Airway obstruction and the risk of myocardial infarction and death from coronary heart disease

A national health examination survey with a 33-year follow-up period

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Abstract

Chronic obstructive pulmonary disease (COPD) has been associated with coronary mortality. Yet, data about the association between COPD and acute myocardial infarction (MI) remain scarce. We aimed to study airway obstruction for its prediction of MI and coronary mortality among 5576 Finnish adults who participated in a national health examination survey between 1978 and 1980. Subjects underwent spirometry, had all necessary data, showed no indications of cardiovascular disease at baseline, and were followed up through record linkage with national registers through 2011. The primary outcome consisted of a major coronary event—that is, hospitalization for MI or coronary death, whichever occurred first. We specified obstruction using the lower limit of normal (LLN) categorization. Through multivariate analysis adjusted for potential confounding factors for coronary heart disease, hazard ratios (HRs) (with the 95% confidence intervals (CIs), in parentheses) of a major coronary event, MI, and coronary death reached 1.06 (0.79–1.42), 0.84 (0.54–1.31), and 1.40 (1.04–1.88), respectively, in those with obstruction compared to others. However, in women aged 30 to 49 obstruction seemed to predict a major coronary event, where the adjusted HR reached 4.21 (1.73–10.28). In conclusion, obstruction appears to predict a major coronary event in younger women only, whereas obstruction closely associates with the risk of coronary death independent of sex and age.

Introduction

Chronic obstructive pulmonary disease (COPD) and coronary heart disease are worldwide problems causing unnecessary premature deaths. Both diseases progress slowly—COPD causes persistent obstruction in the airways and coronary heart disease blocks the coronary arteries [1, 2]. Globally, coronary heart disease stands as the current leading cause of death, while COPD will presumably rank third by 2030 [1–3].

Smoking, the primary cause of COPD, represents an obvious risk factor for coronary heart disease. Other shared risk factors and co-morbidities consist of an increasing age, lower social class, hypertension, diabetes, and hyperlipidemia [1, 2, 4–8]. Additionally, COPD correlates with cardiovascular diseases [1, 4–6, 9–11] as well as death resulting from cardiovascular diseases [1, 12, 13].

Furthermore, an association exists between COPD and coronary heart disease [4–6, 9, 11, 14, 15] and coronary death [13]. The prevalence of coronary heart disease increases alongside the severity of COPD [15]. However, negative outcomes also accompany the association between COPD and coronary heart disease and acute myocardial infarction (MI). For example, a meta-analysis found that COPD associated with MI in cohort studies, but not in case–control studies [7, 8, 10, 16]. Despite the diagnostic differences between studies, the causal association between COPD and MI in particular appears complex and insufficiently studied.

The fact that COPD and coronary heart disease share multiple risk factors, co-morbidities, and supposedly comparable inflammatory reactions in their pathophysiology [4, 5, 8, 17] complicate the inference regarding causality between these diseases. In the present study, we aimed to analyze whether obstruction predicts MI or coronary death in individuals with no indication of baseline cardiovascular disease in a nationally representative population sample followed for 33 years.

Material and methods

Study population and baseline examinations

The Mini-Finland Health Survey was carried out between 1978 and 1980. During the first stage, 40 nationally representative areas were selected for inclusion. During the second stage, a sample representing the Finnish adult population aged 30 years or older (3637 men and 4363 women) was drawn from the population register. We analyzed the data from 5576 subjects (2559 men and 3017 women) who had all pertinent health information collected through interviews, questionnaires, and clinical examinations, and for whom a comprehensive health examination was performed (including spirometry). We excluded from the analysis those with any heart disease, intermittent claudication, or cerebrovascular disease at the baseline examination (Figure 1) [12, 18–20].

