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Impact of occupational exposure to wildfire events on systemic inflammatory biomarkers in Portuguese wildland firefighters

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A R T I C L E I N F O

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A B S T R A C T

While occupational exposure as a firefighter is considered a dangerous occupation, research on the underlying mechanisms remains limited, particularly in wildland firefighters. Inflammation, a key effect of wildfire exposure, plays a significant role in the development of various diseases. The current study aims to investigate the impact of wildland firefighting exposure on the levels of pro-inflammatory systemic biomarkers. A pre-post study design investigated 59 wildland firefighters comparing data collected after participation in a wildfire event (Phase II) with data obtained before wildfire season (Phase I). Data on demographics, lifestyle, health and occupational-related factors were assessed. Exposure factors, such as fire combat (e.g., exposure duration), were also registered. Inflammatory biomarkers (i.e. interleukin-6 [IL-6], interleukin-8 [IL-8], tumor necrosis factor α [TNF-α] and high-sensitivity C-reactive protein [hs-CRP]) and hydroxylated polycyclic aromatic hydrocarbons metabolites (1-OHNaph+1-OHAce, 2-OHFlu, 1-OHPhen, 1-OHPyr) were analysed in blood and urine samples, respectively. Serum IL-8 and IL-6 levels were significantly increased after wildland fire combat. IL-8 levels were 2.62 times higher (95 % CI: 1.96–3.50; $p < 0.01$), whereas IL-6 levels were 1.25 times higher (95 % CI: 1.00–1.57; $p = 0.04$). Furthermore, IL-8 levels were significantly correlated with urinary 2-hydroxyfluorene levels and fire combat duration (>12 h). In addition, the mean hs-CRP level, in both phases, was above 3.0 mg/L, indicating a potential risk for cardiovascular events. Given the long-term health implications of firefighting occupational exposure, biomonitoring and early detection of occupational risks are essential for protecting firefighters' health. Protective measures must be urgently implemented to enhance occupational health and strengthen preventive strategies in this sector.

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1. Introduction

Over recent decades, the intensity and severity of wildland fires have been increasing (Knorr et al., 2017). This trend is expected to persist in a progressively warmer world facing the challenges of global climate change (Ellis et al., 2022). Firefighting is a physically and psychologically demanding occupation, requiring firefighters to face dangerous and complex exposures (Reinhardt and Ottmar, 2004; Adetona et al., 2016; Navarro et al., 2019). Wildfire smoke contains a wide range of toxic compounds (e.g., carbon monoxide, methane, nitrogen oxides) (International Agency for Research on Cancer (IARC), 2023; Naeher et al., 2007) some of which are known carcinogens such as particulate matter (PM2.5), heavy metals and polycyclic aromatic hydrocarbons (PAHs) (International Agency for Research on Cancer (IARC), 2010; Esteves et al., 2022). The exposure to hazardous contaminants, along with long work shifts and high physiological demands in challenging environments, contribute to the occupational health risk observed among wildland firefighters (Adetona et al., 2016; Esteves et al., 2022; Reid et al., 2016). Apart from respiratory and cardiovascular outcomes, firefighters, in general, are at a higher risk than the general population for developing certain types of cancer (International Agency for Research on Cancer (IARC), 2023). In 2022, the International Agency for Research on Cancer (IARC) classified firefighting occupational exposure as "carcinogenic to humans" (Group 1) (International Agency for Research on Cancer (IARC), 2023). However, studies on exposure-induced biological mechanisms among wildland firefighters remain limited (International Agency for Research on Cancer (IARC), 2023). This gap may be attributed to the unpredictability of wildfire events and the difficulty in collecting data in such challenging environments (Taeger et al., 2023). Thus, most available studies have focused on structural fire exposures, simulated/training conditions, or exposure to controlled fire (e.g., prescribed burns) (International Agency for Research on Cancer (IARC), 2023).

Wildland firefighters face various occupational stressors such as heat stress, intensive physical exercise (Aisbett et al., 2012), mental stress (Orysiak et al., 2022), and exposure to woodsmoke-air contaminants (Naeher et al., 2007). Previous studies have found an association between the inhalation of woodsmoke pollutants and local inflammatory responses in both upper and lower airways (Gianniou et al., 2018), linking it to respiratory problems such as asthma, chronic obstructive pulmonary disease, and sinusitis (Naeher et al., 2007). One of the initial responses of the innate immune system is the secretion of pro-inflammatory cytokines, such as IL-6, IL-8, and TNF-α, which are essential for initiating the acute inflammatory response (Abbas, 1991). Some of these pro-inflammatory cytokines (IL-6, TNF-α) stimulate the liver production of acute phase proteins, such as CRP (Akira and Kishimoto, 1992; Shephard and Shek, 1995), which play a fundamental role in the inflammatory response and in the modulation of immune system activity (Nehring et al., 2017). However, when acute inflammation is not effectively resolved by anti-inflammatory mediators (e.g., anti-inflammatory cytokines, glucocorticoids) it can progress to chronic inflammation (Orysiak et al., 2022), particularly in the case of recurrent acute stimuli. This continued over-stimulation of the immune system may lead to chronic low-grade systemic inflammation which has been associated with numerous health implications (Brenner et al., 1994; Bauer, 2005), such as cardiovascular (Guarner and Rubio-Ruiz, 2015; Kim et al., 2018), respiratory (Orysiak et al., 2022), metabolic disorders (Hotamisligil, 2006), mental health (Renna et al., 2018; Passos et al., 2015; Slavich and Irwin, 2014) and cancer (International Agency for Research on Cancer (IARC), 2023; Orysiak et al., 2022; Chen et al., 2018; Singh et al., 2018; Greten and Grivennikov, 2019).

