Independent Impact of Gout on Mortality and Risk for Coronary Heart Disease

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Background—Although gout and hyperuricemia are related to several conditions that are associated with reduced survival, no prospective data are available on the independent impact of gout on mortality. Furthermore, although many studies have suggested that hyperuricemia is associated with cardiovascular disease (CVD), limited data are available on the impact of gout on CVD.

Methods and Results—Over a 12-year period, we prospectively examined the relation between a history of gout and the risk of death and myocardial infarction in 51,297 male participants of the Health Professionals Follow-Up Study. During the 12 years of follow-up, we documented 5,825 deaths from all causes, which included 2,132 deaths from CVD and 1,576 deaths from coronary heart disease (CHD). Compared with men without history of gout and CHD at baseline, the multivariate relative risks among men with history of gout were 1.28 (95% confidence interval [CI], 1.15 to 1.41) for total mortality, 1.38 (95% CI, 1.15 to 1.66) for CVD deaths, and 1.55 (95% CI, 1.24 to 1.93) for fatal CHD. The corresponding relative risks among men with preexisting CHD were 1.25 (95% CI, 1.09 to 1.45), 1.26 (95% CI, 1.07 to 1.50), and 1.24 (95% CI, 1.04 to 1.49), respectively. In addition, men with gout had a higher risk of nonfatal myocardial infarction than men without gout (multivariate relative risk, 1.59; 95% CI, 1.04 to 2.41).

Conclusions—These prospective data indicate that men with gout have a higher risk of death from all causes. Among men without preexisting CHD, the increased mortality risk is primarily a result of an elevated risk of CVD death, particularly from CHD. (Circulation. 2007;116:894-900.)

Key Words: cardiovascular diseases ■ coronary disease ■ gout ■ mortality ■ myocardial infarction

Gout is the most common inflammatory arthritis in adult males, and the overall disease burden of gout remains substantial and may be growing. Many chronic inflammatory disorders are associated with premature death (eg, rheumatoid arthritis, giant cell arteritis, systemic lupus erythematosus, and ankylosing spondylitis). However, it is unknown if gout affects life expectancy. Although gout and hyperuricemia are associated with several conditions that are associated with reduced survival (eg, insulin resistance syndrome, obesity, and hypertension), no large-scale prospective data are available on the potential independent impact of gout on mortality.

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Although many studies investigated the relation between serum urate levels and cardiovascular disorders, little information is available on the relation between gout and cardiovascular outcomes. In the Framingham Study, serum urate levels were not independently associated with the risk of coronary heart disease (CHD), but gout was associated with a 60% increased risk of coronary artery disease. Recently, a study based on the Multiple Risk Factor Intervention Trial (MRFIT) reported that gout was associated with a 26% increased risk of acute myocardial infarction (MI) (multivariate odds ratio, 1.26; 95% confidence interval [CI], 1.14 to 1.40; P<0.001). If an independent association existed between gout and these major outcomes, this information would substantially add to the overall burden of the disease to the society. Furthermore, the information would also be useful for clinicians who care for patients with these disorders (eg, to increase efforts to prevent cardiovascular disease [CVD] and premature deaths).

To address these important issues, we prospectively evaluated the association between gout and the future risk of death and MI in the Health Professionals Follow-up Study, which had a large prospective cohort.

Methods

Study Population
The Health Professionals Follow-up Study is a prospective cohort study of 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians who were predominantly white (91%).

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and were 40 to 75 years old in 1986. The participants returned a mailed questionnaire in 1986 on diet, medical history, and medications. The 51,297 men who provided the baseline questionnaire information were included in our analyses.

Members of the cohort have reported information on various lifestyle factors such as smoking, weight, physical activity, vitamin supplement use, and medical history such as diabetes mellitus, hypercholesterolemia, and hypertension biennially since their enrollment. Dietary and alcohol intake was reported in 1986, 1990, and 1994 with a validated semi-quantitative food-frequency questionnaire.2,3,13,14 Family history of MI before 60 years of age and height were reported at baseline. Follow-up rates have averaged 94% for each 2-year cycle.