Measurements and definition of determinants

Specially trained laboratory technicians followed standard guidelines and instructions when they performed spirometry using a Vitalograph spirometer (Vitalograph Ltd., Buckingham, England). Technicians presented the test procedure individually to each subject. The intention was that for each participant at least two spirometry curves that were as consistent as possible would be recorded. Subjects were instructed to inhale and fill their lungs with air, and, then, to exhale as forcefully and completely as possible to reach an adequate and high-quality forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC). The FEV_1/FVC was determined using the highest readings for FEV_1 and FVC from the technically acceptable efforts recorded for the body temperature and pressure, saturated with water vapor (BTPS) values [12, 19, 21].

Individual results were calculated on the basis of the Global Lung Function Initiative (GLI) reference values. The GLI reference values were determined from a multi-ethnic spirometry records of 97759 healthy non-smokers aged 3 to 95 years based on the corresponding age, sex, and height of the subject. The GLI reference values were determined separately for four ethnic groups, and we used those for Caucasians. Thus, those with FEV_1/FVC values below the lower limit of normal (LLN) were categorized as having obstruction while others had no obstruction. FVC values below LLN were categorized as restriction and over LLN as no restriction. Correspondingly, FEV_1 was categorized as below and over LLN [21, 22].

A standardized methodology was used when measuring height, weight, and blood pressure and when performing electrocardiograms and chest x-rays. Body mass index (BMI) (weight (kg)/height^2 (m^2)) was determined as a measure of relative weight. The basic questionnaire verified the subjects' level of general health, leisure physical activity, and education. General health was categorized as good, moderate, or poor. Leisure physical activity was evaluated using questions about the duration, intensity, and frequency of physical activity and classified as inactive (little physical exercise), occasionally active (exercise in connection with some hobbies or irregular exercise), or regularly active (regular exercise). The level of education was categorized based on the number of years of completed schooling as basic (<8 years), intermediate (8–12 years), and higher (>12 years) [12, 18–20].

Smoking habits were elicited during a standard interview, and subjects were classified as non-smokers, former smokers, or current smokers. Former smokers had quit smoking at least one month prior to the survey. Current smokers included all individuals who reported smoking at least one cigarette, cigar, or pipe daily or almost daily during the last year preceding the survey. These individuals were further classified into two groups according to the number of cigarettes smoked daily: 1 to 19 and ≥20 cigarettes [12, 18–20].

Blood samples were taken to measure the plasma glucose level using the glucose oxidase method (Boehringer Mannheim, GmbH, Mannheim, Germany) [12, 20], and the total serum and high-density lipoprotein (HDL) cholesterol levels using a direct modification of the Liebermann–Burchard method [23]. The level of HDL cholesterol was analyzed from the supernatant of the serum after precipitation of low-density lipoprotein cholesterol and very low–density lipoprotein cholesterol using magnesium/dextran sulphate.

The basic questionnaire elicited the subject´s history of any chronic disease diagnosed by a physician, symptoms of any chronic diseases, and the overall health status and lifestyle. Specially trained physicians performed standardized physical examinations on individuals with any abnormal findings from the questionnaires or examination [12, 19, 20]. In addition, we analyzed subjects´ data collected through the Finnish National Insurance Institution and completed a review of prescribed medications.

During the baseline study, a field physician diagnosed asthma, diabetes, and cardiovascular diseases on the basis of all available information. A subject was categorized as asthmatic if a physician had previously diagnosed asthma, if the subject received medication for asthma, or if a physician monitored the subject due to asthma. Diabetes was determined on the basis of a self-reported history of diagnosed diabetes and being treated by a physician for diabetes, a fasting plasma glucose level ≥6.7 mmol/l, or both [12, 18–20].

Follow-up

We used study subjects´ individual identification numbers and followed them continuously from the baseline examination until any of the following end-points (whichever occurred first): date of hospitalization for MI, death, or through the end of 2011. During the follow-up period, we monitored the causes of death from Statistics Finland [24] and diagnoses of periods of hospital care

from the National Care Register for Health Care [25]. As a nationwide obligatory automated database, this registry contains the hospital discharge diagnosis codes for all medical admissions and is maintained by the Finnish National Institute for Health and Welfare [25].

