
Hypercholesterolemia	37.6	34.0	0.089
Occupational class (%)			0.038
Non-manual workers	25.4	29.4	
Manual workers	74.6	70.6	

Data are presented as n, mean ± standard deviation, geometric mean (interquartile range) or %.
†P-value for Student's t-test for continuous variables and χ^2-test for categorical variables.

factors, such as smoking status, alcohol consumption and total energy intake did not differ significantly according to family history of diabetes.

During the 7-year follow up (20,096 person-years, mean follow-up time 5.7 ± 1.7 years), we documented 228 cases of diabetes; 94 were diagnosed based on high FPG levels, 111 were based on high HbA_{1c} levels, and 23 were based on both high FPG and high HbA_{1c} levels.

Table 2 presents the risk of type 2 diabetes in different categories of a family history of diabetes. After adjustment for age and sex (model 1), the HR for type 2 diabetes in participants with any family history of diabetes was 1.82 (95% confidence interval 1.36–2.43) compared with participants without a family history of diabetes. The HR did not change after further adjustment for BMI (model 2), other lifestyle factors (model 3, 4) and HOMA-IR (model 5). The overall fraction of diabetes incidence attributable to family history in this population was 13.1%.

We found no differences in age, BMI and other lifestyle factors among family-history categories (data not shown); however, the HR for participants with a maternal history of diabetes was the highest among those with a family history of diabetes in first-degree relatives (Table 2).

We found no interactions between family history of diabetes and sex, degree of obesity, degree of insulin resistance and pancreatic β-cell function, lifestyle factors, presence of other chronic diseases, total energy intake, and occupational class in the context of incidence of type 2 diabetes (Table 3).

DISCUSSION

The present cohort study of middle-aged Japanese workers investigated the association between a family history of diabetes

and the incident risk of type 2 diabetes. The results show that participants with a family history of diabetes had an 80% greater risk of incident diabetes compared with those without a family history of diabetes. These associations were independent of other risk factors, such as obesity, insulin resistance, dietary and lifestyle factors, and the presence of other chronic diseases. Additionally, 13% of the incident diabetes in this population was explained by a family history of diabetes. Among individuals with a family of history of diabetes, the risk of diabetes was highest among those with a maternal history of diabetes.

Similar to previous studies in Western countries[9,13,15,16,30–34], a family history of diabetes was significantly associated with the risk of diabetes in Japanese individuals. Family history of diabetes includes environmental factors in addition to genetic factors[9]. Obesity[10–14] and lifestyle factors, such as alcohol consumption[14–16] and diet[15], have been reported to be associated with a family history of diabetes, and these non-genetic factors explain a substantial part of the association between family history and the risk for type 2 diabetes[14,15,17]. However, these reports were from Western countries, and it is not clear to what extent obesity and lifestyle can explain the association between family history and the risk of diabetes in relatively lean Asian people with different lifestyles.

Family history of diabetes was not associated with BMI and insulin resistance in the present study participants, and the association between family history and the risk for diabetes did not change after adjustment for BMI and HOMA-IR. These results differ from those reported in previous studies in Western countries[14,15,17]. A previous study from Asia showed that a positive family history was associated with higher obesity levels and HOMA-IR[35]. However, the study was cross-sectional and

Table 2 | Incidence rate and adjusted hazard ratio for type 2 diabetes during the 7-year follow up according to family history of diabetes in 3,517 Japanese men and women

