The Relationship Between Reduced Lung Function and Cardiovascular Mortality*

A Population-Based Study and a Systematic Review of the Literature

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Study objectives: **Conditions that give rise to reduced lung function are frequently associated with low-grade systemic inflammation, which may lead to poor cardiovascular outcomes. We sought to determine the relationship between reduced FEV_1 and cardiovascular mortality, independent of smoking.**

Design: **Longitudinal population-based study and a metaanalysis of literature.**

Setting: **Representative sample of the general population.**

Participants: **Participants of the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study who were 40 to 60 years of age at baseline assessment (n = 1,861).**

Measurements and results: **We compared the risk of cardiovascular mortality across quintiles of FEV_1. Individuals in the lowest FEV_1 quintile had the highest risk of cardiovascular mortality (relative risk [RR], 3.36; 95% confidence interval [CI], 1.54 to 7.34). Compared to FEV_1 quintile 1, individuals in quintile 5 had a fivefold increase in the risk of death from ischemic heart disease (RR, 5.65; 95% CI, 2.26 to 14.13). We also performed a systematic review of large cohort studies (> 500 participants) that reported on the relationship between FEV_1 and cardiovascular mortality (12 studies; n = 83,880 participants). Compared to participants in the highest FEV_1 category, those with reduced FEV_1 had a higher risk of cardiovascular mortality (pooled RR, 1.77; 95% CI, 1.56 to 1.97).**

Conclusions: **There is strong epidemiologic evidence to indicate that reduced FEV_1 is a marker for cardiovascular mortality independent of age, gender, and smoking history.**

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Key words: cardiovascular mortality; FEV_1; lung function; metaanalysis; National Health and Nutrition Examination Survey

Abbreviations: BMI = body mass index; CI = confidence interval; CRP = C-reactive protein; ICD-9 = International Classification of Diseases, Ninth Revision; NHANES = National Health and Nutrition Examination Survey; NHEFS = National Health and Nutrition Examination Survey Epidemiologic Follow-up Study; RR = relative risk

Nearly 20% of the adult population have reduced FEV_1 values, indicating impaired lung function.[1] The majority of these individuals with reduced FEV_1 have COPD, asthma, or fibrotic lung disease.[1] These conditions are associated with persistent low-grade systemic inflammation.[2–7] In some of these conditions, the blood levels of inflammatory markers, such as C-reactive protein (CRP), fluctuate as a function of the individual's FEV_1. At a population level, individuals with the lowest FEV_1 have the highest levels of CRP, fibrinogen, and other systemic inflammatory markers, while those with the highest FEV_1 have the lowest values.[1,3] Since low-grade systemic inflammation is associated with atherosclerosis, reduced FEV_1 might be an important risk factor for cardiovascular morbidity and mortality, independent of cigarette smoking. Using a large population-based data, we sought to determine the association between FEV_1 and the risk of cardiovas-

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cular hospitalization and deaths in the community, independent of cigarette smoking. The independency of cigarette smoking is important because it is a shared risk factor for both impaired lung function and cardiovascular events[8,9] and may be an important confounder to this relationship. We also conducted a systematic overview (and a metaanalysis) of available evidence from large population-based prospective studies, wherein current and previous cigarette exposure was adjusted for, to determine the nature of the association between cardiovascular mortality and FEV_1 values, independent of smoking status.

Materials and Methods

Study Population

Originally, 20,729 Americans participated in the first National Health and Nutrition Examination Survey (NHANES) from 1971 through 1975; of these, 14,407 persons underwent a detailed medical examination. They were followed up longitudinally until 1992 as part of the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS).[10] The data for the NHEFS were collected in four waves. The details of cohort assemblage and follow-up are provided elsewhere.[10] In brief, the first wave of follow-up occurred between 1982 and 1984, while the second, third, and fourth waves were conducted in 1986, 1987, and 1992, respectively. During each wave, participants' health, vital status, and health service utilization (including hospitalization) information was ascertained. Of the original cohort, 1,116 participants were unavailable for follow-up.[10]