We monitored the diagnostic codes according to the eighth, ninth, and tenth revisions of the *International Classification of Diseases*, (ICD-8, ICD-9, and ICD-10). The end-point of MI includes hospital care periods registered with ICD codes 410 (according to ICD-8 and ICD-9) and I21 and I22 (ICD-10). A major coronary event includes hospital care periods with ICD codes 410 and 411.0 (ICD-8 and ICD-9) and I20.0, I21, and I22 (ICD-10), undergoing coronary artery bypass graft surgery (CABG) or angioplasty, or the cause of death listed using ICD codes 410–414 and 798 (but not 798.0A) (ICD-8 and ICD-9) and I20–I25, I46, R96, and R98 (ICD-10). Coronary death includes a cause of death registered with ICD codes 410–414 and 798 (but not 798.0A) (ICD-8 and ICD-9) and I20–I25, I46, R96, and R98 (ICD-10).

We studied the long-term persistence of obstruction and smoking status among 905 participants from the baseline survey who were re-examined at the next national health examination survey, the Health 2000 [26]. According to Global Initiative for Obstructive Lung Disease (GOLD) fixed cut-off limit for obstruction ($FEV_1/FVC < 0.7$) there were 12 subjects who were obstructive at the baseline. After 21 to 23 years, 9 of them had persisted obstructive while 3 had not. At the Health 2000 Survey, current smokers were 0.8% of those who at baseline had reported as having never smoked, 9.7% of ex-smokers, 50.9% of those who had smoked <20 cigarettes per day and 67.1% of those who had smoked more.

Statistical analysis

We excluded from the analyses those subjects with any heart disease, intermittent claudication, or cerebrovascular disease at the baseline examination. We analyzed cross-sectional associations

between baseline characteristics and a major coronary event using logistic regression and expressed the results as adjusted odds ratios (ORs) with 95% confidence intervals (95% CIs). We used the Cox proportional hazards regression model and estimated the adjusted hazard ratios (HRs) with 95% CIs to estimate the strength of the association between obstruction and MI, a major coronary event, and coronary death during the follow-up period. We also analyzed the effect modification of various determinants by entering their first-degree interaction terms one-by-one into the Cox models. The statistical significance of the interactions was tested using Wald tests and expressed as exact *p* values. We performed all analyses for Mini Finland Survey data using IBM´s SPSS (version 24).

Ethical considerations

The Mini-Finland Health Survey predated the current legislation on ethics in medical research. However, all participants were fully informed about the study, they participated in the study voluntarily, and the use of their information for medical research was explained to them. Agreeing to participate in the baseline health examination was taken to indicate informed consent. The National Institute of Health and Welfare approved the linkage of the National Care Register for Health Care, and Statistics Finland approved the linkage of national mortality data to the survey data used here.

Results

By the end of 2011, 1107 (20%) subjects from our study population suffered a major coronary event (Table 1). Being older and male, currently smoking, having diabetes, a weak general health status, a higher BMI, total cholesterol, systolic and diastolic blood pressures, and a lower educational level and HDL cholesterol all associated with a major coronary event. There was no substantial overlap

between asthma and obstruction: 191 subjects had only obstruction, 67 only asthma, and 19 both asthma and obstruction.

During the follow-up period, 7.7 major coronary events occurred per 1000 person years, and 2517 (45%) subjects from the study population died. Obstruction significantly associated with coronary death but not with MI or a major coronary event in the model adjusted for multiple characteristics (see Table 2). For instance, we found HRs (95% CIs) of 1.40 (1.04–1.88), 0.84 (0.54–1.31), and 1.06 (0.79–1.42), respectively, compared with those without obstruction (HR 1.00). FEV_1/FVC as a continuous variable did not predict major coronary event in the multivariable model, HR (95% CI) was 1.00 (0.93-1.07). Current smoking associated significantly with MI, a major coronary event, and coronary death. Among 126 subjects presenting with BMI ≥ 35, three ~~had an obstruction~~were obstructive, two of whom experienced a major coronary event (HR = 10.63; 95% CI 1.36–83.16). There were 190 subjects with FVC below LLN of whom 49 developed a major coronary event, and comparably 272 subjects with FEV_1 below LLN with 71 major coronary events. FVC or FEV_1 below LLN did not predict major coronary event; in the multivariable model HRs (95% CIs) were 1.11 (0.83–1.48) and 1.08 (0.85–1.38), respectively, when compared to those with FVC or FEV_1 over LLN.

