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REVIEW ARTICLE

Occupational Exposure to Metal Working Fluids and Bladder Cancer: A Systematic Review

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KEYWORDS

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ABSTRACT: Metalworking fluids (MWFs) are complex compounds of oils and chemical additives widely used to cool and lubricate metal machining operations. When sprayed, MWF produces concentrations up to twice the allowable level of US ambient air pollution standards. The study was designed to assess possible relationships between occupational exposure to MWFs and the risk of bladder cancer. Literature entered the study was published from February 2000 to 2021 and provides information on exposure to metalworking fluids and the risk of bladder cancer. We searched PubMed, Scopus, and Web of Sciences from 2000 to 2021. The following subject and keywords were used in the search: "bladder cancer" and "metalworking fluids". Out of 8 studies, 4 were case-control and 4 were cohort and all of them had high NOS scores. The strong exposure-response relationship between bladder cancer and metalworking fluids reinforces the evidence for MWFs as a bladder carcinogen. The literature review in this study also shows that smoking can increase the risk of bladder cancer due to exposure to metalworking fluids.

INTRODUCTION

Metalworking fluids (MWFs) are complex compounds of oils and chemical additives widely used to cool and lubricate metal machining operations [1]. When sprayed, MWF produces airborne particulate matter (PM) at concentrations up to twice the allowable level of US ambient air pollution standards [2]. MWFs, classified as direct (mineral oils), soluble (water-emulsified oils), or synthetic (oil-free), continue to pose potential risks to millions of workers in metalworking jobs. The routes of exposure are dermal, with the bulk liquid phase and

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spraying MWF dust, and inhalation with dust, fog, and vapors. The health effects of MWF exposure have been extensively investigated [3-5].

MWFs contain additives, such as lubricants, extreme-pressure resistant, antimisting, antiwear and coloring agents, corrosion inhibitors, biocides, biostatics or perfumes [6]. In 1998, the National Institute for Occupational Safety and Health (NIOSH) published a standard exposure limit document (REL) for occupational exposure to MWF 0.5 mg / m3 for total PM (TPM) and 0.4 for respirable PM [7]. Potential carcinogens in MWF include hydrocarbons, chlorinated paraffin, aliphatic amines, nitrosamines, PAHs, formaldehyde-releasing agents, diethanolamine, and many other special additives [5]. Efforts to reduce exposure to this potentially carcinogenic MWF have been ongoing for decades [8]. A large number of epidemiological studies show MWFs with numerous concerns for human health, including respiratory and skin diseases for workers [9, 10], malignancies [11], and other related health problems.

The International Agency for Research on Cancer (IARC) has assessed the risk of carcinogenicity due to exposure to semi-refined MWFs as Group A2 [12]. In the literature, an increased risk of bladder cancer has been reported for machinists and mechanics, both of whom use MWF [13-15]. Most of these studies are related to relatively old job periods (before the mid-1990s). However, recent follow-up and exposure studies have also reported an increased risk of bladder cancer among workers who have been exposed to oil dust [13, 16-19].

Based on a review of the literature, this paper reviews and summarizes the most important research on human health risks associated with occupational exposure to MWF. The study was designed to assess possible relationships between occupational exposure to MWFs and the risk of bladder cancer.

MATERIALS AND METHODS

Data sources and searches

The articles used in this study include all cohort and case-control studies that have been published since February 2000 and provide information on exposure to metalworking fluids and bladder cancer risk. The population studied in these articles was mostly automobile manufacturing workers, but other occupations were also considered. We searched PubMed, Scopus, and Web of Sciences from 2000 to 2021. The following subject and keywords were used in the search: “bladder cancer” and “metalworking fluids”.

Data extraction

Mendeley software was used to manage and screen. The title, abstract, and full text were selected based on inclusion and exclusion criteria. Data extraction was performed by two independent authors (ZS and ZM) through a standardized form for extraction of data including study characteristics (author’s name, publication year, starting year (2000)) and characteristics of the study population (sex, occupations, etc.). Studies that included OR, RR, SMR, and HR values were included in the study, and studies that did not have the mentioned items were excluded from the study, even if they had thematic relevance. A total of 8 studies were identified, of which 4 were case-control studies and 4 cohorts. In case-control studies, no direct measurements were made to estimate the exposure of individuals to metalworking fluids. Therefore, the degree of exposure of people to metalworking fluids was estimated with information including employment history, cumulative exposure index, and job-exposure matrix. Also, exposure assessment has been described in previous publications in cohort studies. To provide quantitative combined estimates of standardized mortality ratios (SMRs), the number of cancer deaths observed and SMRs were abstracted from each study. In other articles, relative risk (RR), odds ratio (OR), and hazard ratio (HR) were also considered. For cohort studies with subsequent updates, only the most recent results were considered for consolidated estimates.