Measurements

Spirometry was conducted in a subset of NHANES 1 participants (n = 6,913). Using a spirometer (Model 800; Ohio Medical Instruments; Cincinnati, OH), participants performed five FVC maneuvers from which two reproducible and error-free FEV_1 and FVC values were recorded.[11] We used published prediction equations to calculate predicted FEV_1 and FVC values for each participant.[12] For analytic purposes, the study cohort was divided into quintiles based on the predicted FEV_1. Other measurements were used as covariates, including age, gender, body mass index (BMI), systolic and diastolic BP, total cholesterol, and current smoking status. We also calculated a Framingham risk score[13] and included this as a covariate in the model.

Vital status information was obtained by tracing each participant through telephone contacts, direct mail, in-proxy interviews, and searches of the National Death Index database and state department vital statistics records.[10] Death certificates were available for 96.6% of the decedents and were used to ascertain the principal cause of the mortality, which were codified based on International Classification of Diseases, Ninth Revision (ICD-9) codes. Cardiovascular mortality was defined as deaths in which the principal cause of mortality was cardiovascular in nature, using ICD-9 codes 410–429. Deaths from ischemic heart disease were defined similarly, except we used ICD-9 code 410.

Hospitalization information was initially obtained during the follow-up interviews as part of the NHEFS. The data obtained during the interview were verified by examining inpatient records, discharge summaries, and pathology reports (if any) of the participants. For analytic purposes, we considered only the principal diagnosis of the hospitalization, using codes 410–429 for cardiovascular and code 410 for ischemic heart disease hospitalizations.

Statistical Analysis

To make our cohort as homogenous as possible and to exclude participants who had known or unknown (severe) cardiovascular diseases and other conditions, we excluded all participants who died or were unavailable for follow-up within the first 3 years of the follow-up period. Moreover, we restricted our study sample to those from 40 to 60 years of age, leaving data from 1,861 participants eligible for this study. This cohort was divided into FEV_1 quintiles. Using the highest quintile as the referent group in a Cox proportional hazards model, we compared the cardiovascular and ischemic heart disease mortality rates across the quintiles for the mortality analysis. We performed a similar analysis using cardiovascular and ischemic heart disease hospitalization as the outcome variables. For this analysis, if a sampled person had multiple hospitalization records, only the first hospitalization record was used. Finally, to determine cardiovascular hospitalization-free survival, we calculated the time to the first cardiovascular event (either cardiovascular hospitalization or death) using the Cox proportional hazards model. The covariates considered were age, BMI, gender, race, systolic and diastolic BP, total serum cholesterol level, use of antihypertensive medications, Framingham risk score, and current smoking status. Age was included as both a continuous and categorical variable (in quartiles). As there was little difference in the overall findings, we inserted age as a categorical variable for parsimony. BMI was divided into quintiles (quintile 1, < 21.9 kg/m^2; quintile 2, 21.9 to 24.1 kg/m^2; quintile 3, 24.2 to 26.4 kg/m^2; quintile 4, 26.5 to 29.1 kg/m^2; and quintile 5, ≥ 29.2 kg/m^2). Systolic and diastolic BP values were inserted as continuous variables. Because all of these variables have important effects on cardiovascular outcomes, we forced them into our final model. All analyses were conducted using software (Version 8.02; SAS Institute; Cary, NC; and SAS-callable SUDAAN, Version 8.0; Research Triangle Institute; Research Triangle Park, NC). All tests were two tailed, and $p < 0.05$ was considered statistically significant. Both weighted and unweighted analyses were performed to check the sufficiency of the multivariate model used. The results of the unweighted analyses were very similar to the ones of the weighted analyses, so they are not discussed any further. Plots of estimated survival rates over time were examined to verify that the proportional hazard model assumptions were met.