Human biomonitoring studies are crucial for evaluating the association between occupational exposure and adverse health outcomes (Vorkamp et al., 2021). The evaluation of biomarkers of exposure (i.e., the xenobiotic and/or its metabolites, or the products of the interaction between the xenobiotic and target molecules) is an important tool widely used in occupational health risk assessment and preventive medicine (Esteves et al., 2022), since it quantifies the real dose to which the organism is exposed to, taking in account the individual characteristics. Most of the biomonitoring studies studying firefighting occupational exposure were focused on the assessment of hydroxylated metabolites of PAHs in urine (OHPAHs) (Caux et al., 2002; Fent et al., 2014, 2019; Fernando et al., 2016; Keir et al., 2017), reflecting all the PAH exposure routes (i.e., inhalation, dermal absorption and ingestion) (Wingfors et al., 2018; Hwang et al., 2022).

However, biomarkers of exposure alone do not provide information about the effects that may be induced by the exposure (Esteves et al., 2022), but only estimate the organism's exposure to the xenobiotic. The integration of biomarkers of effect is crucial for evaluating the biological events that occur later in the continuum between exposure and disease (Esteves et al., 2022). A biomarker of effect is defined as a measurable biochemical, physiological, behavioural, functional, or other alteration within an organism that might be elicited by exposure (Costa and Esteves, 2023). It may represent an event that can be correlated with, and possibly predictive of, a deleterious health effect (Costa and Esteves, 2023).

High-sensitivity C-reactive protein (hs-CRP) is a sensitive biomarker of systemic inflammation and a valuable biomarker for predicting cardiovascular risk (Silva and de Lacerda, 2012; Ridker et al., 2007), identifying adults with CRP levels greater than 3.0 mg/L as at higher risk for developing cardiovascular disease (e.g., heart attack, stroke) (Li et al., 2017; Ridker, 2003; Cushman et al., 2009). The application of this effect biomarker in firefighters is particularly interesting because cardiac events have been considered an important cause of death among these professionals (Esteves et al., 2024a). According to the National Fire Protection Association, cardiovascular events such as heart attacks, are among the most common causes of death among on-duty firefighters (Fahy, 2005). Circulating cytokines (e.g., interleukin-6 [IL-6], interleukin8 [IL-8], and tumour necrosis factor-α [TNF-α]) and hs-CRP have been used as biomarkers of inflammation after woodsmoke exposure and ambient particulates (van Eeden et al., 2005; Swiston et al., 2008). Despite some studies have measured inflammatory biomarkers among wildland firefighters (Gianniou et al., 2018; Swiston et al., 2008; Wolkow et al., 2015; Cherry et al., 2021), most have been confined to changes over a single shift/event (Swiston et al., 2008; Adetona et al., 2017a), not considering their assessment in distinct time points of the wildfire season.

The use of biomarkers is of utmost value to understand the possible mechanisms involved in the cellular events resulting from firefighting occupational exposure (Bocato et al., 2019), especially due to the lack of occupational studies among firefighters integrating both biomarkers of exposure and effect (Andersen et al., 2018a; Oliveira et al., 2020; Esteves et al., 2024b). To the best of the authors' knowledge, no studies have explored the association between systemic levels of inflammatory biomarkers and urinary PAH metabolites in the context of wildland firefighters' occupational exposure to real wildfire events.

Thus, this study aims to investigate the impact of wildfire exposure on systemic pro-inflammatory biomarkers in paired samples of wildland firefighters from the northern region of Portugal. Additionally, we aim to examine the potential relationship between levels of systemic inflammatory biomarkers and urinary PAH metabolites following wildfire occupational exposure, as well as with other self-reported exposure-related variables.

2. Material and methods

2.1. Study population

Our study enrolled 59 healthy wildland firefighters from five fire stations located in a predominantly rural district in the Northern region of Portugal. All participants had at least one year of service and were actively involved in wildfire combat activities. This pre-post study design involved paired assessments, with each firefighter serving as their own control. Participation involved biomonitoring the firefighters at two distinct points: Phase I - before the wildfire season, during late spring (low exposure); and Phase II - after wildfire combat, during the wildfire season, in summer (higher exposure). The summer period, specifically from July to September, is recognised as the critical fire season in Portugal (Bergonse et al., 2021). Data collection was carried out between 2021 and 2023 with sampling intervals varying according to wildland firefighters' involvement in firefighting activities. During this period, firefighters were deployed to wildfires occurring in their respective regions assigned to each fire station; besides wildfires considered for the present study, no other major wildfires, in this period, occurred in this region of Portugal.

