



## **Is competitive swimming associated with increased airway inflammation?**

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## Cover

In the course of this project inserted in the Integrated Master`s Degree of Medicine, in addition to the work below “**Is competitive swimming associated with increased airway inflammation?**”, over the past 3 years I have been also co-authored the following works:

- **Prospective assessment of a questionnaire to assess asthma in athletes**

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- **Effect of continuing or finishing swimming on airway inflammation and atopy-related diseases: a 3-year prospective follow-up study of competitive swimmers.**

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## **Abstract**

An increasing body of literature suggests an association between both competitive or recreational swimming and asthma.

We hypothesized that if swimming is causally related with asthma we should then observe a dose dependent relationship between cumulative training exposure and airway inflammation.

A total of 98 swimmers from the two main portuguese teams were included in this cross sectional study. Swimmers were allocated into 3 groups on the basis of their cumulative training exposure defined by the product of number of year involved in national level competition by the number of training hours per week during the last year. Relationships between exhaled nitric oxide (NO) and cumulative training exposure were assessed using spearman correlation, linear regression, and general linear model adjusting on confounding factors: gender, age, atopy, asthma, and use of inhaled steroids.

Spearman correlation showed a significant association between exhaled NO and cumulative training exposure ( $r_s=0.306$ ,  $p=.002$ ). The association was no longer significant after adjustment for confounders both in linear regression ( $p=0.908$ ) and general linear model analysis ( $p=0.489$ ).

In conclusion, we found that swimming is not dose-dependent related with a surrogate marker of eosinophilic airway inflammation such as exhaled NO. Although we cannot rule out an underlying inflammation response driven by cells other than eosinophils our observation does not support competitive swimming as a cause of allergic airway inflammation.

## Background

Allergic asthma, the commonest chronic disease in childhood, is a complex disease with a phenotype that is clinically difficult to define. The main physiological feature of asthma is intermittent and reversible airway obstruction, while the dominant pathological feature is airway inflammation sometimes associated with airway structural changes [1]. Asthma prevalence has reached epidemic proportions in prosperous countries for the last decades suggesting that environmental factors play a role in the aetiology of this disease [2].

In recent years, the observation that regular pool attendance, especially by young children, was associated with lung hyperpermeability and increased risk of developing asthma led to the “pool chlorine hypothesis”. Accordingly, the increasing and largely uncontrolled exposure of young children to chlorination by-products contaminating the air of indoor swimming pools could contribute to the childhood asthma rise in industrialized countries [2]. In Belgian schoolchildren, cumulated pool attendance was inversely related with asthma prevalence, exercise-induced bronchoconstriction and, in a dose dependent manner, with markers of lung epithelium damage [3]. These data led to the hypothesis of higher rates of allergic sensitization and atopic diseases after easier penetration of aeroallergens by the lung damaged epithelium.

An increasing body of literature suggests also an association between competitive swimming and asthma. Although the available evidence is away from consistency to draw clear conclusions, data seems to imply that high level

competitive swimming both increases the risk of incident asthma, and changes prevalent asthma towards a more difficult-to-control phenotype [4]. Specific mechanisms that could contribute to higher incidence and prevalence of asthma in competitive swimmers include airway inflammation induced by chemical exposures, micro aspiration of water droplets, hyperventilation and autonomic nervous system changes [5]. No study yet assessed the “healthy swimmer effect” which probably affects differently recreational and elite swimmers.

We hypothesized that if swimming is causally related with asthma we should then observe a dose dependent relationship between cumulative training exposure and airway inflammation.

## **Methods**

Swimmers from the two main portuguese swimming teams were invited to participate in this cross sectional study. A total of 98 athletes were included, and five athletes were not assessed because missed the evaluation visit. None smoke. Swimmers were then allocated into 3 groups on the basis of their cumulative training exposure defined by the product of number of year involved in national level competition by the number of training hours per week during the last year. Low, medium and high levels exposure groups were defined by the tertis of cumulative exposure. Writen informed consent was obtained for each subject or their parent before entering the study. The local hospital ethical committe aproved the study.

Subjects completed a self-administered questionnaire, including 5 questions adapted from ISAAC questionnaire, reporting allergic symptoms, asthma, physician diagnosis of asthma and asthma medication. Airway inflammation was assessed measuring exhaled nitric oxide (NO) levels before a training session using a portable device, NIOX MINO (Aerocrine AB, Sweden) and expressed in parts per billion (ppb). Through a mouthpiece, participants inhaled to total lung capacity and exhaled at a constant pressure guided by visual and auditory aids to stabilize flow rate. Atopy was defined by positive skin prick testing to at least one out of seven common aeroallergens in the area: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat epithelium, grasses mix, olive, *Parietaria* and *Alternaria* (Leti, Spain).