Systematic Review and Metaanalysis

We conducted a literature search using MEDLINE, EMBASE, and CINAHL. We limited our search to long-term, population-based, prospective studies published before 2004 that reported on the relationship between cardiovascular mortality and FEV_1 values. To identify potentially relevant articles, we combined disease-specific search terms ("forced expiratory volume" or "respiratory function" or "vital capacity"), with outcome-specific terms ("cardiovascular diseases" or "myocardial" or "arrhythmia" or "heart diseases" or "coronary disease" or "sudden death") and design-specific terms (prospective" or "follow-up studies" or "prognosis"). We also scanned the bibliographies and reference lists of the searched articles to identify additional studies that may have been missed by the initial computerized search. We included only those studies that were large (> 500 participants), community based (and not hospital or outpatient clinic based), employed a prospective method of data collection,

and reported on cardiovascular mortality according to FEV_1. We excluded studies in which the study populations were chosen based on disease. From each relevant article, two authors independently reviewed the results and abstracted the following information: year of publication, nature of the study sample, age of the cohort, duration of follow-up, and whether or not adjustments for smoking status were made. Any discrepancies were resolved through iteration and consensus. From the included studies, we compared the risk of cardiovascular mortality among participants in the lowest FEV_1 category (however that was defined in the study) to those in highest FEV_1 category, adjusted for potential confounders including age, gender, and smoking status. In a secondary analysis, we meta-analyzed data from those studies that reported on the relationship between cardiovascular mortality and FEV_1 among lifetime nonsmokers and among men and women, separately. Heterogeneity of results across individual studies was checked for using the Cochran Q test. If significant heterogeneity was observed ($p < 0.10$), we employed the Dersimonian and Laird random effects model to combine the results; otherwise, a fixed effects model was used. We also constructed a funnel plot to assess publication bias. We rated the quality of the study using criteria from the US Preventive Services Task Force and the National Health Service Centre for Reviews and Dissemination.[14,15] A rating of "good" was assigned to studies in which eight or more responses were positive, a rating of "fair" was assigned to studies in which five to seven responses were positive, and a rating of "poor" was assigned to studies in which fewer than five responses were positive. All analyses were conducted using Review Manager version 4.1 (Revman; The Cochrane Collaboration; Oxford, England).

Results

NHEFS

In total, there were 1,861 adult participants in this study. The mean age of the participants was 50 ± 5.7 years; 47.1% (n = 876) were men, 9.4% (n = 174) were African-Americans, and 37.2% (n = 693) were active smokers. The mean systolic and diastolic BP values were 133.8 ± 20.2 mm Hg and 85.3 ± 11.6 mm Hg, respectively (± SD). The mean BMI was 26.0 ± 4.9 kg/m^2. The clinical characteristics of the study participants in the different FEV_1 quintiles are summarized in Table 1.

Overall, 19.1% (n = 355) of the study cohort died during the follow-up period. Cardiovascular disorders were listed as the principal causes of mortality in 45.4% of the deaths (n = 161), ischemic heart disease accounted for 76.4% of all cardiovascular deaths (n = 123), and 9.3% of the cohort experienced at least one hospitalization wherein cardiovascular disorders were listed as the principal discharge diagnosis (n = 173). Finally, 16.6% of the cohort (n = 309) experienced a cardiovascular hospitalization or mortality during the follow-up period.

In all cases, the risk of cardiovascular mortality and hospitalization increased with decreasing FEV_1. In the weighted analysis, individuals in the lowest FEV_1 quintile (quintile 1) had the highest risk of cardiovascular mortality (relative risk [RR], 3.36; 95% confidence interval [CI], 1.54 to 7.34) compared with those in the highest FEV_1 quintile (quintile 5) [Table 1]. The risk was slightly lower in FEV_1 quintiles 2 and 3 (RR, 2.00, 95% CI, 1.03 to 3.89 for quintile 2; RR, 2.22; 95% CI, 1.23 to 4.01 for quintile 3). The relationship between reduced FEV_1 and mortality from ischemic heart disease was even more striking. Compared with FEV_1 quintile 1, individuals in quintile 5 had a greater than fivefold increase in the risk of death from ischemic heart disease (RR, 5.65; 95% CI, 2.26 to 14.13) [Table 1]. Similar findings were observed when we restricted the analysis to nonsmokers (Table 2).