Assessment of Gout and CHD

The 1986 baseline questionnaire inquired about a history of physician-diagnosed gout. Biennial questionnaires mailed between 1988 and 1996 were used to identify newly diagnosed cases of gout. We ascertained incident cases of gout by the American College of Rheumatology (ACR) survey gout criteria, as previously described.2–4 In 2000, we mailed a supplementary questionnaire to those participants with self-reported incident gout diagnosed from 1986 onwards to confirm the report and to ascertain the ACR survey gout criteria.2–4,11,14 The response rate for the supplementary gout questionnaire was 80%, and 69% of the self-reported gout cases who returned the questionnaire met the primary end point definition. The concordance rate of confirmation of the report of gout between the returned questionnaire met the primary end point definition. The questionnaire was 80%, and 69% of the self-reported gout cases who were followed up in 2-year cycles.

We calculated mortality according to history of gout and CHD at baseline. However, when possible, we used confirmed cases in our analyses because our validation of these outcomes was performed among those who reported incident diagnoses during the follow-up after baseline. When possible, we used confirmed cases in our analyses as the analysis for the relation between incident gout and the risk of incident MI.

Ascertainment of Deaths and Incident Myocardial Infarction

Deaths were documented by responses to follow-up questionnaires by family members, the postal service, and a search of the National Death Index. Participants who did not respond were assumed to be alive if they were not listed in the National Death Index. If a death from cancer or CVD was identified, we sought medical records to confirm the cause of death. We obtained death certificates when the cause could not be confirmed by other sources. Cause of death was decided on the basis of all available information, such as death certificates, medical records, and autopsy results. We classified deaths as caused by CHD (International Classification of Diseases, Ninth Revision, codes 410 to 414), CVD (codes 390 to 459), or all other causes. These CVD codes include all CHD and other heart disease, cerebrovascular diseases, hypertension, diseases of arteries and veins, and other diseases of the circulatory system. For the analyses of the risk of incident MI, we used MI cases that were confirmed by review of medical records by physicians with no knowledge of the risk factor status. We used the World Health Organization criteria to define MI: symptoms in addition to either diagnostic electrocardiographic changes or elevated cardiac enzyme levels.18

Statistical Analyses

We calculated mortality according to history of gout and CHD at baseline as well as the diagnoses that were updated with each questionnaire cycle during follow-up. We computed the person-time of follow-up for each man as the interval between the date on which the 1986 questionnaire was returned and the date of death from any cause (or a diagnosis of MI for MI analyses) or the end of the study period, whichever came first. To investigate the link between gout and mortality separately with regard to the presence of CHD, our primary analysis was stratified by history of CHD. Within each stratified group, the relative risk (RR) of death was calculated by a comparison of the rate for the referent category of no gout. Duration of gout was calculated as years since first diagnosis of gout. The variable was updated with each questionnaire cycle and was divided into 4 categories (>5 years, 6 to 10 years, 11 to 15 years, ≥16 years). For the analysis of duration of gout, we used nongout participants as the reference. We employed Cox proportional hazards regression19 in the analyses. To control as finely as possible for confounding by age, calendar time, and any possible 2-way interactions between these 2 time scales, we stratified the analysis jointly by age in months at start of follow-up and calendar year of the current questionnaire cycle. Multivariate models were adjusted for age (continuous), history of hypertension, history of hypercholesterolemia, history of diabetes mellitus, aspirin use (yes/no), diuretic use (yes/no), smoking (never, past, current; 1 to 14, 15 to 24, ≥25 cigarettes/day), body mass index (<21, 21 to 22.9, 23 to 24.9, 25 to 29.9, ≥30), physical activity (quintiles), alcohol intake (nondrinker, <5, 5 to 9, 10 to 14, 15 to 29, 30 to 49, ≥50 g/day), family history of MI (yes/no), total energy intake (quintiles), trans fat (quintiles), dietary cholesterol (quintiles), protein (quintiles), linoleic fatty acid (quintiles), and the ratio of polyunsaturated fat to saturated fat. The SAS PHREG procedure (SAS Institute, Cary, NC) was used for all analysis, and the Anderson-Gill data structure20 was used to handle time-varying covariates efficiently. All covariates except parental history of MI were updated in each questionnaire cycle. We conducted analyses stratified by age (<60, 60 to 69, and ≥70 years), hypertension (yes/no), hypercholesterolemia (yes/no), and family history of MI (yes/no). For all RRs, we calculated 95% confidence intervals (CIs). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

During 576,515 person-years of follow-up in 51,297 men, we documented 5825 deaths (2132 CVD deaths and 1576 CHD deaths). The characteristics of men according to the categories of gout and CHD at baseline are shown in Table 1. In this cohort of men, 4.4% had only gout, 6.9% had only prior CHD, and 1% had both gout and CHD at baseline. Men with CHD and gout were more likely to be smokers. A history of hypertension or hypercholesterolemia was more frequent among those with gout or MI. Men with CHD more often had a parental history of MI and used aspirin.

