Review

SJWEH Suppl 2006;(2):50–53

Ischemic heart disease and welding in Scandinavian studies

by Bengt Sjögren, MD,[1] Finn Gyntelberg, MD,[2] Bjørn Hilt, MD [3]

Sjögren B, Gyntelberg F, Hilt B. Ischemic heart disease and welding in Scandinavian studies. *SJWEH Suppl* 2006;(2):50–53.

This is a review of three Scandinavian studies of ischemic heart disease (IHD) among welders. The three studies were not biased by comparison with national rates. The Copenhagen Male Study, comprising 3321 men, revealed an increased risk of myocardial infarction among workers exposed to both welding and soldering fumes. In a Norwegian study of stainless steel welders and metal workers, an increased risk for myocardial infarction was observed [odds ratio 2.4, 95% confidence interval (95% CI) 1.1–4.9]. Male welders and gas cutters were identified in the Swedish national censuses of 1990 and followed until the end of 1995. The IHD mortality among the welders was compared with that of gainfully employed men. Increased mortality due to IHD was observed (standardized mortality ratio 1.35, 95% CI 1.1–1.6). Additional studies are needed to describe the dose–response relationships between welding fume exposures and the effects on inflammatory markers and the occurrence of IHD.

Key terms ABO blood groups; C-reactive protein; fibrinogen; interleukin-6; review.

Metal welding is associated with the inhalation of gases and respirable particles. In most previous cohort mortality studies of welders, which have used expected numbers of deaths based on national rates, a decreased risk regarding ischemic heart disease (IHD) has been observed. When the death rates of welders are compared with those of the total population, the result may be an underestimation of the true risk, as the general population also includes sick and disabled people unable to work. This selection bias is well known as the healthy worker effect. However, in two previous studies increased mortality among welders due to IHD was observed, despite this biased comparison (1, 2).

This is a review of three Scandinavian studies of welders that were not biased by comparison with national rates.

Denmark

The Copenhagen Male Study was set up in 1970 as a prospective cohort study of 5249 men with a mean age of 48 years. All of the survivors from the 1970 study were traced, and a new baseline was established in 1985–1986 (3). A total of 3387 men agreed to participate, and their mean age was 63 (range 53–75) years. As some data were missing the cohort comprised 3321 men in the analysis. ABO blood groups were determined, as they have been discussed as a genetic risk indicator for IHD. Among men with blood type O (N=1417), 4.7% had a history of myocardial infarction, as compared with 5.7% of the men with other phenotypes (N=1904). According to retrospective information, some occupational exposures were associated with an increased risk of IHD among men with phenotype O. Men with this phenotype who had been exposed to soldering fumes for more than 5 years several times a week had an increased risk of IHD when compared with men with the same phenotype with no occupational exposure to air pollutants [odds ratio (OR) 3.0, 95% confidence interval (95% CI) 1.6–5.8]. Men with phenotype O and exposed to welding fumes several times a week for more than 5 years also had an increased risk of IHD (OR 2.1, 95% CI 1.05-4.3). Among the men with phenotypes

1. Work Environment Toxicology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.
2. Clinic of Occupational and Environmental Medicine, Copenhagen University Hospital, Bispebjerg, Copenhagen, Denmark.
3. Department of Occupational Medicine, St Olav's University Hospital in Trondheim, and Department of Cancer Research and Molecular Medicine at the Faculty of Medicine at the Norwegian University of Technology and Science, Trondheim, Norway.

Reprint requests to: Bengt Sjögren, Work Environment Toxicology, Institute of Environmental Medicine, Karolinska Institutet, PO Box 210, SE-171 77 Stockholm, Sweden. [E-mail: bengt.sjogren@ki.se]

other than O, no association was found between airborne pollutant exposure and IHD risk. In a further analysis, all of the participants with overt cardiovascular disease at baseline (1985–1986) were excluded, and the cohort was followed until 31 December 1993. Men with phenotype O and exposed to soldering fumes for more than 5 years several times a week or more still had an increased risk of IHD when compared with the men with the same phenotype and no occupational exposure to air pollutants (OR 1.8, 95% CI 1.0-3.2). Among the welders no statistically significant increased risk was observed (OR 1.1, 95% CI 0.6-2.2). The calculated odds ratios were based on logistic regression analyses that took several possible confounders into account (eg, smoking habits, serum lipids, body mass index, blood pressure, hypertension, leisure-time activities, and alcohol habits).

One possible explanation of the discrepancy between historical IHD and the prospective follow-up from 1985–1986 until the end of 1993 could be a larger proportion of older (mean age 63 years) retired, and consequently previously exposed but now unexposed persons in the second analysis. Air pollutant exposure could have an effect similar to that of smoking. The mortality of ex-smokers tends to be similar to that of nonsmokers after several years of abstinence (4), and this phenomenon may be valid for other air pollutants as well.