Results were expressed as mean (SD) or, if not normally distributed, as median (interquartile range). Levels of exhaled NO were inverse-transformed because of skewed distribution. Differences between groups were assessed with 1-way ANOVA for normally distributed data, Kruskal-Wallis 1-way ANOVA for non-normally distributed data or Chi-Square for categorical variables. Relationships between exhaled NO and cumulative training exposure were assessed using spearman correlation, linear regression, and general linear model adjusting on confounding factors: gender, age, atopy, physician-diagnosed asthma, and use of inhaled steroids.

## Results

Swimmers in the higher tertile of training exposure were older than the others; otherwise no significant differences in gender, atopy, asthma, or rhinitis prevalence were observed (Table 1).

Spearman correlation showed a significant association between exhaled NO and cumulative training exposure ( $r_s=0.306$ ,  $p=.002$ ). The association was no longer significant after adjustment for age, atopy, and inhaled corticosteroid use in linear regression ( $p=0.908$ ). In general linear model analysis no significant differences in levels of exhaled NO between tertiles of training exposure (median (interquartile range) respectively of 11 ppb (20), 12 ppb (9) and 21 ppb (17);  $p=0.489$ ; Fig 1) were observed with adjustment for variables mentioned above.

## Discussion

The present study showed that swimmers training as much as 17 hours per week in the pool water have no increased levels of airway inflammation measured by exhaled nitric oxide if taken in account their age, atopic and asthma status, and use of inhaled steroids. This is of importance as it has been suggested competitive swimming to increase asthma risk and change prevalent asthma towards a more difficult to control phenotype.

Our study has however some limitations. First, due to its cross nature, a causal relationship cannot be established. Second, it's possible the swimming associated airway inflammation is predominantly of neutrophilic nature [4, 6-7] thus not making the measuring of exhaled NO the best way to access airway inflammation. However, it has been suggested that for each 100 hours spent in the swimming pool for recreational swimmers the risk of asthma in atopics and of elevated exhaled NO in non-atopics increases by thirty percent [3]. On the other hand our study has important strengths: we have adjusted for confounders and known risk factors that affect exhaled NO levels; the approach by ages, number of years of training and even number of hours of practice per week we used are of major importance mainly to figure out whether airway inflammation are mostly related with a sustained exposure during a long period of time or with the highly intensive exercise, or even both; and finally we used a previous validated questionnaire for collecting data [8].

If swimming is causally related with asthma as it has been suggested [9] then we should observe a significant association and temporal sequence, have biological plausibility and coherence with biological background, and finally a biological gradient ought to exist between training and markers of the disease. Although a correlation appeared between cumulative training exposure and levels of exhaled NO, this was no longer significant after adjustment for confounders, particularly age. Exposure and age are for obvious reasons strongly related in competitive swimmers and may be cause of the discrepancy of our findings compared with others [10-11].

A recent study by Belda *et al.* draw attention to the presence of inflammation not mediated by eosinophils related with the degree of bronchial hyperreactivity and the duration of training in the swimming pool in the athlete who practices aquatic, but not land sports, whether or not asthma was present, perhaps due to exposure to chlorine derivatives [12]. This goes along with previous observations that children regularly attending indoor swimming pools for 1 to 2 hours a week no increased levels of exhaled nitric oxide are observed, suggesting that intermittent exposure to chlorine derivatives does not induce eosinophilic airway inflammation [13]. Furthermore, no immediate or delayed changes in exhaled NO were observed in competitive swimmers after two training sessions, independently of the swimmer's atopic or asthmatic status [14]. These data suggests the potential harmful effects of exposure to chlorine derivatives used for swimming pools maintenance are not reflected neither in acute or chronic changes in exhaled NO and other specific mechanisms that could contribute to higher incidence and prevalence of asthma in swimmers may include the microaspiration of water droplets, the hyperventilation and training induced autonomic nervous system changes.