No first-degree interaction between obstruction and age or sex emerged. Yet, we found a significant association between obstruction and a major coronary event in women aged 30 to 49. In a multivariate model, HR for six obstructive cases reached 4.21 (95% CI 1.73–10.28) when compared with women aged 30 to 49 without obstruction (HR 1.00; Table 3). Comparable HRs in women aged 30 to 49 years in a multivariate model for MI reached 5.52 (95% CI 1.77–17.15; 4 cases with MI among obstructed subjects) and 9.57 for coronary death (95% CI 3.18–28.77; 5 coronary deaths among obstructive subjects), when compared with women aged 30 to 49 without an obstruction (HR 1.00).

Among women, 230 (52%) major coronary events occurred 20 years or more after the baseline examination. After excluding the first 20 years' follow-up experience from the multivariate model, no significant association was observed between obstruction and major coronary event. HR (95% CI) for all the women was 1.87 (0.91–3.87) when those without obstruction were as a reference; 9 of those 230 cases with major coronary events were obstructive. Among women aged 30 to 49 years after the same exclusion, the corresponding HR was 5.05 (1.79–14.24); 5 of the 66 cases with a major coronary event were obstructive.

Discussion

We analyzed the association between obstruction and the risk of a major coronary event among those with no cardiovascular disease at the baseline using a population-based survey representative of Finnish adults followed for 33 years. We found that obstruction associated with coronary mortality, but not with a major coronary event. However, obstruction seemed to predict the occurrence of a major coronary event in women aged 30 to 49, especially events evolving 20 years or more after the baseline examination.

Subjects with COPD have an unfavorable cardiovascular risk profile [1, 8]. Furthermore, the predicted 10-year risk for cardiovascular diseases is >20% based on the Framingham score, although smoking plays an important role in this risk [5]. Mortality among subjects with COPD increases, while lung function decreases [12, 13]. Coronary heart disease increases mortality in subjects with COPD [4]; moreover, COPD associates with coronary mortality [11, 13]. We found a strong association between obstruction and coronary mortality independent of smoking history and other relevant known risk factors.

However, the association between COPD and coronary heart disease is more complicated. According to several studies, coronary heart disease and COPD associate, regardless of smoking status and even when COPD is mild [4, 6, 9, 11, 15]. This holds in a model adjusted using the most important risk factors [6] and among subjects with no cardiovascular disease diagnosed at baseline [9, 11]. However, in a systematic literature review, four of nine studies showed no association between coronary heart disease and COPD [10], such as in a model adjusted using relevant confounding factors [8]. The authors of the review cited the insufficient quality and consistency of data as the most important limitations to analysis [10]. In a Danish study, researchers found an association between COPD and coronary heart disease and a previous MI in an unadjusted model; yet, this resulted primarily from the older age of those with COPD, and no significant association emerged in their multivariate model [7].

To our knowledge, only a few relevantly adjusted studies exist detailing the association between COPD and MI and fatal MIs. Register data studies reveal an association between COPD and acute MI [6, 9, 11, 14, 16, 27]. However, studies excluding from analysis subjects with an indication of baseline cardiovascular disease show both an association [9, 11] and no association [28] with COPD and acute MI. These register studies carry weaknesses involving such data, whereby only a few studies included the collection of some background data, such as smoking history and co-morbidities [6, 27]. Since COPD and MI share multiple risk factors and co-morbidities, studies that insufficiently control for confounding factors can provide only part of the correlation. In a recent meta-analysis, subjects with COPD had an increased risk for MI in cohort analyses, but not in the majority of the smoking-adjusted case–control studies; furthermore, the authors considered the role of smoking in this association [16]. In a study with fewer subjects but which included relevant adjustments, COPD did not emerge as an independent predictor for MI [29]; in Denmark, researchers found an association between COPD and MI, although the association diminished after hospitalization for COPD [14].