The RR of death from all causes, CVD, and CHD according to history of gout and CHD at baseline are presented in Table 2. Compared with men without history of gout and CHD at baseline, the multivariate RRs among men with history of gout were 1.28 (95% CI, 1.15 to 1.41) for total mortality, 1.38 (95% CI, 1.15 to 1.66) for CVD deaths, and 1.55 (95% CI, 1.24 to 1.93) for fatal CHD. The corresponding RRs among men with preexisting CHD were 1.25 (95% CI, 1.09 to 1.45), 1.26 (95% CI, 1.07 to 1.50), and 1.24 (95% CI, 1.04 to 1.49) (Table 2). The multivariate RR for non-CVD deaths was 1.25 (95% CI, 1.10 to 1.41) among men without preexisting CHD.

We then updated the status of gout and CHD every 2 years during follow-up. This update resulted in the assignment of more deaths to the categories with history of gout, CHD, or both, as more participants developed these conditions during the study period (Table 3). The overall findings were similar to the results that used baseline information (Table 2). Similarly, when we repeated our analyses with only incident...
cases of gout after exclusion of the prevalent cases of gout at baseline, the results were similar. The multivariate RRs among men with incident gout were 1.28 (95% CI, 1.13 to 1.46) for all-cause mortality, 1.31 (95% CI, 1.08 to 1.59) for CVD deaths, and 1.30 (95% CI, 1.04 to 1.62) for CHD deaths, as compared with those without incident gout.

Risk of total mortality did not change consistently across categories of gout duration. Compared with men without gout, the multivariate RRs for all cause mortality were 1.28 (95% CI, 1.13 to 1.46) for all-cause mortality, 1.31 (95% CI, 1.08 to 1.59) for CVD deaths, and 1.30 (95% CI, 1.04 to 1.62) for CHD deaths, as compared with those without incident gout.

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We examined whether the associations between prior gout and CHD and mortality varied by other potential risk factors (Table 4). For these analyses we used updated gout and CHD status and also updated the stratification variables every 2 years. The RR of death as a result of gout in the oldest age group tended to be lower than in the younger groups. Other subgroup analyses consistently suggested an increased all-cause or CHD mortality among men with gout (Table 4).

The RRs for nonfatal MI according to the presence of incidence gout (both self-reported cases and confirmed cases) are shown in Table 5. Participants with confirmed gout by the ACR criteria15 had a higher risk of nonfatal MI than those without confirmed gout (multivariate RR, 1.59; 95% CI, 1.04 to 2.41). When we used self-reported cases of incident gout in our analysis, the risk was only slightly lower and remained significant (Table 5).

### Discussion

Our objective was to prospectively evaluate the potential associations between history of gout and the risk of mortality and MI. In this large prospective cohort of men, we found that men with gout had a higher risk of death from all causes. Among men without preexisting CHD, the increased mortality risk was caused by elevated risk of CVD deaths, particularly CHD deaths. Of note, the magnitude of the excess risk for CHD deaths (55%) was similar to that for nonfatal MI associated with incident cases of confirmed gout (59%). These associations were independent of age, body mass index, smoking, family history of MI, use of diuretic and aspirin, dietary risk factors, and risk conditions such as diabetes mellitus, hypercholesterolemia, and hypertension. The present study provides the first prospective data about the mortality impact of gout. These findings provide support for aggressive management of cardiovascular risk factors such as hypertension, dyslipidemia, and lifestyle factors in patients with gout.