In conclusion, we found that swimming is not dose-dependent related with a surrogate marker of eosinophilic airway inflammation such as exhaled nitric oxide. Although we cannot rule out an underlying inflammation response driven by cells other than eosinophils our observation does not support competitive swimming as a cause of allergic airway inflammation. More studies are needed to determine the role of specific swimming environment training related factors,

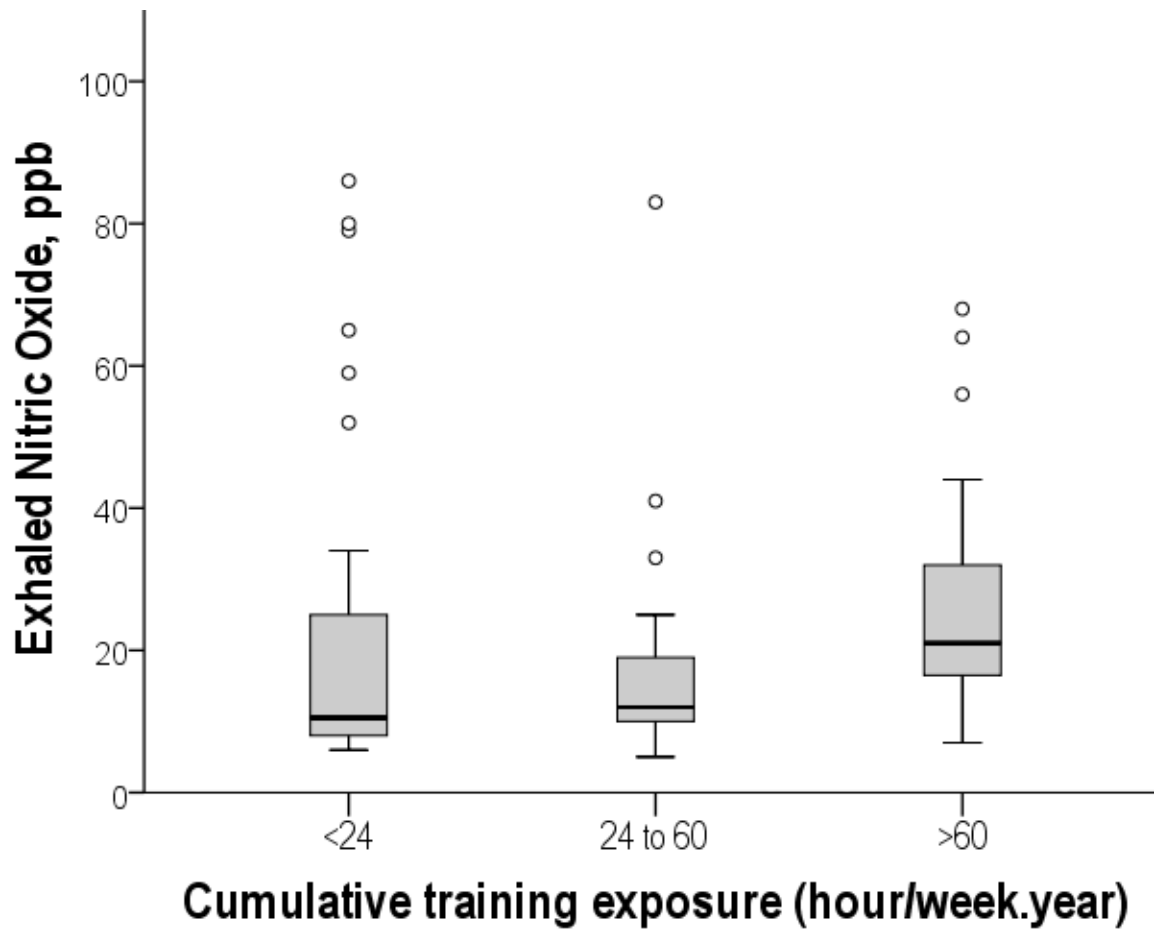
such as the microaspiration of water droplets or hyperventilation among others, as a cause of airway inflammation.

**Table 1.** Characteristics of swimmers according with tertis of cumulative training exposure (less than 24, 24 to 60, and more than 60 hours/week.year of competition).

	<b>Low n=32</b>	<b>Medium n=34</b>	<b>High n=32</b>	<b>p</b>
Age	11±2.5	13±2.3	17±3.1	<0.001*
Gender, female/male	17/15	12/22	11/21	0.225 <sup>£</sup>
Swimming hours/week	6 (5)	12 (4)	17 (5)	<0.001**
Years of competition	2 (3)	4 (2)	7 (4)	<0.001**
Atopy, n (%)	14	12	17	0.345 <sup>£</sup>
Asthma, n (%)	3	5	3	0.729 <sup>£</sup>
Rhinitis, n (%)	3	6	8	0.256 <sup>£</sup>

Data presented as mean±sd or median (interquartile range) unless otherwise stated; \*1-way ANOVA, \*\*Kruskal-Wallis 1-way ANOVA, <sup>£</sup> Chi-Square

**Figure 1.** Levels of exhaled nitric oxide in swimmers according with tertis of cumulative training exposure. The median is the line bisecting the box, the box limits represent 25th and 75th percentiles, and the dots represent outliers.



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