	No family history	Family history	Father only	Mother only	Sibling only	≥2 family members
n	2,887	630	299	181	75	75
Cases	166	62	20	25	8	9
Person-years of follow up	16,465	3,631	1,765	1,027	402	437
Incidence rate (/1,000 person-years)	10.1	17.1	11.3	24.3	19.9	20.6
Hazard ratio (95% CI)						
Model 1	1 (reference)	1.82 (1.36–2.43)	1.26 (0.79–2.01)	2.60 (1.71–3.97)	1.76 (0.86–3.58)	1.98 (1.01–3.87)
Model 2	1 (reference)	1.81 (1.36–2.43)	1.21 (0.76–1.93)	2.75 (1.80–4.19)	1.91 (0.94–3.90)	1.85 (0.95–3.62)
Model 3	1 (reference)	1.78 (1.32–2.37)	1.21 (0.76–1.93)	2.56 (1.67–3.92)	2.06 (1.01–4.20)	1.95 (0.99–3.82)
Model 4	1 (reference)	1.78 (1.33–2.38)	1.21 (0.76–1.93)	2.56 (1.67–3.92)	2.05 (1.00–4.18)	1.95 (0.99–3.81)
Model 5	1 (reference)	1.84 (1.36–2.47)	1.29 (0.80–2.08)	2.56 (1.67–3.92)	1.95 (0.95–4.00)	1.98 (1.01–3.91)

CI, confidence interval;
Model 1, adjusted for age and sex;
Model 2, adjusted for age, sex and body mass index;
Model 3, adjusted for Model 2 variables plus smoking, alcohol consumption, habitual exercise, occupational class, and presence of hypertension, dyslipidemia and hypercholesterolemia;
Model 4, adjusted for Model 3 variables plus total energy intake;
Model 5, adjusted for Model 4 variables plus homeostasis model assessment for insulin resistance.

Table 3 | Interactions between obesity, insulin resistance, lifestyle factors and family history of diabetes in the context of the incidence of diabetes in 3,517 Japanese men and women

	Family history	n	Incidence rate (/1,000 person-years)	Adjusted-HR (95% CI)†	P-value for interaction
Sex					0.344
Men	No family history	1,682	13.5	1.00 (reference)	
	Family history	355	23.1	1.62 (1.14–2.28)	
Women	No family history	1,202	5.6	1.00 (reference)	
	Family history	278	10.7	2.39 (1.36–4.22)	
Body mass index (kg/m²)					0.687
<22	No family history	1,165	4.5	1.00 (reference)	
	Family history	262	6.4	1.75 (0.84–3.62)	
22.0–24.9	No family history	1,032	10.2	1.00 (reference)	
	Family history	223	19.8	1.83 (1.13–2.97)	
≥25	No family history	687	19.9	1.00 (reference)	
	Family history	148	34.1	1.81 (1.16–2.81)	
Fasting plasma glucose (mg/dL)					0.212
<110	No family history	2,773	6.8	1.00 (reference)	
	Family history	601	12.2	1.87 (1.31–2.67)	
110–125	No family history	114	123.6	1.00 (reference)	
	Family history	29	180.3	1.54 (0.88–2.70)	
HOMA-IR (tertiles)					0.478
<0.9	No family history	990	5.2	1.00 (reference)	
	Family history	214	11.2	2.26 (1.17–4.36)	
0.9–1.4	No family history	950	8.2	1.00 (reference)	
	Family history	203	15.0	1.96 (1.12–3.43)	
≥1.5	No family history	808	19.2	1.00 (reference)	
	Family history	179	30.3	1.56 (1.03–2.38)	
HOMA-B (tertiles)					0.495
< 53.0	No family history	906	15.4	1.00 (reference)	
	Family history	203	24.2	1.54 (0.98–2.42)	
53.0–83.5	No family history	939	8.8	1.00 (reference)	
	Family history	197	17.9	2.09 (1.24–3.50)	
≥83.6	No family history	906	6.8	1.00 (reference)	
	Family history	196	12.1	1.99 (1.06–3.76)	
Smoking status					0.584
Never/former smoker	No family history	1,884	7.6	1.00 (reference)	
	Family history	389	13.5	2.00 (1.32–3.05)	
Current smoker	No family history	997	14.8	1.00 (reference)	
	Family history	244	23.8	1.59 (1.06–2.40)	
Alcohol drinking					0.060
Never/occasional drinker	No family history	1,349	7.5	1.00 (reference)	
	Family history	319	16.0	2.74 (1.75–4.29)	
Regular drinker	No family history	1,535	12.4	1.00 (reference)	
	Family history	314	18.7	1.44 (0.97–2.15)	
Habitual exercise					0.288
No	No family history	2,192	10.0	1.00 (reference)	
	Family history	462	15.6	1.55 (1.09–2.20)	
Yes	No family history	692	10.3	1.00 (reference)	
	Family history	171	22.1	2.47 (1.43–4.27)	
Presence of metabolic abnormalities‡					0.835
No	No family history	1,196	4.1	1.00 (reference)	
	Family history	285	8.1	1.99 (1.05–3.78)	
Yes	No family history	1,691	14.7	1.00 (reference)	
	Family history	345	25.2	1.73 (1.24–2.41)	