Norway

In a welding factory, predominantly producing equipment of stainless steel for industry and agriculture, 328 exposed men were eligible for the study (5). All of the men had worked at the plant for more than 1 year between 1960 and 1993, and they were all below 70 years of age at the time of the study. Their main tasks were stainless steel welding and grinding. In the exposed group 236 (72%) men answered a standardized questionnaire. A control group was chosen randomly from the general population matched for age. Among the 1561 men who were eligible for the control group, 1159 answered the questionnaire (74%). Restriction to at least 5 years of occupational activity after 1960 reduced the control group to 989 men. Among the stainless steel welders and other metal workers, an increased risk for myocardial infarction (OR 2.4, 95% CI 1.1-4.9) was observed in a multiple logistic regression analysis adjusting for age, smoking habits, education, and first degree relatives with IHD. The question on myocardial infarction was validated, and the sensitivity was 100% for the exposed group and 90% for the control group. The corresponding specificities were both 90%. The exposed group was further divided into specific work-related exposures or activities. In this analysis, grinding was associated with an increased risk of myocardial infarction (OR 2.5, 95% CI 1.1–5.9), while welding was not (OR 1.8, 95% CI 0.7–4.4).

Sweden

Male welders and gas cutters were identified in the national censuses of 1970 and 1990 (6). The first cohort comprised 31 722 welders in the 1970 national census. The cohort was followed from 1970 until 31 December 1995. The second cohort comprised 28 068 welders in the 1990 national census and was followed until the end of 1995. The reference groups comprised all gainfully employed men identified in the same censuses. The total numbers of referents in the 1970 and 1990 censuses were 2 047 861 and 2 163 967, respectively. The age range of the welders and the referents was 20–64 years at the time of entry.

Increased mortality due to IHD was observed in both the 1970 [standardized mortality ratio (SMR) 1.06, 95% CI 1.02–1.11) and 1990 (SMR 1.35, 95% CI 1.10–1.64) cohorts. Smoking habits were surveyed in the male population between 1986 and 1990. In the general population 29% currently smoked daily compared with 42% among the welders. The observed relative risk in the first cohort could be explained by differences in smoking habits, after calculations proposed by Axelson & Steenland (7). However, the increased relative risk in the second cohort followed from 1990 to 1995 was unlikely to be explained by smoking habits. It was unlikely that the work conditions were worse in 1990 than 20 years before. The 1970 cohort contained a larger proportion of retired men than the 1990 cohort, and this fact may also explain the difference as discussed before.

Lower socioeconomic classes had an increased risk of IHD when compared with higher social classes (8). However, socioeconomic status was not taken into account in this study. Suadicani et al (9) found an increased risk of IHD (relative risk 1.44, 95% CI 1.1–2.0) after adjustment for age among lower social classes when compared with higher classes. After adjustment for age, use of tobacco and alcohol, physical activity, systolic and diastolic blood pressure, hypertension, body mass index, cholesterol, high-density lipoproteins, triglycerides, serum selenium levels, and retirement status, the relative risk decreased to 1.38 (95% CI 1.0–1.9). After further adjustment for two significant occupational exposures (soldering fumes and organic solvents), the relative risk decreased to 1.24 (95% CI 0.9–1.8) (9). Thus exposure to particles and irritant gases may have been one factor explaining the difference between the social classes.

Discussion

This review of three studies of welders in Scandinavia, not based on comparisons with national mortality rates, indicated an increased risk for IHD. However, none of the studies addressed dose–response relations or postexposure risks.

The proportion of female welders was generally small. However, the total number of female welders in Sweden increased from 761 (2%) in 1970 to 1932 (6%) in 1990. These cohorts have also been followed until 1995. In the first cohort the total number of deaths due to IHD was 15 versus 11.9 expected, and in the second cohort it was none versus 0.9 expected.

Welders are sometimes exposed to metal fumes associated with fever. Zinc oxide is the most well known inducer of metal fume fever. The inhalation of zinc oxide fume increases the plasma concentration of interleukin-6 (10). Interleukin-6 is known to stimulate hepatocytes to produce and secrete fibrinogen (11). A high plasma level of fibrinogen is an established risk factor for coronary heart disease (12, 13). A general hypothesis has linked the inhalation of particles to the occurrence of IHD in the following way: the inhalation of air pollutants retained in the lungs will hypothetically create a low-grade inflammation in association with an increase in plasma fibrinogen. The high concentration of fibrinogen and possibly other factors associated with blood coagulation will increase the likelihood of blood clotting and thereby the risk of myocardial infarction and IHD (14, 15).