In those with COPD, mortality appears to increase after MI [16, 27, 30]. Some researchers have considered the role of co-morbidities, background factors, and smoking in this association [16, 30]; yet, in a case-controlled study, COPD did not predict mortality after MI [29]. Here, we found no significant association between obstruction and hospitalization for MI or a major coronary event in a multivariate model adjusted using the potential confounding factors among those without cardiovascular disease at the baseline examination.

Women with COPD carry an increased risk for MI, other cardiovascular events, and coronary mortality compared to women without COPD [6, 11, 13, 14]. Additionally, the risk for MI, fatal MI, and coronary heart disease increases among the youngest population with COPD (aged 40–64, below 45 or 50) compared to older subjects or those without COPD [6, 11, 13, 14]. We showed in a multivariate model that obstruction seemed to predict a major coronary event in women aged 30 to 49 years, especially events evolving 20 to 33 years after the baseline examination.

We could neither disclose the cause for these particular associations nor why obstruction predicted coronary mortality but not a major coronary event among the entire study population. Presumably, comparable systemic inflammatory reactions, which are suspected to underlie COPD and coronary heart disease, play some role in such reactions [4, 5, 8, 17]. Coronary heart disease in men and women carries different indications; in women coronary heart disease is concentrated among older populations, but fatal MIs occur more frequently among younger women [31, 32]. This sex difference, as well as the co-morbidity in subjects with COPD, may have affected our results [1, 4]. However, our sample size was limited and the results from the subgroup analyses should be extremely cautiously interpreted. Thus, future studies should seek to replicate our study in another sample to determine if this relationship holds or if it was a coincidence.

Unfortunately, no single internationally agreed upon definition exists for obstruction. The definition used by the Global Initiative for Obstructive Lung Disease (GOLD) identifies a clear fixed cut-off

311 (FEV_1/FVC <0.7) for the limit of obstruction [1]; yet, this definition tends to over-diagnose
312 obstruction among the elderly [21]. To avoid over-diagnosing, we used the LLN criterion for
313 international GLI reference values which specifies the FEV_1/FVC limit for obstruction according to
314 age, sex, and height [22]. However, the reference studies we use in our analysis relied on various
315 definitions of obstruction (GOLD, LLN, register data with variable COPD definitions, or other),
316 thus affecting those previous results. Therefore, the results across studies (including our own) may
317 not be directly comparable.

318 We followed a population sample representative of Finnish adults continuously until the end of
319 2011 from a study with participation rates exceeding 90% [12, 18]. Well-trained experienced
320 professionals performed examinations using standardized methods [18–20]. Further strengthening
321 our results, this study relied on data from the National Care Register for Health Care, which is
322 validated for MI patients [33]. Furthermore, the causes and dates of death were obtained from death
323 certificates as documented by attending physicians [20, 24].
324 While our sample was quite large, the small number of obstructed subjects limited our analysis of
325 the effect of different factors, such as the degree of obstruction, sex, and age more specifically.
326 Additionally, no bronchodilation test was performed; therefore, we may have misclassified some
327 reversible obstructions as chronic conditions, although, there was no overlap between categories
328 asthma and obstruction. Unfortunately, no data about lifetime smoked pack years was collected. In
329 addition, we had no data about some possible confounders, such as birth weight, duration of
330 pregnancy, and prematurity, which associate with both cardiovascular diseases and obstruction [34,
331 35]. Other limitations of our study include those generally associated with retrospective health
332 examination surveys. Baseline characteristics, such as smoking habits, weight, and leisure physical
333 activity, may have changed during the last 30 years, thus affecting our results. Such effects include
334 changes in medical treatments for various diseases, in particular for cardio-vascular disease, and the
335 possible minor changes to causes of death and their documentation.