In Phase I, during the off-season, firefighters were fully informed about the study objectives, procedures, potential benefits, and associated risks. They were also instructed on data confidentiality and protection, as well as the possibility to withdraw from the study at any time without any consequences. Each participant who agreed voluntarily to participate signed an informed consent form before the start of the study. A self-administered questionnaire was used in Phase I to collect data on sociodemographic characteristics (e.g., sex, age), lifestyle habits (e.g., smoking), anthropometric measurements (i.e., weight and height) and occupational-related information (e.g., shift duration, years of service). In this Phase (off-season), firefighters did report no recent occupational exposure to fire occurrences.

In Phase II, after the wildfire combat, firefighters were asked to complete a brief questionnaire with questions about the fire event and activities (e.g., exposure duration). Our study was conducted under the Declaration of Helsinki (World Medical Association, 2013; Williams, 2008). Ethical approval was granted by the Ethics Committee of the University of Porto, Portugal (reference number 92/CEUP/2020).

2.2. Biological sample collection

Blood and urine samples were collected simultaneously for each individual during Phase I and Phase II. In Phase I, blood samples were collected by venipuncture, between 10 and 11 a.m., and transported to the laboratory under refrigerated conditions (4 °C, transport within 2 h) to be immediately processed and consecutively stored at −80 °C for further analysis; a spot urine sample was also collected in sterile polyethylene containers (100 mL) and frozen at −20 °C until analysis.

During Phase II, post-exposure biological samples (blood and urine) were collected from firefighters involved in wildland fire combat/post-combat activities, once they returned to the fire station. After collection, all samples were transported in a cooler to the laboratory to be processed.

2.3. Urinary OHPAHs analysis

Quantification of urinary OHPAHs was performed as in Barros et al. (2024) solid-phase extraction and high-performance liquid chromatography with a fluorescence detector. The following urinary PAH biomarkers were determined: 1-hydroxynaphthalene (1-OHNaph) 1-hydroxyacenaphthene (1-OHAce), 2-hydroxyfluorene (2-OHFlu), 1-hydroxyphenanthrene (1-OHPhen) and 1-hydroxypyrene (1-OHPyr). Calibration curves, along with the limits of detection (LOD) and limits of quantification (LOQ), were defined for each biomarker. Quality control was ensured by assessing intra-day and inter-day precision using relative standard deviation (RSD). Samples were analysed in triplicate for reliability. The methodology's accuracy was verified through recovery assays, with recovery rates ranging from 70 % to 117 %. Concentrations of OHPAHs were normalised to creatinine levels (μmol/mol creatinine).

2.4. Serum IL-6, IL-8, TNF-α evaluation

Whole blood collected in serum tubes (Vacuette® Ref#456092) was allowed to coagulate at room temperature for 1–2 h. After clotting, samples were centrifuged at 720 rcf for 10 min and serum was then aliquoted and frozen at −80 °C until analysis. Pro-inflammatory biomarkers (TNF-α, IL-6, IL-8) were evaluated using multiplex immunoassays on a Luminex 200™ xMAP™ analyser (Luminex Corporation, Austin, TX, USA), following the protocol of the Human High Sensitivity T Cell Magnetic Bead Panel (Milliplex® MAP kit, Millipore Corporation, Billerica, MA, USA). Raw data analysis (mean fluorescence intensity, MFI) was performed using a standard five-parameter logistic (5-PL) curve fit generated by the Luminex xPONENT® Software (version 3.1).

2.5. Plasma hs-CRP quantification

Plasma was obtained from whole blood collected in K2EDTA tubes (Vacuette® Ref#367864) after centrifugation at 720 rcf during 10 min. Afterward, plasma was aliquoted and kept at −80 °C. Plasma levels of hs-CRP were measured by a particle-enhanced immunoturbidimetry method (CRP LX HS, Roche Diagnostics, Rotkreuz, Switzerland) in a Cobas Integra® 400 plus analyser (Roche Diagnostics, Switzerland) according to the manufacturer's instructions with a detection limit of 0.01–2.00 mg/dL.

2.6. Statistical analysis

Descriptive statistics were performed for quantitative and qualitative variables. Individual characteristics, stratified by sex, are presented as mean ± standard deviation (SD) for continuous variables and as absolute numbers and frequencies for categorical variables. For comparisons between sex groups, the independent *t*-test was used for continuous variables, and the chi-square test of independence was applied for categorical variables. For smoking habits participants were categorised as current smokers and non-current smokers. Non-current smokers included individuals who had never smoked or those who had ceased smoking for more than one year. The normality of data distribution was assessed using the one-sample Kolmogorov-Smirnov test and data dispersion graphs. Data that were not normally distributed are presented as medians with interquartile ranges (IQR). Univariate analysis was conducted to investigate potential associations between inflammatory biomarkers (i.e. IL-6, IL-8, TNF-α, and hs-CRP) and questionnaire retrieved variables (i.e., individual characteristics, lifestyle, and occupational-related factors). Whenever the data did not follow a normal distribution, statistical differences were assessed using the Mann-Whitney *U* test (for two groups) or the Kruskal-Wallis test (for more than two groups). The difference in biomarkers within paired samples (i.e., before and after fire exposure) was evaluated using the Wilcoxon test for non-normally distributed endpoints. Possible correlations among continuous variables were explored using Spearman's rank correlation test. The frequency ratio (FR) (i.e., post-/pre-exposure) and its asymptotic 95 % confidence intervals (95 % CI) were calculated for the studied endpoints i.e. IL-6, IL-8, TNF-α, and hs-CRP.