Risk of bias assessment

Three independent reviewers (ZM, MV & GH) assessed the study quality based on the nine-star Newcastle Ottawa scale (NOS) [20, 21]: selection (representativeness of the population), comparability of groups (adjustment for confounders such as age, sex) and ascertainment of the outcome. The NOS assigns four stars for selection, two stars for comparability, and three stars for outcome. The NOS score of more than 7 was acknowledged as high quality.

RESULTS

For this study, three databases PubMed, Scopus, and Web of Science were examined. A total of 2679 articles were found from these three sites. After applying the filter by limitation of words, the number of articles found decreased to 384. In the next step, duplicate articles were removed and the total number of articles reached 359. These articles were reviewed by the research team and most of the articles were removed due to irrelevance, lack of inclusion criteria, and lack of necessary information. Finally, 8 articles were reviewed. Table 1 shows the characteristics of the studies including the author's name, Workers' Gender, sample size, Working Context, Study year, Risk Adjusted for Smoking Habits, and exposure assessment.

Table 1. Characteristics of the studies (n = 8) included in the review.

Working Context	Workers' Gender	Sample Size	Adjusted Risk for Smoking Habits	Exposure Assessment	Reference
French steel-producing factories	Male	cases=84 controls=251	Yes	job-exposure matrix	[6]
Various	Male	cases=895 controls=1031	Yes	Occupational history data	[13]
Various	Male Woman	cases=1158 controls=1402	Yes	Historical measurements data	[22]
autoworkers	Woman	4825	Not	Occupational history data	[23]
automobile manufacturing plants	Male Woman	38549	Not	Historical measurements data	[8]
French carbon steel-producing factory	Male Woman	17701	Yes	job-exposure matrix	[24]
Automotive workers	Male	21999	Not	Historical measurements data	[17]
Various	Male Woman	cases=1171 controls=1418	Not	Occupational history data	[25]

Out of 8 studies, 4 were case-control and 4 were cohort and all of them had high NOS scores (Table 2). Four studies considered different types of metalworking fluids. 3 studies reported OR, 2 studies SMR, 2 studies HR, and one study RR. In total, half of the studies also considered smoking habits.

Table 2. Results of the included studies (study design, NOS Score, and statistical results achieved).

Study Design	Statistical Results	NOS Score	Reference
case-control	Straight MWFs OR=1.13 (1.02–1.25) frequency- weighted duration of exposure to straight MWFs OR=1.44 (0.97–2.14) Current smoker OR= 10.87 (3.39-34.9)	7	[6]
case-control	Straight MWFs OR=1.7 (1.1–2.8) soluble MWFs= 50% elevated risk (95% CI=0.96–2.5) synthetic MWFs= Nonsignificant	7	[13]
case-control	precision metalworkers OR= 2.2 (1.4-3.4) metalworking/plastic working machine operators OR= 1.6 (1.01- 2.6) use of metalworking fluids= OR 1.7 (1.1 to 2.5) smoker precision metalworkers OR= 2.9 (2.2- 3.7) smoker metalworking/plastic working machine operator OR= 2.9 (2.3- 3.8) smoker automobile mechanics OR= 3.1 (2.4- 3.9)	7	[22]
Cohort	Female autoworkers SMR= 0.7 (0.14- 2.05)	8	[23]
Cohort	Bladder and urinary organ cancers SMR= 0.95 (0.81- 1.12) straight metalworking fluids HR=> 1.8 soluble metalworking fluids HR= > 11.1 synthetic metalworking fluids= > 0.5	8	[8]
Cohort	metalworking fluids RR=2.44 (1.06 to 5.60) Current smoker RR= 6.22 (6.50- 105.8)	8	[24]
Cohort	straight metalworking fluids HR= 2.07 (1.19-3.62) soluble metalworking fluids HR= 1.02 (0.56-1.88) synthetic metalworking fluids= 0.78 (0.38-1.61)	8	[17]
case-control	---	7	[25]

DISCUSSION

We conducted a review of the association between exposure to metalworking fluids and the incidence of bladder cancer in potentially exposed individuals. In none of the articles reviewed, the exposure to metalworking fluids was directly measured. Instead, exposure information is extracted through a job-exposure matrix, occupational history data, and Historical measurements data. The working context of these studies is also related to industry and occupational exposure.

