LITERATURE REVIEW

Calcification of the Aortic Arch
Risk Factors and Association With Coronary Heart Disease, Stroke, and Peripheral Vascular Disease

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Many radiologists note aortic arch calcification on chest radiograph reports. Since calcium deposits in extracoronary arterial beds can reflect underlying atherosclerosis, is this finding predictive of cardiovascular disease or mortality on long-term follow-up?

METHODS

The study cohort consisted of 60,393 women and 55,916 men aged 30–89 years at baseline. The subjects were enrolled in a California health maintenance organization and attended voluntary comprehensive health assessments from 1964 through 1973. The incidence of hospitalization and/or mortality data were determined using discharge diagnosis codes and death records through December 31, 1997 (median follow-up was 28 years). The main outcome measure was hospitalization for or death due to coronary heart disease, ischemic stroke, hemorrhagic stroke, or peripheral vascular disease as associated with aortic arch calcification found on the chest radiograph obtained at the initial comprehensive health evaluation. About 36% of the study participants were followed up until the closing date.

RESULTS

Aortic arch calcification was present in 1.9% of men and in 2.6% of women. Its prevalence increased with age in both sexes. In persons 65 years and older, 10.6% of men and 15.9% of women had aortic arch calcification. During the median follow-up of 28 years and after multivariate analysis for age, race/ethnicity, educational attainment, cigarette smoking, alcohol
consumption, body mass index, serum cholesterol level, hypertension, diabetes, and family history of myocardial infarction, aortic arch calcification was associated with an increased risk for coronary heart disease (in men, relative risk [RR], 1.27; 95% confidence interval [CI], 1.11–1.45; in women, RR, 1.22; 95% CI, 1.07–1.38). In addition, calcification conferred a significant increase in risk for ischemic stroke among women (RR, 1.45; 95% CI, 1.28–1.67). In men, no significant associations were found for ischemic or hemorrhagic stroke. Associations of borderline significance were seen for peripheral vascular disease in both men and women.

**DISCUSSION**

In this population-based cohort of adults, aortic arch calcification found on routine chest radiographs was positively associated with the traditional cardiovascular risk factors and was an independent predictor of coronary artery disease risk and increased risk of cardiovascular events.
Cognitive Impairment in Older People: Prevalence, Vascular Factors, Impact on Disability

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Individuals with problems with memory or other areas of cognition that are not sufficiently severe to meet the criteria for dementia are diagnosed as having cognitive impairment, no dementia (CIND). These individuals are judged to be distinct from individuals with normal cognitive ability for their age. A subgroup of CIND without any neurological or psychiatric disease is classified as age-related cognitive decline (ARCD).

This condition is receiving more attention today as a possible precedent to dementia. This study evaluates the prevalence of dementia and CIND in a general population, whether there are risk factors associated with CIND, and whether CIND is associated with disability.

STUDY METHODOLOGY

This work is part of the Italian Longitudinal Study on Aging, a population-based survey begun in 1992. A sample of size 5462 was randomly selected from the registry. This registry includes a detailed database with direct clinical evaluation for hypertension, angina, myocardial infarct, arrhythmia, diabetes, and peripheral artery disease. Smoking history, alcohol use, and activities of daily living were based on self-report. They were stratified by 5-year age groups, age 65–84, and equal numbers of each sex and both rural and urban areas of Italy were represented.

Participation of this sample in the phase 1 screening using the Mini-Mental State Examination (MMSE) was 83%. Individuals with a score <24 were suspected of cognitive impairment and were examined in phase 2 of the study.

Phase 2 was a clinical assessment by trained neurologists using sections B and H of the Cambridge Mental Disorders of the Elderly Examination (CAMDEX), the Pfeffer Functional Activities Questionnaire, the Hamilton Depres-
sion Scale, and a detailed review of personal history and physical examination. Section H of the CAMDEX includes a structured interview with a relative or caregiver for confirmation of functional activities.

Use of the CAMDEX Section B generates a score for memory, orientation, language, praxis, attention, judgment, abstract thinking, constructional abilities, perception, and calculation. A total score of less than 80 has 92% sensitivity and 96% specificity for detecting cognitive impairment. Dementia was ruled in or out using the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised (DSM-IIIR) criteria. All clinical tools were used to provide the global context of the patient’s condition.

Results are reported as prevalence rates with 95% confidence intervals. Analysis of differences in the frequency of categorical variables was carried out using the chi-squared test. Logistic regression analysis identified variables independently associated with cognitive impairment, and a multiple logistic regression model evaluated the net effect of cognitive impairment on disability controlling for other variables.