In a recent study of welders, the median exposure to $PM_{2.5}$ (particulate matter <25 μm in diameter) was 1.66 mg/m^3. Among the nonsmokers, welding fume exposure was associated with a significant increase in white blood cell and neutrophil counts immediately following exposure. A significant decrease in fibrinogen levels was observed in nonsmokers. Sixteen hours after welding exposure, CRP (C-reactive protein) levels were found to be significantly increased in both nonsmokers and smokers. The increase in inflammatory markers represented a response to the air pollutants (16). The decrease in fibrinogen concentrations is somewhat surprising but has been observed in a study of environmental air pollutants. This decrease may indicate the consumption of fibrinogen and an increase in blood coagulation (17).

In previous studies, it has been observed that chronic bronchitis is more prevalent among welders than among different reference groups (18). In the original Framingham Heart Study (19) chronic cough was associated with the occurrence of myocardial infarction after adjustment for age, gender, smoking, forced vital capacity, diabetes mellitus, systolic blood pressure, angina pectoris, and total cholesterol level. In a Finnish study chronic bronchitis was also associated with an increased risk of coronary disease after adjustment for three major risk indicators (20). A tentative interpretation of these results could be that exposures associated with chronic bronchitis are also associated with IHD.

Additional studies are needed to describe the dose–response relations between welding fume exposures and the effects on inflammatory markers such as interleukin-6 and fibrinogen and the occurrence of IHD.

References

1. Newhouse ML, Oakes D, Woolley AJ. Mortality of welders and other craftsmen at a shipyard in NE England. Br J Ind Med. 1985;42:406–10.
2. Moulin JJ, Wild P, Haguenoer JM, Faucon D, De Gaudemaris R, Mur JM, et al. A mortality study among mild steel and stainless steel welders. Br J Ind Med. 1993;50:234–43.
3. Suadicani P, Hein HO, Gyntelberg F. Airborne occupational exposure, ABO phenotype and risk of ischaemic heart disease in the Copenhagen Male Study. J Cardiovasc Risk. 2002; 9:191–8.
4. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ. 1994;309:901–11.
5. Hilt B, Qvenild T, Rømyhr O. Morbidity from ischemic heart disease in workers at a stainless steel welding factory. Norsk Epidemiologi. 1999;9:21–6.
6. Sjögren B, Fossum T, Lindh T, Weiner J. Welding and ischemic heart disease. Int J Occup Environ Health. 2002;8:309–11.
7. Axelson O, Steenland K. Indirect methods of assessing the effects of tobacco use in occupational studies. Am J Ind Med. 1988;13:105–18.
8. Rosengren A, Wedel H, Wilhelmsen L. Coronary heart disease and mortality in middle aged men from different occupational classes in Sweden. BMJ. 1988;297:1497–500.
9. Suadicani P, Hein HO, Gyntelberg F. Do physical and chemical working conditions explain the association of social class with ischaemic heart disease? Atherosclerosis. 1995;113:63–9.
10. Fine JM, Gordon T, Chen LC, Kinney P, Falcone G, Beckett WS. Metal fume fever: characterization of clinical and plasma IL-6 responses in controlled human exposures to zinc oxide fume at and below the threshold limit value. J Occup Environ Med. 1997;39:722–6.
11. Akira S, Kishimoto T. IL-6 and NF-IL6 in acute-phase response and viral infection. Immunol Rev. 1992;127:25–50.
12. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA. 1998;279:1477–82.
13. Danesh J, Lewington S, Thompson SG, Lowe GDO, Collins R, the Fibrinogen Studies Collaboration. Plasma fibrinogen level and the risk of major cardiovascular diseases and nonvascular mortality: an individual participant meta-analysis. JAMA. 2005;294:1799–809.
14. Seaton A, MacNee W, Donaldson K, Goddon D. Particulate air pollution and acute health effects. Lancet. 1995;345:176–8.
15. Sjögren B. Occupational exposure to dust: inflammation and ischaemic heart disease. Occup Environ Health. 1997;54:466–

69.
16. Kim JY, Chen J-C, Boyce PD, Christiani DC. Exposure to welding fumes is associated with acute systemic inflammatory responses. Occup Environ Med. 2005;62:157–63.
17. Seaton T, Soutar A, Crawford V, Elton R, McNerlan S, Cherrie J, et al. Particulate air pollution and the blood. Thorax. 1999;54:1027–32.
18. Sjögren B. Effects of gases and particles in welding and soldering. In: Zenz C, Dickerson OB, Horvath EP, editors. Occupational medicine. 3rd ed. St Louis (MO): Mosby Year Book, Inc; 1994. p 917–25.
19. Haider AW, Larson MG, O'Donnell CJ, Evans JC, Wilson PWF, Levy D. The association of chronic cough with the risk of myocardial infarction: the Framingham Heart Study. Am J Med. 1999;106:279–84.
20. Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Symptoms of chronic bronchitis and the risk of coronary disease. Lancet. 1996;348:567–72.