Inflammatory biomarkers that showed statistically significant differences after fire exposure were further analysed. Linear regression analysis was conducted to identify possible statistically significant associations with exposure variables (i.e. duration of exposure and urinary OHPAHs) and the difference (post-exposure - pre-exposure) of log-transformed inflammatory biomarkers i.e., variation (Δ) inflammatory biomarker = log(post-exposure) - log(pre-exposure). Logarithmic transformation was applied to normalise data distribution and facilitate the calculation of FR using exponentiated coefficients (e^{β}) from linear regression analysis. A statistical significance level of 0.05 was considered. The statistical software used for all analyses was IBM SPSS Statistics 29.0 for Windows (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Population characterisation

Table 1 summarises the general characteristics of the study population. Despite the traditionally male-dominated nature of the firefighting occupation with women often under-represented (International Agency for Research on Cancer (IARC), 2023), nearly a quarter of our participants were women (22.0 %). The overall mean age was 35.5 ± 9.0 years.

Regarding Body Mass Index (BMI) [weight (kg) × height (m)$^{-2}$] the average was 26.5 ± 3.3 kg/m^2. Half of our participants were overweight, 11.9 % were obese, and 37.3 % had a normal weight, according to the World Health Organization classification (World Health Organization, 2022). In terms of smoking habits, 54.2 % reported being current smokers, with males accounting for the larger proportion.

Average years of service as a firefighter was 15.9 ± 8.9 years, with no significant differences between males (16.1 ± 9.4 years) and females (14.8 ± 6.7 years). Of the participants, 44.8 % (n = 26) were members of the Permanent Intervention Team (full-time contracted firefighters), while the remaining firefighters were volunteers, with no contract. Moreover, as shown in Table I, a significant association between sex and permanent intervention teams was observed, with a higher proportion of males in these teams. The Permanent Intervention Team members had an average of 16.35 ± 8.59 years of service, while volunteers had an average of 15.37 ± 9.49 years of service (data not shown). On average, firefighters engaged in wildfire suppression activities for 11 h, with 28.8 % (n = 17) of them spending more than 12 h in the field. Wildland firefighters under the age of 36 years spent an average of 10 h at the fire scene, whereas those aged 36 and older spent an average of 12 h in wildfire suppression activities (data not shown).

3.2. Inflammatory biomarkers (IL-6, IL-8, TNF-α and hs-CRP)

Descriptive statistics for the concentrations of IL-6, IL-8, TNF-α, and hs-CRP in both Phase I and Phase II are presented in Table S1 of the supplementary material. A statistically significant increase in IL-8 and IL-6 serum levels was observed after the fire combat compared with the levels accessed before the wildfire season ($p < 0.01$ and $p = 0.04$, respectively). The analysis was performed using paired samples t-tests. Data are presented as mean ± standard error (SE), and p-values reflect these comparisons between pre- and post-fire combat measurements. Despite no statistically significant difference in hs-CRP levels being observed (Phase I: 3.65 ± 1.05 mg/L; Phase II: 3.24 ± 0.70 mg/L) the mean level of hs-CRP in both phases was greater than 3.0 mg/L indicating a higher risk for cardiovascular events, according to cut-offs values suggested for adults (Silva and de Lacerda, 2012; Cushman et al., 2009; Pearson et al., 2003).

When studying the influence of sex, age, smoking habits, or occupational variables (e.g., years of service, permanent intervention teams) on our endpoints, no significant effect was found (Table S2, Supplementary material). However, TNF-α levels were found to be significantly different between BMI groups ($p < 0.05$). TNF-α levels were significantly increased in overweight firefighters compared to colleagues with normal BMI.

The Phase I/Phase II-observed variations in the individual levels of inflammatory biomarkers, represented as FR, are illustrated in Fig. 1. IL-8 serum levels were significantly increased following the wildfire-combat exposure (FR: 2.62; 95 % CI: 1.96–3.50, $p < 0.01$), showing levels almost three times higher than those found during the pre-wildfire season. IL-6 levels were also significantly increased after the wildfire combat (FR: 1.25; 95 % CI: 1.00–1.57) reflecting a 25 % higher risk of increased IL-6 levels post-exposure ($p = 0.04$). No significant variation was found for TNF-α and hs-CRP between both study phases, with FRs of 0.99 (95 % CI: 0.94–1.04) and 0.89 (95 % CI: 0.60–1.30), respectively.

Correlation between the different variables and endpoints was also tested. A significant positive association was found between Phase II levels of serum TNF-α and IL-6 levels ($r = 0.31$; $p = 0.02$) (data not shown).

3.3. Urinary OHPAHs biomarkers

Creatinine-corrected urinary OHPAHs concentrations within both

Table 1
General characteristics of the study population (n = 59).