Several potential mechanisms exist for the observed excess cardiovascular deaths in patients with gout. Hyperuricemia,
the culprit of gout pathogenesis, is associated with CVD in humans, although whether it is an independent risk factor with a pathogenic role in CVD or only a marker for associated CVD risk factors, such as insulin resistance, obesity, diuretic use, hypertension, and renal disease, remains unclear.\textsuperscript{21,22} Approximately two thirds of previous epidemiological studies reported an independent link between serum uric acid levels and cardiovascular outcomes after adjustment for various covariates.\textsuperscript{22} For example, the National Health and Nutrition Examination Survey (NHANES) I Follow-Up Study reported that serum uric acid was an independent predictor of cardiovascular mortality in subjects \textsuperscript{45} years old regardless of sex, menopausal status, diuretic use, presence of CVD, or race.\textsuperscript{23} In the Framingham Study, serum

<table>
<thead>
<tr>
<th>Disease Status</th>
<th>No CHD</th>
<th>CHD</th>
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<tbody>
<tr>
<td></td>
<td>No Gout</td>
<td>Gout</td>
</tr>
<tr>
<td>Deaths from all causes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>4017</td>
<td>410</td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.43 (1.29 to 1.58)</td>
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<tr>
<td>Multivariate RR (95% CI)</td>
<td>1.0</td>
<td>1.28 (1.15 to 1.41)</td>
</tr>
<tr>
<td>All cardiovascular deaths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>1067</td>
<td>137</td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.76 (1.47 to 2.10)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)</td>
<td>1.0</td>
<td>1.38 (1.15 to 1.66)</td>
</tr>
<tr>
<td>Fatal CHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>646</td>
<td>90</td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.95 (1.57 to 2.44)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)</td>
<td>1.0</td>
<td>1.55 (1.24 to 1.93)</td>
</tr>
</tbody>
</table>

RRs were adjusted for age (continuous), history of hypertension, history of hypercholesterolemia, history of diabetes mellitus, aspirin use (yes/no), diuretic use (yes/no), smoking (never, past, current; ≥14, 15 to 24, ≥25 cigarettes/day), body mass index (<21, 21 to 22.9, 23 to 24.9, 25 to 28.9, ≥29), physical activity (quintile), alcohol intake (non-drinker, <5, 5 to 9, 10 to 14, 15 to 29, 30 to 49, ≥50 g/day), family history of MI (yes/no), total energy intake (quintile), trans fat (quintile), dietary cholesterol (quintile), protein (quintile), linoleic fatty acid (quintile), and ratio of polyunsaturated fat to saturated fat.

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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Gout</td>
<td>Gout</td>
</tr>
<tr>
<td>Deaths from all causes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>3379</td>
<td>451</td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.36 (1.23 to 1.50)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)</td>
<td>1.0</td>
<td>1.25 (1.13 to 1.38)</td>
</tr>
<tr>
<td>All cardiovascular deaths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>784</td>
<td>124</td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.61 (1.33 to 1.94)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)</td>
<td>1.0</td>
<td>1.32 (1.09 to 1.60)</td>
</tr>
<tr>
<td>Fatal CHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>434</td>
<td>71</td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.73 (1.35 to 2.23)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)</td>
<td>1.0</td>
<td>1.44 (1.12 to 1.86)</td>
</tr>
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The diagnoses of gout and CHD were updated every 2 years. RRs were adjusted for the same covariates as in Table 2.
urate levels were not independently associated with the risk of CVD,10 but gout was associated with a 60% increased risk of CHD in men, primarily attributed to a 2-fold excess of angina pectoris.11 Furthermore, a recent Finnish prospective study of middle-aged men found that the RR of CVD death between extreme tertiles of baseline urate levels was 3.7 after adjustment for various potential confounders such as biomarkers commonly associated with gout, CVD, and metabolic syndrome.24 Further adjustment for markers related to the metabolic syndrome (such as triglyceride and high-density lipoprotein cholesterol level) increased the RR to 4.8. Recently, a novel rodent model of arteriolopathy and hypertension induced by mild hyperuricemia has brought new insight into this possible association.21,22,25,26 The rodent model showed that uric acid could cause renal afferent arteriolopathy and tubulointerstitial disease, which leads to hypertension.25,26 The renal lesions and hypertension were prevented or reversed by a reduction of uric acid levels.25,26 Furthermore, hyperuricemia that occurred as a complication of diuretic therapy has been implicated as a risk factor for CVD events. The Systolic Hypertension in the Elderly Program (SHEP) trial27 found that participants who developed hyperuricemia while on chlorthalidone therapy sustained CVD events at a rate similar to participants treated with placebo. Data from the Losartan Intervention for End Point Reduction in Hypertension (LIFE) trial indicated that treatment with losartan (a uricosuric angiotensin receptor blocker) attenuated the time-related increase in serum uric