Table 3 | (*Continued*)

	Family history	n	Incidence rate (/1,000 person-years)	Adjusted-HR (95% CI)†	P-value for interaction
Total energy intake (kcal/day, tertiles)					0.526
<1,744	No family history	963	9.3	1.00 (reference)	
	Family history	216	9.4	1.48 (0.78–2.81)	
1,745–2,194	No family history	952	8.8	1.00 (reference)	
	Family history	217	21.0	2.19 (1.34–3.59)	
≥2,195	No family history	969	12.0	1.00 (reference)	
	Family history	200	22.1	1.75 (1.10–2.80)	
Occupational class					0.485
Non-manual worker	No family history	732	5.4	1.00 (reference)	
	Family history	185	11.0	2.21 (1.05–4.67)	
Manual worker	No family history	2,155	11.5	1.00 (reference)	
	Family history	445	19.4	1.69 (1.23–2.33)	

†Adjusted for age, sex, body mass index, smoking, alcohol consumption, habitual exercise, and presence of hypertension, dyslipidemia and hypercholesterolemia.
‡Metabolic abnormalities included hypertension, dyslipidemia and hypercholesterolemia.
HOMA-B, homeostasis model assessment for pancreatic β-cell function; HOMA-IR, homeostasis model assessment for insulin resistance.

could not evaluate how these factors affect each other and the association between family history and risk for diabetes. Our prospective observations suggest that the association is not confounded by the presence of obesity and insulin resistance. Among relatively lean Asian people, not only obesity and insulin resistance, but also impaired insulin secretion is thought to be an important risk factor for diabetes[5–8]. Associations between family history of diabetes and obesity/insulin resistance, and the interaction between these factors and incidence of diabetes might differ from those identified in Western people. Similarly, family history was not associated with HOMA-B. HOMA-IR and HOMA-B are calculated using fasting plasma insulin and glucose levels. A family history of diabetes was reported to be associated with insulin response after glucose load[36–39], and postprandial glucose metabolism, rather than fasting glucose/insulin regulation, might be strongly associated with the family history-related incidence of diabetes in Asian people.

Two previous studies of Asian populations suggested that insufficient physical activity and family history of diabetes might jointly increase the risk of diabetes[40,41]. However, these studies did not evaluate the interaction between physical activity and family history. The present study found no significant interaction between habitual exercise and family history of diabetes, and family history was associated with an increased risk of diabetes independent of habitual exercise.

Among individuals with a family history of diabetes in different first-degree relatives, those with a maternal history of diabetes had the highest risk of diabetes in the present study. A greater risk from maternal diabetes compared with paternal diabetes has been reported in some previous studies[13,16,30,32], but not in all studies[9,15,33,42]. The explanations for this greater importance of maternal diabetes have included the following:

genomic imprinting (i.e. the differential expression of inherited susceptibility genes in the paternal or maternal generation[43]); mutations in mitochondrial DNA, which are maternally inherited[44]; and metabolic programming during intrauterine exposure[45]. Furthermore, mothers might have a greater influence on their children's eating habits and other lifestyle behaviors, because they might spend more time with their children during childhood and in later life as compared with fathers. However, excess maternal transmission of type 2 diabetes was not observed in a hospital-based cross-sectional study from Korea[42]. Our prospective study suggests that Asian individuals with a maternal history of diabetes have a greater risk of type 2 diabetes. Because these associations were similar after adjustment for lifestyle factors, genetic background appears to have strongly affected the maternal transmission of diabetes.