Study participant characteristics	Wildland Firefighters (n = 59)	Male (n = 46)	Female (n = 13)
Individual characteristics			
Age (years)[a]	35.5 ± 9.00 (20.0–55.0)	35.6 ± 9.3 (20.0–55.0)	35.1 ± 8.0 (21.0–45.0)
Body Mass Index (BMI) (kg m^{-2})[a]	26.5 ± 3.3 (19.4–35.9)	26.7 ± 3.3 (19.4–35.9)	26.0 ± 8.0 (21.2–33.0)
Normal weight, *n* (%)	22 (37.3 %)	17 (37.0 %)	5 (38.5 %)
Overweight, *n* (%)	30 (50.8 %)	23 (50.0 %)	7 (53.8 %)
Obesity, *n* (%)	7 (11.9 %)	6 (13.0 %)	1 (7.7 %)
Lifestyle-related			
Smoking habits			
Non-current smoker	27 (45.8 %)	19 (41.3 %)	8 (61.5 %)
Current smoker	32 (54.2 %)	27 (58.7 %)	5 (38.5 %)
Cigarettes/day[a]	16.91 (1.0–35.0)	18.22 (1.0–35.0)	9.80 (4.0–20.0)
Occupational-related			
Years of service[a]	15.9 ± 8.9 (3.0–34.0)	16.1 ± 9.4 (3.0–34.0)	14.8 ± 6.7 (7.0–28.0)
Permanent Intervention Teams			
No, n (%)	32 (55.2 %)	21 (45.7 %)	11 (91.7 %)
Yes, n (%)	26 (44.8 %)	25 (54.3 %)	1 (8.3 %) *
Active wildfire exposure			
Exposure duration (hours)[a]	11.0 ± 11.7 (1.0–55.0)	11.7 ± 12.3 (1.0–55.0)	8.7 ± 9.2 (1.0–24.0)
≤12 h, *n* (%)	42 (71.2 %)	32 (69.6 %)	10 (76.9 %)
>12 h, *n* (%)	17 (28.8 %)	14 (30.4 %)	3 (23.1 %)

*Statistical significance was determined using the Chi-square test ($p < 0.05$).
[a] Values are expressed as mean ± SD (standard deviation), with the range presented as min – max.

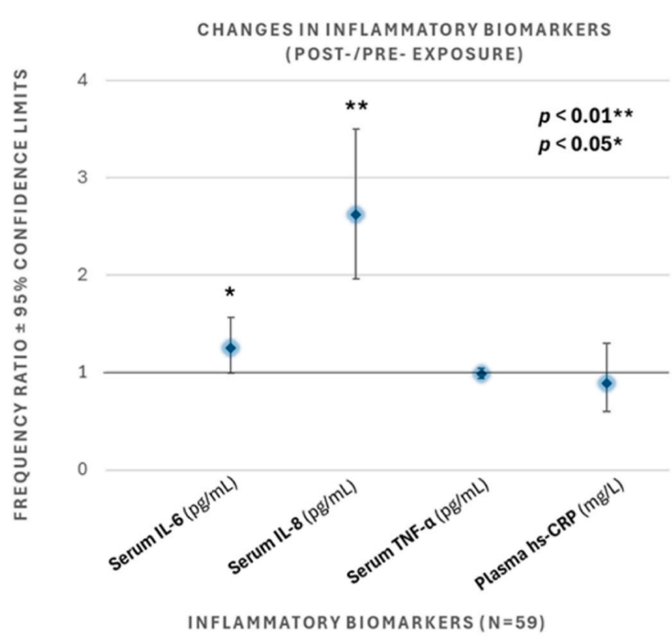

Fig. 1. Frequency ratios showing changes in inflammatory biomarkers [ratio within post (Phase I) and pre-exposure levels (Phase II)]. * and ** indicate the statistical significance of post/pre-exposure ratios, with p-values <0.05 and <0.01, respectively.

phases are presented in Table S3 (Supplementary material). An increase of each studied urinary OHPAHs was observed after firefighting intervention, namely 1-OHNaph+1-OHAce (µmol/mol creatinine) (pre: 16.15 ± 2.32 vs. post: 40.34 ± 6.00; $p < 0.01$), 2-OHFlu (µmol/mol creatinine) (pre: 0.17 ± 0.03 vs. post: 0.21 ± 0.04; $p = 0.07$), 1-OHPhen (µmol/mol creatinine) (pre: 0.07 ± 0.01 vs. post: 0.13 ± 0.03; $p = 0.05$) and 1-OHPyr (µmol/mol creatinine) (pre: 0.04 ± 0.01 vs. post: 0.06 ± 0.01; $p < 0.01$).

3.4. *Impact of firefighting in inflammatory response*

The contribution of each exposure-related variable to the variation (Δ) observed on the IL-6 and IL-8 levels was investigated. Δ IL-8 levels were significantly influenced by the exposure duration of the fire-event combat (Phase II). Firefighters who were more than 12 h in the field had approximately two times higher IL-8 levels [FR (95 % CI) = 2.07 (1.12–3.84); $p = 0.02$)] compared to those who were 12 h or less (Fig. 2). No significant influence was found for Δ IL-6, regarding exposure-related factors (data not shown).

