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Review

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Is vaping better than smoking for cardiorespiratory and muscle function?

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ABSTRACT

Cigarette smoking is a risk factor for respiratory disorders, cardiovascular diseases and even decrements in muscle function. Electronic cigarette use (vaping) is considered a healthier alternative to cigarette smoking and may help in smoking cessation. However, the effects of vaping are not clear yet and particularly the long-term effects of vaping are largely unknown. Some reports suggest that vaping maybe as harmful for *e.g.* respiratory function, as cigarette smoking. In this narrative review the effects of vaping and cigarette smoking on respiratory, cardiovascular and muscle function are compared. Overall, vaping has been found to cause similar effects as smoking on lung function and cardiovascular function. Future studies are needed to clarify the severity of smoking- and vaping-induced decrements on muscle function.

Key words: Vaping; electronic cigarette; cardiorespiratory; lung function; smoking; muscle function.

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Introduction

Cigarette packages contain warning labels like 'Smoking kills' and 'Smoking clogs the arteries and causes heart attacks and stroke'. These labels illustrate the tragic truth that smoking is a major risk factor for the development of cancer, cardiovascular diseases and respiratory disorders. It causes more than 7 million deaths per year globally [1] and in 2016, 77,900 deaths in the United Kingdom (UK) were directly or indirectly attributable to smoking [2]. Yet, these labels do not appear enough of a deterrent as about 7.2 million of the UK population are smokers [3]. These disastrous effects of smoking develop unperceivably slowly and only later in life the detrimental health issues become evident [4], a phenomenon referred to as 'the smoking time-bomb'. To make matters worse, 'The beneficial cognitive effects of nicotine have implications for initiation of smoking and maintenance of tobacco dependence' [5].

Any means to administer nicotine, but without the concomitant inhalation of the more than 4,000 toxic substances in cigarette smoke, such as acrolein, carbon monoxide, acetaldehyde and cyanide, would thus be preferable to cigarette smoking. E-cigarettes containing nicotine are considered to do this. The success of e-cigarettes in reducing smoking is reflected by the fact that about 54.1% of the current 3.6 million adult e-cigarette users in the UK are ex-smokers [6].

There is, however, concern that e-cigarettes may singularly stimulate uptake of smoking, particularly in youth, and have an acute effect on cardiorespiratory health, even in the absence of smoking [7,8]. Additionally, there are potential risks with vaping during pregnancy and lactation on the development of the child in the womb and health of the newborn baby [9-11]. Indeed, vapours from e-cigarettes contain, besides nicotine and the respiratory irritant propylene glycol, toxic substances also seen in cigarette smoke, such as acrolein, acetaldehyde, formaldehyde, and reactive oxygen species. As seen in animal studies, these toxic substances may well cause oxidative stress and negative effects on cardiovascular and respiratory function after vaping [7], casting doubt on the idea that e-cigarettes are a suitable 'healthy' alternative to normal cigarettes. Yet, there are only basic regulations for the composition of e-cigarette liquids (as described in https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products).

The potential health risk of e-cigarettes led the Forum of International Respiratory Societies to release a position statement that concluded*:* *'*As a precaution, electronic nicotinic delivery devices should be restricted or banned until more information about their safety is available' [8]. There is, thus an unmet need to know the effects of vaping on cardio-respiratory function in humans, and how this is related to the daily vaping volume and/or for how long one has been vaping. Therefore, the aim of this narrative review is to compare the effects of vaping and cigarette smoking on cardiovascular, respiratory and muscle function.

Vaping and smoking cessation

Since 1963 cigarette companies have been working to invent a new smoking system such as electronic nicotine delivery systems (ENDS) that heats, instead of burns, tobacco to reduce harm, and presents as a socially acceptable alternative to smoking [12,13]. The credit of inventing the e-cigarette as an alternative to smoking goes to Hon Lik, a Chinese pharmacist and inventor, whose heavy-smoking father died from lung cancer [14,15]. Many companies worldwide have adopted this technology and started marketing e-cigarettes as an harmless and safe alternative to cigarette smoking [16]. The focus of this review is therefore on e-cigarettes rather than heated tobacco products (HTPs) like *e.g.* iQOS.

Most smokers are aware of the harmful effects of cigarette smoking. Since the introduction of e-cigarettes in 2003, many smokers have turned to electronic cigarettes as they are thought to be less harmful, instead of nicotine replacement therapy (NRT) to help them quit smoking [17-22]. In 2019, 7.1% of the adult population of Great Britain used e-cigarettes [6] and in the European Union (EU), the use of e-cigarettes increased from 7.2% in 2012 to 11.6% in 2014 [23]. The potential of e-cigarettes or vaping to facilitate smoking cessation is illustrated by the 80% decrease in the use of normal cigarettes after 6 months of vaping [24], and other studies showing an up to 50% decrease in smoked cigarettes 24 months after taking up vaping [25, 26]. In addition, smoking cessation was reported to be as high as 8.7% 52 weeks after taking up vaping [26]. In the UK, a recent trial for smoking cessation showed that using e-cigarette accompanied by behavioural support, such as face-to-face support, was more effective than NRT [27]. This is a strong evidence that vaping indeed can reduce smoking.