The strengths of the present study were its prospective cohort design and large sample size as compared with other Asian studies. Furthermore, several previous cohort studies used information about incident diabetes collected from self-administered questionnaires, whereas our conclusions are based on more reliable data obtained from annual examinations and determination of fasting blood glucose and HbA_{1c}. The present study had several limitations. First, the family history of diabetes was self-reported and was evaluated only once, at the baseline examination. This might have caused misclassification errors. A family history of diabetes was observed in 18% of the present study participants; this percentage was similar to those in previous studies of Asian people (10–20%)[40–42], and any misclassification does not therefore appear to have been excessive. Second, the sample included only people who were employed. Poor health can prevent some individuals from working. Thus, the prevalence of obesity or the incidence of diabetes might be lower in our sample than in the general Japanese population.

However, in previous population-based cohort studies in Japan, the number of incident cases of diabetes was reported to be 67 in a group of 926 men followed for 9 years[46], and 65 in a group of 827 men and women followed for 9–10 years[47], these rates seem to be similar to that in our workplace cohort. Third, we did not measure waist circumference at baseline, which might have provided more information about abdominal fat accumulation and insulin resistance than was provided by BMI measurements. Fourth, oral glucose tolerance tests were not carried out, and we cannot evaluate the interaction between family history and glucose/insulin levels after glucose load in the context of diabetes incidence. A further limitation is that we did not determine whether the diabetes that developed was type 1 or type 2. However, the study participants were middle-aged men and, as the condition was detected in an annual medical check-up and was relatively mild, it is most likely that the cases were type 2 diabetes.

In conclusion, a family history of diabetes was significantly associated with the incident risk of diabetes in Japanese men and women, and this association was independent of interactions with obesity and lifestyle factors. Although family history of diabetes is an unmodifiable risk factor, detection and early intervention in these high-risk people would also be useful for the primary prevention of type 2 diabetes in the relatively lean Asian population.

ACKNOWLEDGMENTS

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ORIGINAL ARTICLE

Correlation between Shift-work-related Sleep Problems and Heavy Drinking in Japanese Male Factory Workers

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Abstract — Aims: To investigate the effects of shift work on increased alcohol intake associated with poor sleep quality. **Methods**: This cross-sectional survey evaluated the correlation between work schedule, poor sleep quality and heavy drinking among 909 factory workers aged 35–54 years in Japan. Subjects included 530 day workers, 72 shift workers who did not work at night and 290 shift workers who engaged in night work. Heavy drinking was defined as a mean volume of alcohol consumption exceeding 60 g/day. **Results**: Compared with other workers, night-shift workers who suffered poor sleep quality exhibited the highest frequency of heavy drinking (17.6%). Multiple logistic regression analysis demonstrated that compared with day workers with good sleep, night-shift workers who experienced poor sleep had more than twice the odds of heavy alcohol consumption (odds ratio 2.17 [95% confidence interval (CI), 1.20–3.93]). Shift workers who did not work at night and day workers with poor sleep were not at increased odds of heavy drinking. **Conclusion**: Shift workers who engage in night work may try to modify their health behavior to cope with sleep problems. Such modification may be a risk factor for heavy drinking.

INTRODUCTION

Moderate alcohol consumption may help in preventing coronary disease in older individuals (Rimm *et al.*, 1999; Murray *et al.*, 2002). Conversely, excessive intake of alcohol has been linked to major morbidity, including neuropsychiatric disorders, gastrointestinal illness, cancer and cardiovascular disease, as well as both intentional and unintentional injury (Rehm *et al.*, 2010). According to the World Health Organization, alcohol consumption is the world's leading risk factor for mortality among working males ages 15–59 years (WHO, 2011). Therefore, identifying risk factors for heavy drinking in the work force is essential for preventing alcohol-related health problems. Numerous studies have assessed the association between occupational factors and alcohol consumption or excessive drinking. (Siegrist and Rodel, 2006) Job stress arising from perceived imbalances between work effort and rewards, protracted working hours and job insecurity is a well-known risk factor for heavy drinking (Head *et al.*, 2004; Siegrist and Rodel, 2006; Hiro *et al.*, 2007; Biron *et al.*, 2011; Marchand *et al.*, 2011). However, other studies examining the relationship between work schedule and alcohol consumption have generally produced equivocal findings (Ragland *et al.*, 1995; Lasfargues *et al.*, 1996; Bøggild and Knutsson, 1999; Hermansson *et al.*, 2003; Hiro *et al.*, 2007; Bushnell *et al.*, 2010).