Literature Review

The initial MEDLINE search produced 340 "hits." The abstracts of all these articles were se-

Table 1—*Relative Risk of Various Cardiovascular Events Across The FEV_1 Quintile Groups (Weighted Analysis)

Variables	p Value for Trend‡	p Value for Trend§	FEV_1 Quintile† 1	2	3	4	5
Mean FEV_1, % predicted			63	80	88	96	109
Cardiovascular mortality	< 0.001	< 0.001	3.36 (1.54–7.34)	2.00 (1.03–3.89)	2.22 (1.23–4.01)	0.93 (0.39–2.25)	1.0
Cardiovascular hospitalization	0.024	0.049	1.69 (0.84–3.40)	1.44 (0.78–2.65)	1.60 (0.88–2.90)	0.99 (0.52–1.88)	1.0
Cardiovascular death or hospitalization	< 0.001	< 0.001	2.44 (1.37–4.33)	1.70 (1.08–2.67)	1.78 (1.18–2.70)	1.06 (0.62–1.82)	1.0
Mortality from ischemic heart disease	< 0.001	< 0.001	5.65 (2.26–14.13)	3.11 (1.38–7.03)	3.69 (1.50–9.06)	1.50 (0.54–4.20)	1.0
Hospitalization from ischemic heart disease	0.103	0.182	1.52 (0.67–3.42)	1.39 (0.66–2.91)	1.25 (0.61–2.59)	0.95 (0.45–2.02)	1.0

*Data are presented as RR (95% CI) and have been adjusted for various factors including modified Framingham risk score for coronary heart disease, age, smoking status, gender, diabetes, systolic and diastolic BP, cholesterol, BMI, race, and treated hypertension.

†In all analyses, quintile 5 is the referent.

‡Test of tread is not adjusted for any covariates.

§Test of tread is adjusted for covariates listed above.

Table 2—*RR of Various Cardiovascular Events in Nonsmokers Across the FEV_1 Quintile Groups (Weighted Analysis)

Variables	p Value for Trend‡	p Value for Trend§	FEV_1 Quintile†				
			1	2	3	4	5
Mean FEV_1, % predicted			63	80	88	96	109
Cardiovascular mortality	< 0.001	0.003	2.68 (1.17–6.15)	1.86 (0.88–3.94)	1.95 (0.90–4.23)	0.74 (0.30–1.84)	1.0
Cardiovascular hospitalization	0.031	0.085	1.71 (0.78–3.77)	1.17 (0.56–2.45)	1.79 (0.89–3.59)	0.91 (0.39–2.12)	1.0
Cardiovascular death or hospitalization	< 0.001	0.002	2.16 (1.18–3.96)	1.47 (0.88–2.44)	1.77 (1.05–2.98)	0.95 (0.51–1.75)	1.0
Mortality from ischemic heart disease	< 0.001	< 0.001	3.98 (1.29–12.23)	3.17 (1.12–8.98)	3.59 (1.25–10.35)	0.86 (0.23–3.21)	1.0
Hospitalization from ischemic heart disease	0.126	0.278	1.61 (0.62–4.20)	1.05 (0.44–2.52)	1.53 (0.67–3.50)	0.86 (0.35–2.14)	1.0

*Data are presented as RR (95% CI) and have been adjusted for various factors including modified Framingham risk score for coronary heart disease, age, smoking status, gender, diabetes, systolic and diastolic BP, cholesterol, BMI, race, and treated hypertension.
†In all analyses, quintile 5 is the referent.
‡Test of tread is not adjusted for any covariates.
§Test of tread is adjusted for covariates listed above.