The association between each urinary OHPAHs on Δ IL-8 was also studied. A significant positive correlation was observed between Δ IL-8 (post- vs. pre-exposure) and post-exposure urinary 2-OHFlu levels ($r = 0.37$; $p < 0.01$) (Fig. 3).

Data from regression analysis confirmed this association, indicating that for every unit increase of 2-OHFlu (µmol/mol creatinine), △ IL-8 increased by 16 % (95 % CI: 1.00, 1.34), after adjusting for age, sex, and smoking habits [FR (95 % CI) = 1.16 (1.00 1.35); $p \leq 0.05$] (data not shown).

In addition, despite no significant differences, a proportional increase in urinary OHPAHs levels was observed across different categories of hs-CRP for cardiovascular risk (low < intermediate < high) as shown in Table 2.

4. Discussion

Our study shows a significant increase in firefighters' serum levels of IL-6 and IL-8 following the wildfire combat. This positive inflammatory response aligns with the scarce previous literature comprising wildland firefighters (Swiston et al., 2008; Main et al., 2020; Adetona et al., 2017b). Swiston et al. (2008) observed a significant increase in both serum IL-6 and IL-8 levels in forest Canadian firefighters ($n = 52$) after an 8-h shift of firefighting activities in a real wildfire scenario. Another study, conducted during prescribed burns in the southeastern United States, also found a significant increase in IL-8 levels in a group of

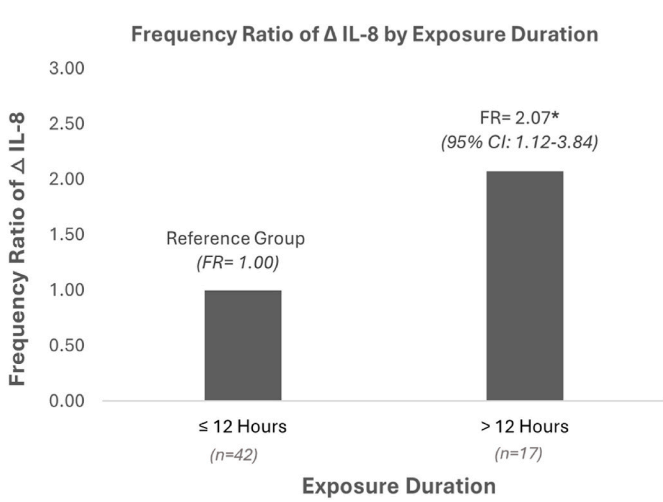

Fig. 2. Frequency ratio of Δ IL8 (post-vs. pre-exposure) by exposure duration: ≤12 h vs. >12 h *Statistically significant <0.05.

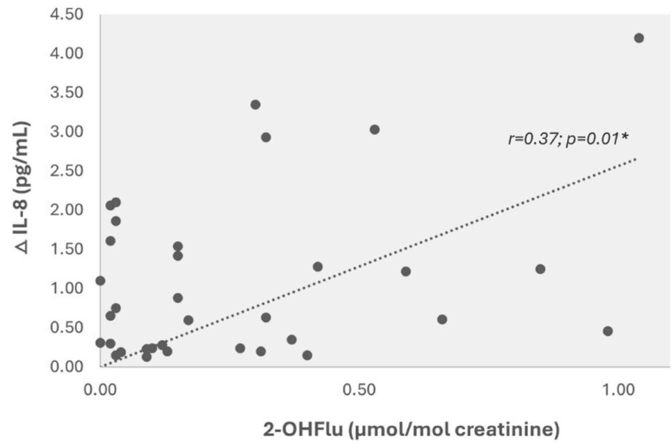

Fig. 3. Correlation within △ IL-8 levels (pg/mL) with exposure urinary 2-OHFlu levels (µmol/mol creatinine). *Statistically significant <0.05.

wildland firefighters after their work shift (Hejl et al., 2013). More recently, Main et al. (2020) conducted a study with 38 Australian firefighters enrolled in a real wildfire event, both plasma IL-8 and IL-6 levels were significantly higher after a 12-h shift. Furthermore, Greven et al. (2012) observed among 51 Dutch municipal firefighters (not wildland) an increase in serum IL-8 levels ($p < 0.05$), persisting for up to 3 months.

We also found that, among our group of wildland firefighters, those part of the Permanent Intervention Teams (full-time firefighters) exhibited higher serum IL-8 levels compared to colleagues in Phase I, although this difference was not statistically significant. This finding aligns with previous research, conducted in Greece, reporting greater inflammatory biomarkers (including IL-8) among career firefighters (Gianniou et al., 2016). Our study also showed that firefighters who spent more than 12 h at the wildfire scene had significantly higher IL-8 levels than those with lower exposure duration, showing a potential dependent effect of exposure duration on IL-8 levels. These findings agree with those of Gianniou et al. (2018), who also observed an association between longer participation in forest firefighting and intense systemic inflammation levels among Greek firefighters. Indeed, wildland firefighters' work shifts during a real scenario of wildland fires can last several consecutive days (Betchley et al., 1997). The long-lasting work shifts can place firefighters at greater risk for health effects associated with occupational exposures (Ebert, 2013).