It is well established that most shift workers experience at least occasional or long-lasting sleep problems (Åkerstedt, 2003; Åkerstedt and Wright, 2009). Particularly, shift work extending into the night can exert pronounced negative effects on sleep hours and sleepiness (Pilcher *et al.*, 2000), reduce performance (Torsvall and Åkerstedt, 1987) and increase the risk of accidents (Smith *et al.*, 1994; Åkerstedt *et al.*, 2002). Thus, learning how to effectively cope with sleep problems is an important goal for many night shift workers.

Alcohol is commonly used as a sleep aid, since ingestion of alcohol can initially be associated with improved sleep onset. An international collaborative study conducted by 10 countries found that 19.4% of subjects who thought they did not sleep well drank alcohol (Soldatos *et al.*, 2005). However, many individuals can become tolerant to the sedative effects of alcohol, which in turn, may lead to increased consumption and more detrimental abuse (Roehrs and Roth, 2001). Accordingly, we hypothesized that shift workers who suffer from sleep problems and depend on alcohol as a sleep aid may be at risk of heavy drinking. To investigate this hypothesis, we conducted a cross-sectional survey examining the effects of shift work and related sleep problems on alcohol intake among male factory workers in Japan.

MATERIALS AND METHODS

Subjects

The study population consisted of male manual workers employed at a factory that produces light metal products. In 2009, a self-administered survey on sleep and alcohol intake was carried out in 4736 employees, of whom, 3715 (78.4%) provided valid responses. The analysis included data from a subset of 909 employees, aged 35–54 years, who engaged in manual work, such as the operation of machinery or the processing or construction of aluminum products. This study was approved by the Ethics Committee for Epidemiologic Research at the Kanazawa Medical University (Ishikawa, Japan).

The employees worked one of three shift schedules: (1) a non-continuous two-shift schedule; (2) a non-continuous three-shift schedule and (3) a continuous three-shift schedule. The three-shift workers rotated in a counterclockwise manner: 75% had a non-continuous shift schedule (five day shifts, five night shifts and five evening shifts with weekend

holidays) and 25% had a continuous-shift schedule (three or four day shifts, three or four night shifts and three or four evening shifts, with one rest day between successive shifts). Workers adhering to three-shift schedules changed shifts at 08h00, 16h30 and 00h15, or 06h30, 13h00 and 21h30. The two-shift workers followed a non-continuous shift schedule (five day shifts and five evening shifts or five night shifts).

Data collection

Heavy drinking was defined as the mean volume of alcohol consumption exceeding 60 g/day in accordance with the Japan Ministry of Health, Labor and Welfare guideline, '21st Century Measures for National Health Promotion'. (Ministry of Health, Labour and Welfare, 2001). Alcohol intake during the preceding month was assessed using a self-administered diet history questionnaire (DHQ) (Sasaki *et al.*, 1998). The DHQ was developed to estimate the dietary intakes of macronutrients and micronutrients in epidemiological studies in Japan. A detailed description of the methods used for calculating dietary intake and the validity of the DHQ have been previously published (Sasaki *et al.*, 1998). The DHQ includes questions about the nature of alcohol intake, including weekly or monthly frequency and the amount of alcohol consumed on each occasion by the type of alcoholic beverage. The mean volume of alcohol consumption per day was calculated over a one-month period using an *ad hoc* computer algorithm developed for the DHQ, which is based on the Standard Tables of Food Composition in Japan.

The subjects were queried about the presence of sleep problems during the past month. On the basis of the nature of their responses, the subjects were judged to have poor sleep quality if they reported any one or more of the following: fairly bad or very bad sleep quality, short sleep duration (6 h or less), sleep disturbances (waking up in the middle of the night or early morning at least once a week) and the use of sleep medication at least once a week. Further, the subjects were also asked about the use of alcohol as an intentional means of achieving good sleep. Data on work characteristics (skilled manual versus non-skilled manual), smoking habits and the use of medication for hypertension, diabetes and dyslipidemia were also collected.