Conclusions

In conclusion, obstruction appears to predict a major coronary event only in younger women. However, obstruction remains independent of known risk factors closely associated with the risk of coronary death among the adult population in general. Therefore, treating physicians should note the increased risk for coronary death among obstructed subjects.

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Declaration of interest

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Table 1

Baseline characteristics and the incidence of a major coronary event[a]

Characteristics		No major coronary event (n)	Major coronary event (n)	OR[b]	95% CI
Age	Years, ±1 SD	Mean = 46.4 ±12.4 SD[c]	Mean = 52.9 ±12.1 SD[c]	1.68	1.57–1.80
Sex	Men	1891	668	1.00	
	Women	2578	439	0.43	0.37–0.49
Smoking	Non-smoker	2556	522	1.00	
	Former smoker	859	245	1.05	0.86–1.27
	Current smoker, 1–19 cigarettes/day	653	200	1.42	1.16–1.74
	Current smoker, ≥20 cigarettes/day	401	140	1.53	1.20–1.94
Obstruction[d]	No	4308	1058	1.00	
	Yes	161	49	0.78	0.55–1.10
Asthma	No	4402	1088	1.00	
	Yes	67	19	1.10	0.65–1.88
General health	Good	2580	482	1.00	
	Moderate	1491	476	1.32	1.14–1.54
	Poor	398	149	1.36	1.09–1.70
Leisure physical activity	Inactive	1406	386	1.00	
	Occasionally active	2272	548	0.94	0.81–1.09
	Regularly active	791	173	0.89	0.72–1.10
Educational level	Basic	2741	832	1.00	
	Intermediate	1075	200	0.79	0.66–0.94
	Higher	653	75	0.51	0.39–0.66
BMI	<20	238	31	1.00	
	20–24.9	2053	395	1.19	0.79–1.78
	25–29.9	1611	498	1.62	1.08–2.43
	30–34.9	481	143	1.58	1.02–2.45
	≥35	86	40	3.03	1.75–5.25
Diabetes	No	4375	1050	1.00	
	Yes	94	57	1.71	1.20–2.43
Systolic pressure	mmHg, ±1 SD	Mean = 140.6 ±21.4 SD[e]	Mean = 152.0 ±23.5 SD[e]	1.42	1.33–1.56
Diastolic pressure	mmHg, ±1 SD	Mean = 85.7 ±11.2 SD[f]	Mean = 90.2 ±11.3 SD[f]	1.34	1.24–1.43
Fs-Cholesterol	mmol/l, ±1 SD	Mean = 6.8 ±1.3 SD[g]	Mean = 7.3 ±1.3 SD[g]	1.40	1.31–1.50
Fs-HDL Cholesterol	mmol/l, ±1 SD	Mean = 1.7 ±0.4 SD[h]	Mean = 1.6 ±0.4 SD[h]	0.85	0.79–0.91

[a] Hospitalization for acute myocardial infarction (MI) or coronary death.

[b] Odds ratio (OR) for a major coronary event with 95% confidence intervals (CIs). Age adjusted for sex, sex adjusted for age, and the other factors adjusted for age and sex.

[c] SD, standard deviation; range for no major coronary event, 30–91 years of age; range for a major coronary event, 30–87 years of age.

[d] FEV_1/FVC over or below the lower limit of normal (LLN).

[e] Range for no major coronary event, 92–264 mmHg; and a major coronary event, 94–250 mmHg.

[f] Range for no major coronary event, 46–140 mmHg; and a major coronary event, 54–130 mmHg.

[g] Range for no major coronary event, 2.8–13.9 mmol/l; and a major coronary event, 3.6–12.7 mmol/l.

[h] Range for no major coronary event, 0.6–5.0 mmol/l; and a major coronary event, 0.6–3.5 mmol/l.