lected and reviewed. Thirty articles met the inclusion and exclusion criteria and were selected for a detailed review. Eighteen articles were excluded for the following reasons: no reporting of cardiovascular mortality or FEV_1 (n = 14) or multiple publications from the same cohort (n = 4). This left 12 original articles meeting the inclusion and exclusion criteria for analysis. Table 3 summarizes the abstracted data from the chosen studies.[16–27] Although there was a marked heterogeneity in the way in which the studies defined "low" FEV_1 and the referent FEV_1 groups, all the studies nevertheless reported a significant association between reduced FEV_1 (as defined by each of the studies) and cardiovascular mortality (n = 83,880 participants). Overall, reduced FEV_1 was associated with increased cardiovascular mortality (pooled RR, 1.99; 95% CI, 1.71 to 2.29) [Table 3]. In an analysis of studies that made statistical adjustments for smoking status (seven studies, n = 63,690 participants), the results were similar (pooled RR, 1.77; 95% CI, 1.56 to 1.97; test for heterogeneity, p = 0.15). When only those studies that divided the study population into quintile groups based on FEV_1 were meta-analyzed (n = 22,530), the pooled RR of cardiovascular mortality of the lowest FEV_1 quintile group compared to the highest quintile group was 1.75 (95% CI, 1.54 to 2.01; p = 0.63 for heterogeneity) [Fig 1]. In a secondary analysis, we analyzed data from studies that reported on the relationship between FEV_1 and cardiovascular mortality among lifetime nonsmokers. The results of this analysis were very similar to the main analysis: RR, 1.67; 95% CI, 1.35 to 2.01 (p = 0.84 for heterogeneity) [Fig 2]. Moreover, the relationship between reduced FEV_1 and cardiovascular mortality was similar among men (RR, 1.64; 95% CI, 1.48 to 1.84; p = 0.17 for heterogeneity) and women (RR, 2.14; 95% CI, 1.75 to 2.59; p = 0.40 for heterogeneity).

Discussion

The NHANES 1 follow-up data indicate that reduced FEV_1 is a marker for future cardiovascular morbidity and mortality. The relationship between reduced FEV_1 and mortality from ischemic heart disease was particularly striking. Even a modest decline in FEV_1 (from a mean of 109% of predicted to 88% of predicted) was associated with a fivefold increase in deaths from ischemic heart disease, independent of baseline smoking status and other potential confounding factors such as age, gender, and Framingham risk scores.

These data are consistent with other published population-based studies, in which investigators systematically examined the relationship between FEV_1 and cardiovascular mortality.[16–27] Our pooled analysis of the studies that categorized FEV_1 in quintiles demonstrated that individuals in the lowest FEV_1 quintile (approximately < 75 to 80% of predicted) have a 75% increase in the risk for cardiovascular mortality compared with those in the highest FEV_1 quintile. Even among lifetime nonsmokers, this relationship held, indicating that reduced lung function independent of smoking is a significant marker for cardiovascular mortality.

There are three potential explanations for the relationship between various lung conditions that give rise to reduced FEV_1 and cardiovascular disease. The first possibility is that there is a common offending agent (associated with reduced FEV_1) that affects both pulmonary and cardiovascular systems

Table 3—*Baseline Characteristics of Included Studies and Their Reported Association Between FEV_1 and Cardiovascular Mortality