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| TABLE 4. Subgroup Analysis of Multivariate RRs of Death From All Causes and CHD According to the Status of Gout and CHD at Baseline and During Follow-Up in the Health Professionals Follow-Up Study (1986–1998) |
|-----------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Disease Status                          | No CHD          | CHD             | No CHD          | CHD             |
|                                          | Gout, RR (95% CI) | Gout, RR        | No Gout, RR     | Gout, RR (95% CI) |
| All-cause deaths                        |                 |                 |                 |                 |
| Age, y                                 |                 |                 |                 |                 |
| <60 (n=845)                            | 1.0             | 1.30 (0.96 to 1.74) | 1.0             | 1.59 (1.02 to 2.49) |
| 60 to 69 (n=1816)                      | 1.0             | 1.35 (1.13 to 1.61) | 1.0             | 1.47 (1.21 to 1.79) |
| ≥70 (n=3164)                           | 1.0             | 1.16 (1.01 to 1.32) | 1.0             | 1.31 (1.15 to 1.50) |
| Hypertension                           |                 |                 |                 |                 |
| No (n=2991)                            | 1.0             | 1.25 (1.06 to 1.47) | 1.0             | 1.53 (1.26 to 1.86) |
| Yes (n=2878)                           | 1.0             | 1.24 (1.09 to 1.41) | 1.0             | 1.30 (1.14 to 1.48) |
| Hypercholesterolemia                   |                 |                 |                 |                 |
| No (n=3758)                            | 1.0             | 1.30 (1.15 to 1.47) | 1.0             | 1.16 (0.98 to 1.37) |
| Yes (n=2067)                           | 1.0             | 1.15 (0.96 to 1.37) | 1.0             | 1.50 (1.30 to 1.72) |
| Family history of MI                   |                 |                 |                 |                 |
| No (n=5087)                            | 1.0             | 1.29 (1.16 to 1.43) | 1.0             | 1.32 (1.17 to 1.49) |
| Yes (n=738)                            | 1.0             | 0.90 (0.63 to 1.29) | 1.0             | 1.47 (1.15 to 1.89) |
| CHD Deaths                             |                 |                 |                 |                 |
| Age, y                                 |                 |                 |                 |                 |
| <60 (n=168)                            | 1.0             | 1.84 (0.93 to 3.61) | 1.0             | 1.73 (1.00 to 3.01) |
| 60 to 69 (n=489)                       | 1.0             | 2.10 (1.38 to 3.18) | 1.0             | 1.58 (1.22 to 2.04) |
| ≥70 (n=919)                            | 1.0             | 0.98 (0.68 to 1.41) | 1.0             | 1.24 (1.03 to 1.49) |
| Hypertension                           |                 |                 |                 |                 |
| No (n=626)                             | 1.0             | 1.55 (0.98 to 2.47) | 1.0             | 1.72 (1.32 to 2.25) |
| Yes (n=950)                            | 1.0             | 1.26 (0.93 to 1.71) | 1.0             | 1.30 (1.09 to 1.54) |
| Hypercholesterolemia                   |                 |                 |                 |                 |
| No (n=816)                             | 1.0             | 1.31 (0.93 to 1.83) | 1.0             | 1.17 (0.92 to 1.47) |
| Yes (n=760)                            | 1.0             | 1.55 (1.05 to 2.30) | 1.0             | 1.47 (1.22 to 1.77) |
| Family history of MI                   |                 |                 |                 |                 |
| No (n=1298)                            | 1.0             | 1.41 (1.07 to 1.85) | 1.0             | 1.24 (1.05 to 1.46) |
| Yes (n=278)                            | 1.0             | 1.68 (0.84 to 3.36) | 1.0             | 1.82 (1.34 to 2.47) |

RRs were adjusted for the same covariates as in Table 2.
acid in a statistically significant manner, and this difference seemed to account for 27% of the total treatment effect on the composite CVD end points.\(^2\)^\(^{11,28}\) Furthermore, presence of gout per se may pose an increased risk of CVD beyond these potential contributions from hyperuricemia, as suggested by the recent study based on MRFIT.\(^12\) One possible explanation for this excess risk independent of uric acid levels is that ongoing low-grade inflammation among patients with gout may promote atherogenesis and thrombogenesis, as seen in other inflammatory rheumatic disorders associated with higher risk of CVD (eg, RA or lupus).\(^2\)^\(^{12}\)