Table 2

Association between airway obstruction and the incidence of myocardial infarction (MI), a major coronary event, and coronary death in a multivariate model[a]

Characteristics		Total (n)	MI (n)	HR[b]	95% CI	Major coronary event (n)	HR[b]	95% CI	Coronary death (n)	HR[b]	95% CI
Age	Years, ±1 SD	Mean = 47.7 ±12.6 SD[c]		2.21	1.97–2.49		2.32	2.14–2.52		3.95	3.57–4.42
Sex	Men	2559	339	1.00		668	1.00		463	1.00	
	Women	3017	229	0.46	0.38–0.57	439	0.43	0.37–0.50	358	0.46	0.38–0.55
Smoking	Non-smoker	3078	274	1.00		522	1.00		389	1.00	
	Former smoker	1104	120	1.01	0.79–1.28	245	1.09	0.92–1.29	171	1.18	0.96–1.45
	Current smoker, 1–19 cigarettes/day	853	103	1.65	1.29–2.11	200	1.75	1.47–2.09	153	2.33	1.89–2.87
	Current smoker, ≥20 cigarettes/day	541	71	1.77	1.32–2.38	140	1.90	1.54–2.34	108	2.98	2.32–3.82
Obstruction[d]	No	5366	547	1.00		1058	1.00		772	1.00	
	Yes	210	21	0.84	0.54–1.31	49	1.06	0.79–1.42	49	1.40	1.04–1.88
Asthma	No	5490	556	1.00		1088	1.00		804	1.00	
	Yes	86	12	1.36	0.76–2.43	19	1.04	0.66–1.64	17	1.27	0.78–2.06
General health	Good	3062	237	1.00		482	1.00		315	1.00	
	Moderate	1967	247	1.19	0.99–1.44	476	1.15	1.01–1.32	385	1.15	0.99–1.35
	Poor	547	84	1.32	1.01–1.72	149	1.18	0.97–1.43	121	1.07	0.85–1.33
Leisure physical activity	Inactive	1792	198	1.00		386	1.00		319	1.00	
	Occasionally active	2820	286	1.00	0.83–1.20	548	0.94	0.82–1.07	400	0.84	0.72–0.98
	Regularly active	964	84	1.06	0.81–1.39	173	1.05	0.87–1.27	102	0.85	0.67–1.08
Educational level	Basic	3573	439	1.00		832	1.00		648	1.00	
	Intermediate	1275	95	0.77	0.62–0.97	200	0.84	0.72–0.99	126	0.83	0.68–1.01
	Higher	728	34	0.56	0.39–0.81	75	0.64	0.50–0.82	47	0.67	0.50–0.92
BMI	<20	269	15	1.00		31	1.00		23	1.00	
	20–24.9	2448	198	0.80	0.46–1.42	395	0.72	0.49–1.06	275	0.74	0.47–1.18
	25–29.9	2109	256	0.82	0.46–1.46	498	0.75	0.50–1.10	360	0.75	0.47–1.19
	30–34.9	624	77	0.81	0.44–1.47	143	0.72	0.47–1.09	128	0.90	0.55–1.46
	≥35	126	22	1.19	0.59–2.41	40	1.04	0.63–1.72	35	1.23	0.70–2.18

Diabetes	No	5425	532	1.00		1050	1.00		766	1.00	
	Yes	151	36	2.40	1.70–3.40	57	2.09	1.59–2.74	55	2.55	1.93–3.38
Systolic pressure	mmHg, ±1 SD	Mean = 142.8 ±22.3 SD[e]		1.28	1.14–1.43		1.33	1.22–1.43		1.39	1.28–1.56
Diastolic pressure	mmHg, ±1 SD	Mean = 86.6 ±11.4 SD[f]		1.03	0.93–1.15		1.08	1.01–1.17		1.06	0.98–1.16
Fs-Cholesterol	mmol/l, ±1 SD	Mean = 6.9 ±1.3 SD[g]		1.26	1.16–1.37		1.29	1.21–1.37		1.25	1.17–1.35
Fs-HDL Cholesterol	mmol/l, ±1 SD	Mean = 1.7 ±0.4 SD[h]		0.76	0.69–0.84		0.83	0.77–0.89		0.89	0.82–0.96

[a] Hospitalization for acute MI; hospitalization for acute MI, or coronary death; coronary death.
[b] Hazard ratios (HRs) with 95% confidence intervals (CIs) in a multivariate model, adjusted for all of the characteristics listed in this table.
[c] SD, standard deviation; range, 30–91 years.
[d] FEV_1/FVC over or below the lower limit of normal (LLN).
[e] Range, 92–264 mmHg.
[f] Range, 46–140 mmHg.
[g] Range, 2.8–13.9 mmol/l.
[h] Range, 0.6–5.0 mmol/l.