Source (quality rating)	Publication Year	Study Population	Sample Size	Age, yr	Male Gender, %	Mean FEV_1, L or % of predicted	Current Smokers	FEV_1 Categorization (% predicted or L)	Follow-up, yr	RR of Cardiovascular Mortality (95% CI)	Covariates Adjusted for in the Analysis
Marcus et al[19] (good)	1989	Honolulu Heart Program, US (Japanese American)	5,924	54	100	2.71 (94%)	48%	Quintiles (2.10 L vs 3.28 L)	15–18	1.93 (1.46–2.54)	Age, gender, smoking history
Higgins and Keller[17] (fair)	1970	Tecumseh, US	5,140	16–75	47.7	NA	NA	< 2.0 L (1.4‡) vs ≥ 2.0 L (1.4‡)	2–6	5.03 (3.07–8.22)	None
Hole et al[16] (good)	1996	Renfrew & Paisley, UK	15,411	45–64	45.8	2.83† 1.99‡	36%	Quintiles (≤ 73 to 75% vs ≥ 108 to 113%)	15	1.56 (1.26–1.92)† 1.88 (1.44–2.47)‡	Age, gender, cigarette smoking, diastolic BP, cholesterol concentration, body mass index, and social class
Beaty et al[18] (fair)	1985	Baltimore Longitudinal Study of Aging, US	874	50.7	100	95.6%	21%	≤ 80% vs ≥ 80%	24	1.58 (0.96–2.60)	None
Schunemann et al[20] (good)	2000	Buffalo/Erie County, US	1,195	46.8	46.4	2.8	58.3%	Quintiles (< 80% vs ≥ 109 to 114%)	29	2.11 (1.20–3.71)† 1.96 (0.99–3.88)‡	Age, gender, education, smoking history, systolic BP, BMI
Ebi-Kryston[21] (fair)	1988	Whitehall Civil Servants, UK	17,717	40–64	100	NA	NA	< 65% vs ≥ 65%	10	1.49 (1.24–1.80)	Age, smoking history
Lange et al[22] (good)	1991	Copenhagen City Study, Denmark	12,511	53.1	NA	NA	NA	< 60% vs > 80%	6.5	1.8 (1.4–2.4)	Age, gender, diabetes, systolic BP, cholesterol, BMI, smoking history
Tockman et al[23] (fair)	1989	Washington County, Maryland	884	NA	100	NA	32.3%	Quartiles (< 65% vs > 100%)	10	3.66 (1.76–7.61)	None
Krzyzanowski and Wysocki[24] (fair)	1986	Cracow, Poland	3,047	19–70	59	NA	38.4%	< 65% vs 76–100%	13	2.56 (1.35–4.85)† 1.99 (0.95–4.18)‡	Age, gender, height, smoking history, health status
Hospers et al[25] (good)	1999	Vlagtwedde-Vlaardingen, Netherlands	5,382	36	54	98%	55%	< 80% vs ≥ 100%	~25	1.82 (1.42–2.34)	Eosinophilia, positive skin tests, age, gender, smoking history, and city of residence
Kuller et al[26] (good)	1989	Multiple risk factor intervention trial	7,368§	46	100	3.38	64%	Quintiles (< 2.8 to 3.0 L vs ≥ 3.8 to 4.0 L)	7	2.33 (1.35–4.03)‖	Age, diastolic BP, smoking history, LDL, HDL, leisure time, education, height
Speizer et al[27] (good)	1989	Harvard Six Cities Study	8,427	49	45	2.85	39.9%	Quartiles (2.0 to 2.6 L vs 2.9 to 4.1 L)	12	1.42 (1.07–1.90)† 2.74 (1.93–3.90)†	Age, respiratory symptoms, gender, smoking history
Pooled summary			83,880							1.99 (1.71–2.29)	

*NA = not available; LDL = low-density lipoprotein; HDL = high-density lipoprotein. Test for heterogeneity, p = 0.001.
†Male values.
‡Female values.
§Although 12,866 participants were originally enrolled in the study, only 7,368 participants had an acceptable pulmonary function test result.
‖Although the smoking-adjusted RR was reported, its 95% CI was not provided; thus, the adjusted data could not be used for the metaanalysis.