Several strengths and potential limitations of the present study deserve comment. Our study was considerably larger than previous studies on gout,\(^1,11,29–33\) and our exposure data and covariate information were prospectively collected. Because we did not validate baseline cases of gout, we used self-reported gout diagnosed by a physician as our primary definition, which leaves some misclassification inevitable. Nonetheless, it is unlikely that misclassification of the gout diagnosis would explain the associations observed in the present study, as the definition was also successfully used in previous studies, such as the Johns Hopkins Precursor Study\(^1\) and the recent MRFIT report.\(^12\) We also have included this definition as a secondary definition in our own previous studies for risk factors for gout\(^2\)^\(^3\) and found that suspected associations became even stronger when we used more specific case definitions such as cases that meet the ACR criteria or crystal-proven or tophaceous gout.\(^2\)^\(^{3}\) This notion is further supported by our finding of the significant association with the risk of MI by use of the incident cases of gout confirmed by the ACR criteria. Although studies have shown that xanthine oxidase inhibition (eg, allopurinol use) improves endothelial function in patients with chronic heart failure, coronary artery disease, or diabetes mellitus,\(^34–38\) the present study does not address the impact of gout therapy or disease severity. There was no clearly increased association with increased duration of gout for all-cause mortality and for the top duration category in CHD mortality. Potential explanations for this include survival cohort effects (ie, removal of those most susceptible), certain treatment effect (eg, endothelial benefit of allopurinol\(^34–38\)), increased screening and treatment of preventable conditions among long-standing gout cases, confounding of unmeasured covariates (eg, disease severity), and a threshold effect of gout on the outcomes. Similarly, potential explanations for the trend of a larger RR for death among younger patients with gout include a survival cohort effect and increased disease severity among early-onset gout cases. Evaluation of these factors in future studies would be valuable.

The restriction to health professionals in our cohort is both a strength and a limitation. The cohort of well-educated men minimizes potential for confounding by socioeconomic status, and we were able to obtain high-quality data with minimal loss to follow-up. Although the absolute rates of death and CVD and distribution of gout may not be representative of a random sample of US men, the biological effects of gout on these outcomes should be similar. Our findings are most directly generalizable to men \(\geq\) 40 years old (the most gout-prevalent population\(^29\)). Given the potential influence of female hormones on the risk of gout and CVD in women, prospective studies of women would be valuable.

In conclusion, the present prospective data indicate that individuals with gout have a higher risk of death from all causes. Among men without preexisting CHD, the increased mortality risk is primarily caused by an elevated risk of CVD death, particularly from CHD. The present findings provide support for aggressive management of cardiovascular risk factors in patients with gout.

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Disclosures
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References


**CLINICAL PERSPECTIVE**

Gout is the most common inflammatory arthritis in adult males, and the overall disease burden of gout remains substantial and may be growing. However, it is unknown whether gout affects life expectancy. Although gout and hyperuricemia are associated with several conditions linked to reduced survival (eg, insulin resistance syndrome, obesity, and hypertension), no large-scale prospective data are available on the potential independent impact of gout on mortality. Furthermore, although many studies have suggested that hyperuricemia is associated with cardiovascular disease, limited data are available on the impact of gout on cardiovascular disease. Over a 12-year period, the present study prospectively examined the relation between a history of gout and the risk of death and myocardial infarction in 51 297 male participants of the Health Professionals Follow-Up Study. The present study found that men with gout have a 28% higher risk of death from all causes, a 38% higher risk of cardiovascular disease death, and a 55% higher risk of death from coronary heart disease than men without gout. Furthermore, men with gout had a 59% higher risk of nonfatal myocardial infarction than men without gout. These associations were independent of age, body mass index, smoking, family history of myocardial infarction, use of diuretic and aspirin, dietary risk factors, and risk conditions such as diabetes mellitus, hypercholesterolemia, and hypertension. These results provide the first prospective data about the mortality impact of gout and further support the link between hyperuricemia, gout, cardiovascular disease, and death. The present findings provide support for aggressive management of cardiovascular risk factors in patients with gout.
Independent Impact of Gout on Mortality and Risk for Coronary Heart Disease
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