Exposure to metalworking fluids has been linked to several cancers [23, 26-28]. In a study, Friesen et al. examined the association between exposure to metalworking fluids and cancer. In this study, SMR= 0.7 was reported for exposure to metalworking fluids and bladder cancer [29]. Sadie Costello et al. also followed up with 38,549 automobile manufacturing workers in potential exposure to metalworking fluids in a cohort study. The SMR for bladder cancer in this study was also < 1 and equal to 0.95 (0.81-1.12) [8]. Although SMR is < 1 in both studies, their values are different. Especially in the Sadie Costello et al. study, its value is very close to 1. In the literature, an increased risk of bladder cancer has been reported for machinists and mechanics exposed to MWF [30].

Four studies examined the types of metalworking fluids, two of which were case-control studies that reported OR and two were cohort studies that reported HR. Workers at six French steel-producing factories were studied for exposure to metalworking fluids by Colin et al. in 2018. According to the results of this study, in the 25 years before diagnosis, OR increased significantly with the duration of straight MWF exposure (OR = 1.13 (1.02-1.25)). The study by Colt et al. confirms this result and the risk of bladder cancer for straight metalworking fluids was high (OR= 1.7 (1.1–2.8)). In addition, the use of soluble MWFs increased the risk by 50% (95% CI = 0.96-2.5). [13]. In both studies, the authors suggested that metalworking fluids are a bladder carcinogen. In the case of cohort studies, the HR for bladder cancer was higher concerning soluble metalworking fluids in the Sadie Costello et al. study (straight HR=> 1.8, soluble HR> 11.1, synthetic = > 0.5) [8]. The results of the study of Friesen et al. were not in line with the study mentioned above. In the study by Friesen et al., straight metalworking fluids had the highest risk of bladder cancer (straight HR= 2.07 (1.19-3.62), soluble HR= 1.02 (0.56-1.88), synthetic = 0.78 (0.38-1.61)) [17]. The association with direct oils, seen here, illustrates the role of PAHs in the etiology of bladder cancer as observed in other PAH-exposed industries [31, 32].

Simultaneous exposure to metalworking fluids and smoking has also been investigated in four studies. In the study by Colin et al., ORs increased with the duration of smoking (P <0.001), the average number of cigarettes consumed per day (P = 0.002), and the number of packs per year (P <0.001) (Current smoker OR= 10.87 (3.39-34.9)) [6]. In the study by Colt et al., The simultaneous effects of smoking and metalworking fluids were investigated. In this study, there was a significant interaction between smoking and precision metalworking (OR= 2.9 (2.2- 3.7)), and the increased risk of bladder cancer was significantly higher among smokers [13]. Another study by Bourgkard et al. found that the relative risk increased with an increasing number of cigarettes per day. The relative risk for smoking more than 20 cigarettes per day was estimated to be 53.5 (95% CI 12.9 to 222.7).

Studies show an increased risk of bladder cancer among workers who are exposed to straight MWFs and secondarily to soluble MWFs, which may be explained by the presence of carcinogens. In addition, the literature review in this study generally shows that smoking can increase the risk of bladder cancer due to exposure to metalworking fluids.

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ETHICAL CONSIDERATION

Ethical approval was approved by the Shahid Beheshti University of Medical Sciences Ethics Committee (IR.SBMU.RETECH.REC.1400.977).

Conflict of interests

None declared.

Author contribution

Zahra Moradpour: investigation, writing original draft, and writing—review and editing. Mahdi Jalali, Sajjad Farhadi, Masoomeh Vahabi Shekarloo: data collecting and writing. Zahra Sedaghat: writing—review, and editing. Seyed Alireza Mosavi Jarrahi: data collecting and writing. Mohammad Reza Taherian: writing—review, and editing. Ghasem Hesam: investigation, writing original draft, and writing—review and editing.

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