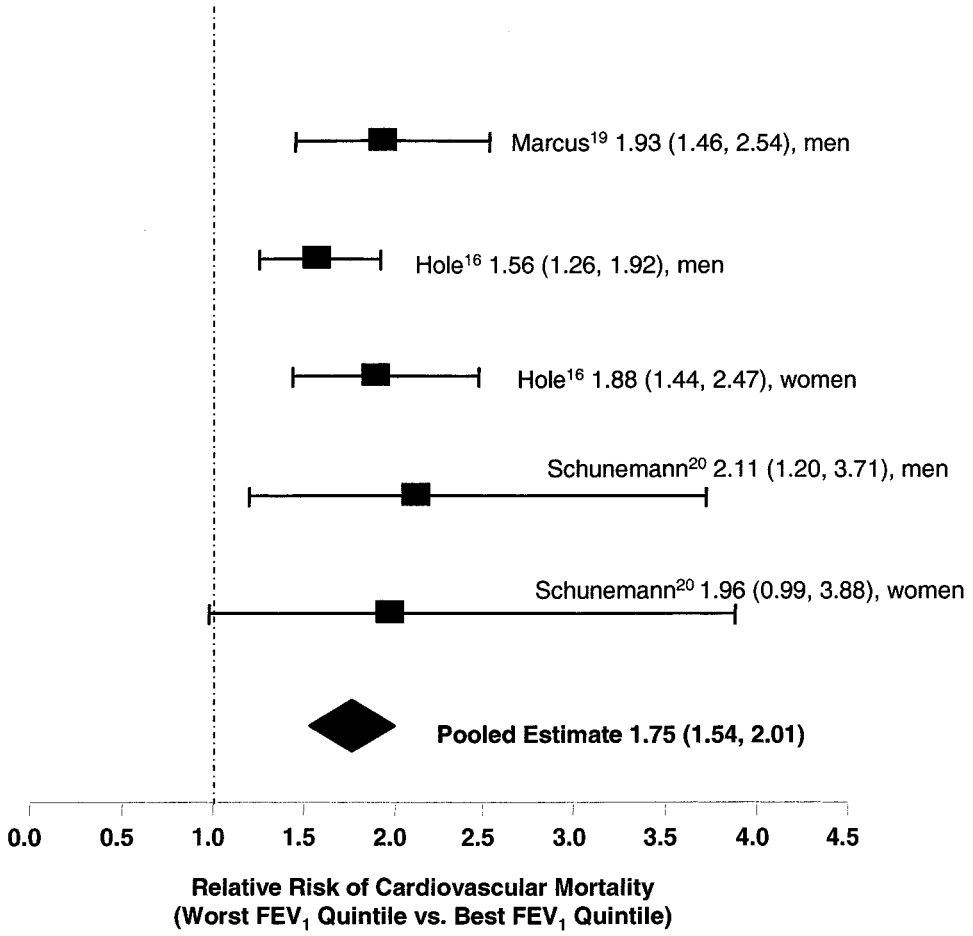

FIGURE 1. Metaanalysis of studies that reported RR of cardiovascular mortality based On FEV_1 quintiles.

such that reduced FEV_1 serves as an epiphenomenon of this "third" factor. A second possibility is that the relationship is confounded by various measured and unmeasured variables. The third possibility is that the lung processes may be causally linked to cardiovascular disease. There are several lines of evidence that suggest a causal association is possible. Although fibrotic lung and obstructive airway diseases are disparate conditions, both can give rise to systemic inflammation and increased systemic levels of CRP and fibrinogen.[3,28–30] In these conditions, CRP and other acute-phase proteins may increase in response to certain cytokines and growth factors that may be overexpressed in the lung tissue.[7,31] Although the precise mechanism by which this occurs is unknown, in rabbit models, Suwa and colleagues[32] have shown that induction of airway inflammation can incite and propagate systemic inflammation, which in turn may contribute to the progression of atherosclerosis. This observation is consistent with the notion that low-grade systemic inflammation is a major risk factor for plaque genesis, progression, and rupture.[33]

There are limitations to the current study. Because the present review relied on published reports of data, residual confounding by other risk factors is a concern. Moreover, for the metaanalysis, we did not have access to individualized data; thus, we could not determine the appropriateness of FEV_1 cut-off values used across the studies and we could not determine the exact shape of the relationship between FEV_1 and cardiovascular mortality. A pooled analysis of individualized data from these studies may be of value in addressing the shortcomings of the present study. Furthermore, future large prospective studies are needed to determine whether differential changes in FEV_1 over time can modify the risk of cardiovascular events. Second, for the NHEFS analysis, we relied on ICD-9 coding on hospital records and death certificates to ascertain cardiovascular event rates in the cohort. Previous studies[34,35] suggest that this approach may overestimate the burden of cardiovascular events in the community. Random misclassification of cardiovascular event data across FEV_1 quintiles would have biased the findings toward the null value. Therefore, the results from the