RESULTS

The MMSE was administered to 3425 individuals, with 845 having a total score less than 24. Phase 2 testing was done on 780 individuals (92%), with 46% being male. Dementia was diagnosed in 226 (29%), CIND in 391 (50%), and normal cognitive function in 163 (21%).

CIND was attributed to neurological disease in 13%, depression in 10%, other psychiatric causes in 2%, and sociocultural factors in 6%. The remaining 69% were assessed as age-related cognitive decline (ARCD).

Table 1 reports the prevalence of dementia, CIND, and ARCD for all age groups.

Women had a higher prevalence in all age groups considered. Individuals with CIND were more likely to be women, older, and less educated than those without cognitive decline.

### Table 1. Prevalence of Cognitive Impairment by Age

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Dementia (n = 226)</th>
<th>CIND (n = 391)</th>
<th>ARCD Subgroup of CIND (n = 270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65–69</td>
<td>1.0 (0.3–1.6)</td>
<td>5.5 (4.0–7.0)</td>
<td>4.2 (2.9–5.5)</td>
</tr>
<tr>
<td>70–74</td>
<td>2.5 (1.5–3.5)</td>
<td>8.3 (6.5–10.1)</td>
<td>5.8 (4.2–7.3)</td>
</tr>
<tr>
<td>75–79</td>
<td>7.6 (5.8–9.4)</td>
<td>18.8 (14.9–22.7)</td>
<td>11.0 (8.8–13.2)</td>
</tr>
<tr>
<td>80–84</td>
<td>18 (15.3–20.7)</td>
<td>19.2 (16.4–22.0)</td>
<td>13.2 (10.8–15.6)</td>
</tr>
<tr>
<td>All ages</td>
<td>5.5 (4.7–6.3)</td>
<td>10.7 (9.6–11.7)</td>
<td>7.5 (6.6–8.4)</td>
</tr>
</tbody>
</table>

Increasing age, previous myocardial infarction, stroke, heart failure, and atrial fibrillation were significantly and positively associated with CIND. Smoking history was negatively associated with CIND. Alcohol use, hypertension, and diabetes did not correlate with CIND.

ARCD was positively associated in the multivariate model only with age (odds ratio [OR] 1.08; 95% CI, 1.05–1.11) and myocardial infarction (OR 1.95; 95% CI, 1.21–3.14). It was negatively associated with education (OR 0.6; 95% CI, 0.55–0.65) and smoking (OR 0.64; 95% CI, 0.45–0.90).

The presence of both CIND and ARCD was linked to functional decline with at least 1 activity of daily living (ADL) impaired in 57.7 and 51.5%, respectively. Of normal individuals, 26.7% had loss of at least 1 ADL.

DISCUSSION

This study documents the magnitude and pattern of cognitive decline in the older population. It is based on a detailed medical database with a detailed neuropsychological evaluation of the participants. The MMSE was used only for screening, and 21% of those failing this test had normal cognitive function.
The estimate of cognitive decline may be conservative. Mild cases of CIND may escape detection. A second source of underestimation is the number of individuals who refused phase 2 testing. The attrition rate was 8% (65 of 845 scoring <24 on MMSE). In this study, these individuals were older than those completing phase 2, and a bias toward reduction in strength of associations was introduced.

The Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), defines age-related cognitive decline (ARCD) as decline that is normal for the person’s age. “Individuals with this condition may report problems remembering names or appointments or may experience difficulty in solving complex problems.” The relationship of ARCD to dementia is not precisely known. This study demonstrates that the presence of ARCD is significantly associated with impairments of ADLs.

There are two surprising findings. While showing an association with stroke, this study failed to show an association of CIND with hypertension. The negative correlation with smoking history also seems contradictory to the known risk it contributes for stroke.

One question that is raised by this study is whether there is a significant rate of progression from CIND, and from ARCD in particular, to dementia. A longitudinal study with follow-up on this cohort would be needed to answer this question.
LITERATURE REVIEW

Prevalence, Clinical Characteristics, and Mortality Among Patients With Myocardial Infarction Presenting Without Chest Pain

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E arly in the course of most physician’s training, they are exposed to the concept of a silent myocardial infarction (MI), the MI that occurs without chest pain. Traditionally that has usually been in the context of a patient with diabetes. This association between diabetes and heart disease has been known for generations. However, the incidence that silent MIs occur in the general population has never been fully studied. The research presented in this landmark article establishes that the rate of silent MI is much higher than estimated, is associated with a longer time to diagnosis, contributes to suboptimal care, and leads to higher mortality.

STUDY DESIGN

A total of 167 hospitals participated in the National Registry of Myocardial Infarction 2 study from June 1994 through March 1998. A total of 434,877 myocardial infarction patients were enrolled in the study. Observations were made prospectively to determine the outcome of those patients who did not experience chest pain during their cardiac event.