No significant differences were found among our group for plasma hs-CRP levels. The same finding was obtained by two previous studies enrolling wildland firefighters exposed to prescribed burn shifts (controlled fire) (Hejl et al., 2013; Wu et al., 2020). Plasma hs-CRP is an acute-phase protein produced downstream of cytokines release and, thus, likely to undergo a delayed systemic release (van Eeden et al., 2005). IL-6 levels rapidly increase in response to inflammatory stimuli, serving as an early indicator of the systemic inflammatory response (Orysiak et al., 2022). CRP is synthesised by the liver in response to IL-6 and other cytokines, resulting in a delayed peak in its levels (Kramer et al., 2008). However, in both phases, our wildland firefighters had a mean level of hs-CRP above 3.0 mg/L - classified as a high risk for developing cardiovascular disease (Ridker et al., 2007; Li et al., 2017). As described in the literature, wildland firefighters are at high risk of cardiovascular disease due to long-term exposures to cardio-toxic smoke-released pollutants, such as PM2.5 and carbon monoxide (Esteves et al., 2024a). Additionally, a sedentary lifestyle, unhealthy diet, high BMI and smoking habits are known risk factors that contribute to high cardiovascular risk (Esteves et al., 2024a). To the best of our knowledge, this is the first study assessing hs-CRP levels - a clinical biomarker of inflammation and cardiovascular risk - among wildland firefighters involved in fire combat of real wildfire scenario.

In accordance with previous studies, urinary PAH levels were

Table 2
Concentration of urinary OHPAHs metabolites after wildfire exposure by hs-CRP categories for cardiovascular risk (Low < Intermediate < High).

	1-OHNaph+1-OHAce (μmol/mol creatinine)		2-OHFlu (μmol/mol creatinine)		1-OHPhen (μmol/mol creatinine)		1-OHPyr (μmol/mol creatinine)	
	n	*Median (IQR[a])*	*n*	*Median (IQR[a])*	*n*	*Median (IQR[a])*	*n*	*Median (IQR[a])*
Low Risk (<1.0 mg/L hs-CRP)	17	22.23 (9.96–40.96)	17	0.06 (0.02–0.31)	17	0.04 (0.02–0.09)	17	0.03 (0.02–0.06)
Intermediate Risk (1.0–3.0 mg/L hs-CRP)	23	36.79 (12.58–43.45)	23	0.10 (0.03–0.17)	23	0.09 (0.04–0.12)	23	0.04 (0.04–0.06)
High Risk (>3.0 mg/L hs-CRP)	15	47.63 (4.34–82.35)	15	0.13 (0.03–0.42)	15	0.10 (0.03–0.07)	15	0.05 (0.03–0.07)

[a] Interquartile range (IQR). The Kruskal-Wallis test was used to determine statistical differences between groups.

increased after exposure to woodsmoke (Adetona et al., 2017c). We found a statistically significant association between urinary 2-OHFlu post-fire-levels and IL-8 suggesting that IL-8 may serve as a viable biomarker for monitoring occupational exposure among wildland firefighters. So far, no occupational biomonitoring studies have explored this association, thus, further research is needed to confirm our result.

The use of adequate personal protective equipment (PPE) is essential to mitigate exposure to woodsmoke air contaminants (Esteves et al., 2024a). According to two previous studies conducted by Andersen et al., 2018a,b, no significant changes in IL-8 and IL-6 levels were found in structural firefighters after fire-combat activities. However, in both these studies, firefighters used self-contained breathing apparatus (SCBA). The use of air-supplied SCBA in a wildfire context is not feasible (Esteves et al., 2022), and therefore the lack of complete respiratory protection among wildland firefighters combating a real wildfire may result in a higher pollutant exposure gradient through inhalation.

It is important to note that our study group of wildland firefighters was predominantly male, reflecting the traditionally male-dominated nature of firefighting (International Agency for Research on Cancer (IARC), 2023). Most studies in this field have focused on male firefighters (International Agency for Research on Cancer (IARC), 2023), resulting in limited data on female firefighters. This underscores the need for further research including both sexes. In the present study, we observed no significant differences in the biological endpoints between females and males, though caution is warranted due to the small sample size of female firefighters. Regarding other findings of the present study, no significant association was found between our endpoints and years of service. However, it cannot be dismissed that over the years, firefighters may become less active in combat, potentially leading to a balance in exposure levels. In addition, we observed a significant correlation between IL-6 and TNF-α, confirming their relationship as key pro-inflammatory mediators in response to wildfire exposure. This aligns with earlier research indicating a linked activation of the inflammatory cascade (Abbas, 1991).