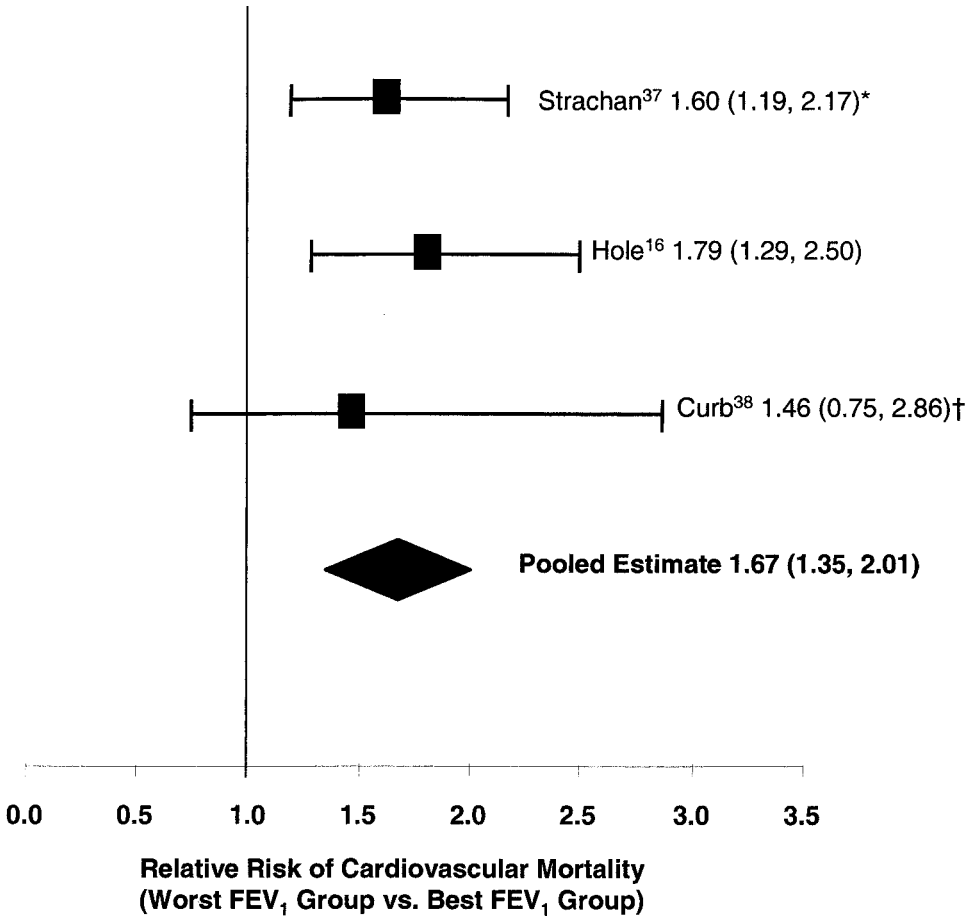

FIGURE 2. Metaanalysis of studies that reported RR of cardiovascular mortality among nonsmokers. *Data from the Whitehall cohort.[21] †Data from the Honolulu Heart Program.[19]

current analysis may be a conservative estimate of the impact of FEV_1 on cardiovascular outcomes. Third, we cannot entirely rule out the possibility of publication bias in the systematic review.[36] Therefore, the findings of the metaanalysis should be interpreted cautiously.[36]

In summary, the NHEFS as well other published population-based data suggest that reduced FEV_1 is a marker for cardiovascular mortality, independent of smoking history. FEV_1, which is easily measurable in ambulatory clinic settings, provides additional prognostic information, which may help to better risk-stratify patients and populations for future cardiovascular events. Future work is needed to determine whether lung conditions giving rise to reduced FEV_1 can contribute to atherosclerosis and whether treatment of these conditions can improve cardiovascular outcomes in such patients.

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