Statistics

The subjects were classified into three groups according to their work schedule: (1) day workers ($n = 530$); (2) two-shift workers without night shift ($n = 72$) and (3) two-shift or three-shift workers including night shift ($n = 307$, including 42 two-shift workers and 265 three-shift workers). After adjusting for age and other confounding factors, a multiple logistic regression model was employed to evaluate the correlation between work schedule, the presence of poor sleep quality and heavy drinking. Potential confounding factors tested included age group (35–39 years/40–44 years/45–49 years/50–54 years), smoking (non-smoker/ex-smoker/current-smoker) and the use of medication for hypertension, diabetes and dyslipidaemia.

The frequencies of categorical variables were compared using the χ^2-test. Continuous variables were compared using the one-way analysis of variance (ANOVA) or the Kruskal–Wallis test.

Statistical analyses were performed using IBM SPSS 19.0 (SPSS, Inc., Chicago, IL, USA). All the probability values were two-tailed and $P < 0.005$ was defined to be statistically significant.

RESULTS

Table 1 presents the age, lifestyle habits and the frequency of sleep problems reported for all subjects as well as for the subjects stratified by shift. Workers who engaged in night shift work were generally younger than workers comprising the other two groups. Skilled manual workers were more prevalent among the daytime workers than the other groups. The frequency of short sleep duration (<6 h) varied among the three groups; a post hoc test showed that shift workers who worked at night were affected significantly more often than daytime workers (22.1 versus 13.8%, respectively; $P = 0.002$). However, the frequency of sleep disturbance and poor sleep quality did not differ significantly between shift workers and day workers.

Table 1. Characteristics of subjects by work schedule

Variables	All ($n = 909$)		Day workers (a) ($n = 530$)		Shift workers without night shift (b) ($n = 72$)		Shift workers with night shift (c) ($n = 307$)		P^*	a/b	a/c	b/c
Age (years), mean (SD)	45	(6.0)	45.4	(5.9)	46.2	(6.1)	44.2	(5.9)	0.003	0.563	0.014	0.032
Skilled worker, n (%)	134	(14.7)	115	(21.7)	6	(8.3)	13	(4.2)	<0.001	0.007	<0.001	0.224
Sleep problems, n (%)												
Short sleep duration, <6 h	157	(17.3)	73	(13.8)	16	(22.2)	68	(22.1)	0.005	0.078	0.002	1.000
Sleep disturbance ≥1/week	215	(23.7)	119	(22.5)	17	(23.6)	79	(25.7)	0.56	—	—	—
Poor sleep quality, fairly bad or very bad	314	(4.5)	168	(31.7)	29	(40.3)	119	(38.8)	0.052	—	—	—
Use of sleeping medication, ≥1/week	24	(2.6)	21	(4.0)	1	(1.4)	2	(0.7)	0.012	0.5	0.004	0.469
Alcohol intake												
Alcohol use for good sleep ≥1/week, n (%)	220	(24.2)	116	(21.9)	14	(12.8)	90	(29.3)	0.033	0.76	0.02	0.107
Alcohol intake (g/day), median [25 and 75 percentile]	13.0	[0.6, 31.7]	12.8	[0.6, 30.6]	13.2	[0.5, 37.5]	12.6	[0.8, 31.4]	0.765	—	—	—
Alcohol intake, >60 g/day, n (%)	94	(10.3)	49	(9.2)	5	(6.9)	40	(13.0)	0.137	—	—	—
Smoker												
Ex-smoker, n (%)	183	(20.1)	118	(22.3)	13	(18.1)	52	(16.9)	0.137	—	—	—
Current smoker, n (%)	426	(46.9)	230	(43.4)	38	(52.8)	158	(51.5)				

*P-value tested by one-way ANOVA, χ^2-test or Kruskal–Wallis test.
Sleep problems: self-evaluation during the past one month.