RESULTS

To the surprise of many, one third (142,445 patients, 33%) of the patients enrolled in the study did not have chest pain on presentation to the hospital. Several characteristics were noted about this group. On average,

- they were 7 years older (74.2 versus 66.9 years old),
- there was a higher proportion of women (49.0 versus 38.0%),
- there was a history of diabetes (32.6 versus 25.4%).
there was a history of prior heart failure (26.4 versus 12.3%).

As one might expect, this unusual presentation led to longer delays before presentation to the hospital (7.9 versus 5.3 hours). In addition, those patients without chest pain were less likely to be diagnosed as having a confirmed MI at the time of admission (22.2 versus 50.3%), receive thrombolytics or angioplasty (25.3 versus 74.0%), or other traditional MI treatments including aspirin, beta blockers, or heparin. As might be expected given these delays in diagnosis and treatment, in-hospital mortality was significantly higher in those who did not present with chest pain (23.3 versus 9.3%).

**DISCUSSION**

Medical science has known for decades that myocardial infarction can occur without chest pain. It has generally been felt that diseases such as diabetes, which can cause autonomic dysfunction, also needed to be present for such presentation to occur. This large, multicenter prospective study challenges that concept. One third of the MI patients did not have significant chest pain. Six characteristics were noted to be associated with those patients without chest pain. Those were (in order of importance) prior heart failure, prior stroke, older age, diabetes, female sex, and nonwhite racial/ethnic group.

In our day-to-day underwriting of cases, we are often presented with the EKG tracing that suggests prior ischemic disease, which is usually refuted by the applicant or broker with the statement that the applicant “has never had a chest pain in his life.” This study gives warning to us all that ignoring such data or giving too much credence to a patient’s testimony can lead to serious consequences such as misdiagnosis or inaccurate risk determination.
LITERATURE REVIEW

Low Dose Inhaled Corticosteroids and the Prevention of Death from Asthma

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Both the incidence and deaths related to asthma have increased in the United States. The rate of death from asthma clearly increases with severity of disease. Corticosteroids have long been associated with reduction in both airway inflammation and hyperresponsiveness. There is a positive correlation between corticosteroids and measurement of asthma endpoints such as impaired lung function, days of symptoms, and hospitalization frequency.

This study is a population-based (Canadian) epidemiological study to determine whether inhaled corticosteroids prevent asthma-related deaths.

STUDY DESIGN

Of the 2 million people covered by the Saskatchewan Health Universal Insurance Plan, 30,569 were identified as having received 3 or more prescriptions for antiasthma medication (1975–97). These were followed until death, age 55, emigration from the province, or the end of the study in December 1997.

There were 562 deaths in the cohort, 77 of which were classified as asthma related. Eleven deaths were during a period in which medication data was not collected and thus were eliminated from the study group. The 66 remaining deaths were matched with 2681 controls.

RESULTS

In 47% of the deaths and 54% of the controls, there was no inhaled corticosteroid usage in the 12 months prior to the event. Using 6 or more canisters within the previous year was present in only 1 death (1.5%) as compared with 7.5% of the controls. Within the 6 months prior to death, 56% used no inhaled corticosteroids compared with 65% of controls.
Thirteen patients that had asthma-related deaths had discontinued the inhaled corticosteroids within 1–3 months prior to their event. This represented 19.7% of the death occurrences compared with 9% of the controls.

**STUDY CONCLUSIONS**

The authors conclude that inhaled corticosteroids at several doses a day decrease asthma-related deaths. Mortality was markedly increased in the first 3 months after medication discontinuance.

**STUDY LIMITATIONS**

There are significant limitations to this study. Even though there were some 30,000 patients that received prescriptions for antiasthma medications, the number of deaths in the study was only 66. This group of deaths is small for analysis. The statistical power of such small numbers remains questionable. Since only one half of the deaths had used inhaled corticosteroids, the remaining subset (n = 35) seems too small to make conclusions on the death rate per dosage. In the case group who had used 6 or more inhaled canisters in a 6-month period, there was only 1 patient. The entire province was used as a population, and one wonders the difference in prescribing practices since there were no standard clinical protocols used. There was also a lack of pulmonary function testing as an objective measure. This may have added credibility to their observations on the effects of inhaled corticosteroids to the endpoint of asthma-related mortality.

Since 20% of the deaths occurred within 3 months from the discontinuance of inhaled corticosteroids, this medication change may be a red flag rather than a marker of clinical improvement. One half of the deaths were in the subset of patients who were not using inhaled corticosteroids in the previous 12 months. This group should be evaluated regarding whether the asthma is undertreated or whether patients are simply noncompliant.