Our study has some limitations. Information bias may have been introduced using self-reported questionnaires for data collection. Moreover, the nature of firefighting makes it challenging to isolate other factors that may trigger inflammation, as firefighters are consistently exposed to various co-stressors such as physical exertion, smoke inhalation, psychological stress, heat stress, and sleep restriction, either individually or in combination, which may have contributed to the observed changes. Wildfires are unpredictable events, characterised by variability in timing, intensity, and duration. Wildland firefighting environments are complex and present numerous challenges. Factors such as duration of post-wildfire activities (e.g., mop-up operations), uncertainty regarding return times to the fire station, the need for rest after extended periods of activity, and the fluctuating nature of volunteer firefighter work shifts all contribute to the variability in sample collection timing. Biomarkers such as OHPAHs and inflammatory markers exhibit dynamic temporal patterns following exposure, making the timing of sample collection critical for accurate detection. In our study, although blood and urine samples were collected within a similar time window for all participants, variations in timing may have influenced the biomarker levels observed, potentially leading to an underestimation of some results. In addition, some of our results may potentially be underestimated since we did not have a "true baseline", for that only including firefighters before the beginning of their careers. Furthermore, we acknowledge the potential influence of seasonal variations.

However, our study has also significant strengths: This is the first study i) evaluating differences in systemic inflammatory biomarkers among wildland firefighters longitudinally at two distinct time points of wildfire season: during the pre-wildfire season and after fire combat in a real wildfire scenario; ii) evaluating hs-CRP among wildland firefighters – a known clinical marker for cardiovascular risk – considering exposure to real wildfires fire-combat; iii) accessing the association between systemic levels of inflammatory biomarkers and urinary PAH metabolites exposure on wildland firefighters in real scenarios of wildfires. Furthermore, the pre- and post-study design with paired active wildland firefighters enhances the study's robustness by establishing a temporal relationship between exposures and outcomes. The integration of effect biomarkers with exposure data provides a comprehensive assessment of the inflammatory response.

Evaluation of firefighting occupational exposure is complex and may depend upon multiple factors, such as tasks performed (e.g., front-line firefighter, fire engine driver), duration of exposure, and decontamination procedures after wildfire suppression activities equipment/materials (International Agency for Research on Cancer (IARC), 2023; Fabian et al., 2014). Moreover, other individual factors (e.g., sleep, smoking habits, psychological stress) and external factors (e.g., environmental pollution) may affect inflammatory response (Abbas, 1991). Nonetheless, promoting healthy modifiable behaviours can be an effective strategy to reduce such impact. This involves periodic training sessions, decontamination measures, proper use of PPE, a healthy diet, physical activity, strategies to reduce psychological stress, frequent medical examinations, and healthy sleep hygiene (Esteves et al., 2024a).

5. Conclusions

Although exposure during firefighting is recognised as carcinogenic to humans, the risks associated with this activity are poorly investigated. It is paramount to establish a panel of biomarkers to monitor wildland firefighters' occupational exposure worldwide, particularly in countries significantly affected by wildfires. The integration of biomarkers of effect with those monitoring exposure in human studies is of utmost value for assessing long-term potential health impacts. Understanding the dynamics of inflammatory biomarkers through time is crucial for their accurate interpretation in acute settings such as wildfire exposure.

Our study found an increased firefighters' systemic inflammatory response after wildland firefighting activities, a key factor in the development of cardiovascular and other chronic diseases. The data found within exposure-related variables and IL-8 levels suggest it is a suitable biomarker for monitoring occupational exposure of wildland firefighters.

The implementation of preventive strategies and occupational safety measures is crucial to mitigate health risks among firefighters. These strategies should consider the proper use of PPE and adequate postfire decontamination practices. Many occupational diseases, including work-related cancers, have long latency periods, making it difficult to recognise these conditions before clinical symptoms appear. Early detection of occupational risks can significantly reduce the harmful effects on workers' health, reduce the corresponding health and cost burdens, and improve their quality of life. Further research addressing the risks associated with firefighters' exposure during wildfire season, including the effect of different roles/tasks, is essential to better understand and mitigate occupational hazards, ultimately safeguarding firefighters' health.

CRediT authorship contribution statement

Filipa Esteves: Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Joana Madureira:** Writing – review & editing, Writing – original draft, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Bela Barros:** Methodology, Data curation. **Sara Alves:** Methodology, Data curation. **Joana Pires:** Methodology, Data curation. **Sandra Martins:** Software, Resources, Methodology, Data curation. **Marta Oliveira:** Methodology, Data curation. **Josiana Vaz:** Writing – review & editing, Resources, Project administration, Methodology, Investigation, Data curation. **Klara Slezakova:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Maria do Carmo Pereira:** Project administration, Funding acquisition. **Adília Fernandes:** Resources, Project administration, Methodology, Funding acquisition, Data curation. **Simone Morais:** Writing – review & editing, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation. **João Tiago Guimarães:** Software, Resources, Methodology, Data curation. **Stefano Bonassi:** Writing – review & editing, Supervision, Software, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **João Paulo Teixeira:** Writing – review & editing, Resources, Project administration, Funding acquisition. **Solange Costa:** Writing – review & editing, Writing – original draft, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Ethics approval

This work received approval for research ethics by the Accredited Ethics Committee of the University of Porto, Portugal, Report Nr. 92/CEUP/2020, under the project BioFirEx project (PCIF/SSO/0017/2018): "A panel of (bio)markers for the surveillance of firefighter's health and safety".

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2025.121608.

Data availability

The authors do not have permission to share data.

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