Nicotine replacement therapies expose users to low doses of nicotine [7 to 14 mg/24-hour patch or 2 to 4 mg per piece of gum) and have been approved as medicinal products by the United States (US) Food and Drug Administration (FDA) [28]. E-cigarettes are not approved by the FDA and can be bought over the counter or online also in Europe [28]. The liquid in e-cigarettes have widely different nicotine concentrations, varying from 8 to 24 mg/ml per cartridge, but even doses up to 100 mg/ml are readily available [28] and pose a real risk of nicotine poisoning [29]. There is, indeed, not enough evidence that vaping is safe and has no, or minor, negative health effects. On the contrary, a study using online forums reported 326 negative health-related effects of vaping, including effects on the respiratory, circulatory, sensory, digestive and neurological systems [30].

The dangers of nicotine in e-cigarettes

An e-cigarette is composed of a rechargeable lithium battery, vaporizing chamber and a cartridge that contains the vaping liquid that consists, among other substances, of nicotine, glycerol, propylene glycol, glycerine, and tobacco flavouring [31,32], although some vaping liquids may be free of nicotine. Nicotine is easily absorbed by the mucus membrane, skin, gastrointestinal tract and respiratory airways [33] and acts as a neurotransmitter that in turn stimulates the release of dopamine, which contributes to the feeling of pleasure and satisfaction as part of the reward pathway [34]. It is this effect of nicotine that makes smoking so addictive [35]. As mentioned above, the dose of nicotine in e-cigarettes can be very high; typically, a 5-mL bottle of e-cigarette refill solution consists of 20 mg/ml nicotine (that is 100 mg/bottle) [36]. The life threatening dose of nicotine is around 30 to 40 mg in adults and 10 mg in children [36]. This high dose combined with unlimited vaping poses a potential health risk as it has been shown that acute contact to high concentrations of inhaled nicotine, or even skin contact e.g. after spills of nicotine-containing solutions, may cause nausea, vomiting or dizziness [33,37]. Such risks are even higher in vaping than in smoking, where such poisonous nicotine levels rarely occur [38]. In fact, many successful and unsuccessful suicide attempts through intravenous and oral intake of the nicotine solution intended for e-cigarette cartridges have been reported [39-41].

Chemical components of e-cigarettes

Besides nicotine there are other chemicals in the vaping liquids, where propylene glycol constitutes 90% of the e-cigarette liq-

uid [42]. While propylene glycol is often used to produce the smoke in special events like rock concerts and is considered harmless, prolonged and repeated exposure to propylene glycol vapour has been reported to cause cough, irritations of the eyes and lungs [43], and to increase the risk of acquiring asthma [44]. Vaping liquid also contains 1% diethylene glycol, a known carcinogen [31, 45], when non-pharmaceutical grade propylene glycol is used [46]. While many of the flavours in e-liquids are safe when ingested and widely used in the food industry, the potential dangers of inhaling flavours are not yet fully investigated, but there are indications they may have a negative effect on lung health. For example, diacetyl is used in butter and safe when ingested, but when heated and inhaled it might cause bronchiolitis [47]. In addition, some studies have shown that e-cigarettes release aromatic, particularly the carcinogenic component, polycyclic hydrocarbons, that have a pathogenic effect on human lung cells [48], and contain esters, aldehydes, acids or saccharides that are cariogenic [49]. In addition to these compounds, there are many more carcinogenic compounds in e-cigarette liquids [45, 50], particularly trace metals (*i.e.*, cadmium, arsenic, chromium, nickel, and lead), and tobacco-specific N-nitrosamines, and all these substances can in some cases reach concentrations even higher than in cigarette smoke [51]. Perhaps most surprising, given that smoking is a primary risk factor for pulmonary diseases, is that the most common used e-cigarette refill liquids are classified as respiratory irritants, allergens, inducers of asthmatic symptoms or potentially causing breathing difficulties if inhaled [52].

There is as yet no strong evidence that passive exposure to vaping has adverse effects on health. However, the detrimental effects of passive smoking and the observation that nicotine released into the environment does not only affect those who inhale it, but may also affect non-smokers and non-vapers *via* nicotine left on surfaces *e.g.* furniture, carpets and clothes [53], strongly hints to the dangers of passive exposure to the e-cigarette aerosols.

Effects of vaping and smoking on respiratory function

Cigarette smoke irritates the lining of the bronchial tubes causing them to swell and produce mucus to remove smoke particles [54]. Emphysema may develop when smoke particles irritate the alveolar walls and inflammation stimulates the release of proteases, enzymes that lead to the destruction of elastic fibres and collagen, which subsequently culminate in the destruction of the alveolar walls [54, 55]. Over time, this can lead to a decreased elastic recoil of the lung, chronic bronchitis and narrowing of the bronchial tubes that increases the resistance, and hence, cost of breathing [54, 56]. Ultimately, this progressive decrease in lung function can develop into COPD [57] that is diagnosed in 6.6% of the US population, of which 75% are smokers [58].