Table 3

Hazard ratios (HRs) for a major coronary event[a] by airway obstruction, sex, and age

	Obstruction[b]	Total (n)	Major coronary event (n)	HR[c]	95% CI	HR[d]	95% CI	HR[e]	95% CI
Men, age in years									
30–49	No	1569	321	1.00		1.00		1.00	
	Yes	47	7	0.88	0.42–1.87	0.76	0.36–1.60	0.78	0.36–1.67
50–69	No	729	281	1.00		1.00		1.00	
	Yes	71	20	0.97	0.62–1.54	0.89	0.56–1.41	0.80	0.50–1.28
70–91	No	123	33	1.00		1.00		1.00	
	Yes	20	6	2.71	1.10–6.68	2.46	0.94–6.49	1.97	0.61–6.36
Women, age in years									
30–49	No	1634	97	1.00		1.00		1.00	
	Yes	33	6	3.31	1.45–7.54	2.81	1.22–6.45	4.21	1.73–10.28
50–69	No	1093	262	1.00		1.00		1.00	
	Yes	28	6	1.10	0.49–2.46	0.75	0.31–1.77	0.77	0.32–1.85
70–91	No	218	64	1.00		1.00		1.00	
	Yes	11	4	1.51	0.55–4.19	1.54	0.56–4.26	2.77	0.89–8.57

[a] Hospitalization for acute MI or coronary death.

[b] FEV_1/FVC over or below the lower limit of normal (LLN) .

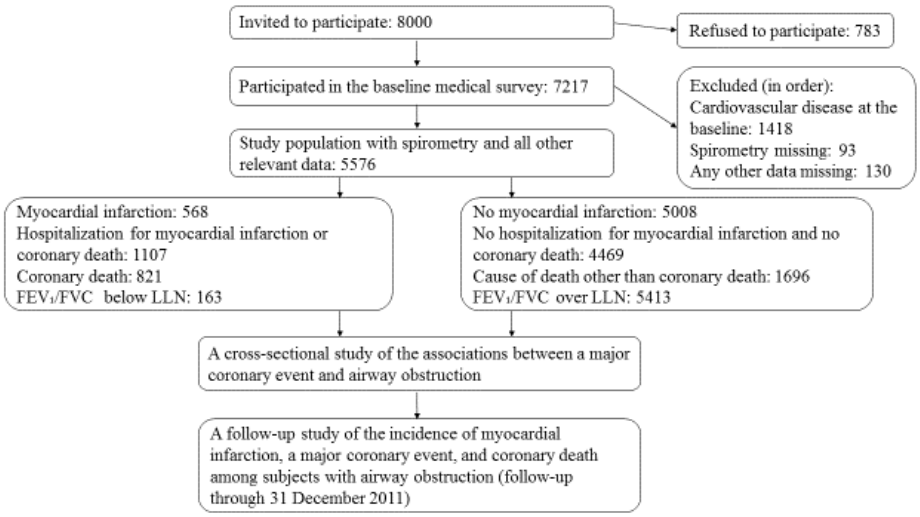
[c] Hazard ratios (HRs) with 95% confidence intervals (CIs), adjusted for age.

[d] HRs, adjusted for age and smoking.

[e] HRs in a multivariate model, adjusted for age, smoking, asthma history, general health, leisure physical activity, educational level, BMI, diabetes, systolic and diastolic pressures, and total and HDL cholesterol.

Figure 1.

Flow chart of the study population.



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