In contrast to smoking, the effects of vaping on human health and respiratory function are poorly investigated [59], but it has been shown that vaping for just 5 min increased peripheral airway resistance [60]. This is, however, not unequivocal, as another study found no acute effects of active vaping on lung function [61]. Whatever the cause of the discrepancy, it has been suggested that the increased peripheral airway resistance after 5 min of vaping [60] is partially caused by nicotine [59]. Indeed, nicotine inhalation (0-64 mg/ml) showed a dose-dependent increase in the amount of coughing and airway obstruction in non-smokers, which may be a consequence of the stimulation of afferent nerve endings in the bronchial mucosa by nicotine, which in turn triggers parasympathetic cholinergic pathways leading to bronchoconstriction [62]. Nicotine is, however, not the whole explanation, as respiratory symptoms, and airway inflammation were even found in vapers who used nicotine-free e-cigarettes [63].

Over time, the above effects of vaping may cause acute small-airway constriction and airway epithelial injury [64] that may be linked to increased risk of wheezing and respiratory symptoms similar to those seen in cigarette smokers [65]. McCauley *et al.* [66] presented a case study of a 42-year old woman diagnosed with exogenous lipoid pneumonia due to vaping. She had a history of 7-months productive cough, fevers and dyspnoea which occurred at the same time of her use of e-cigarettes. After several laboratory tests, glycerine, which is a component added to e-cigarette liquid to produce visible smoke to simulate the cigarette smoking experience, was found to be the causative agent. The symptoms improved by vaping cessation [66]. The above example may be considered anecdotal, but in a study of 30 vapers who never smoked, it was seen that the forced expiratory volume in one second (FEV_1) and forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) were significantly lower than those in controls (non-vapers and non-smokers) [67], similar to that seen in smokers [68, 69] (Figure 1).

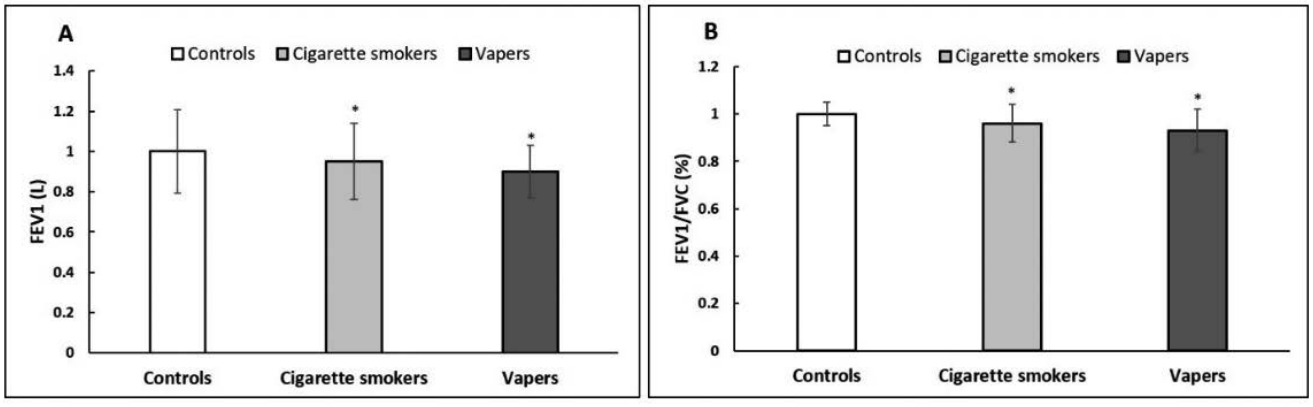

Figure 1. The effect of vaping on A) forced expiratory volume in one second (FEV_1) and B) FEV_1:FVC (forced vital capacity). Data are mean ± SD. Data are from Meo *et al.* [67], and Sparrow *et al.* [69]. To make the data between the two studies comparable, in each study the data were normalised to the control group. *Different from controls at p<0.05.

In contrast to the above cross-sectional study where vapers and non-vapers were compared [67], in a 3.5-year prospective study no significant decrements in spirometry or diffusion capacity were found in vapers [70]. Perhaps studies with a larger sample size are needed, as there are studies that have also not seen any significant effect of smoking on respiratory function [71]. Overall, combined with the detrimental impact of vaping on the lungs of mice [72] the data suggest that vaping has a detrimental effect on lung function.

Effects of vaping and cigarette smoking on cardiovascular function

Smokers suffer from a reduced exercise capacity that is not only attributable to a reduction in aerobic capacity, but also in increased metabolic cost of breathing [73-75]. Smoking increases blood pressure (BP), heart rate (HR), the risk factor for atherosclerosis [76,77] and has been shown to impair cardiovascular function, increase vascular resistance, and decrease vasodilation and hence tissue blood flow [76]. The impaired vasodilation [78] can even occur after short-term smoking [79]. Such an effect is not limited to the peripheral vasculature. Indeed, a narrowing of the coronary arteries, and hence decrease in coronary blood flow and increase coronary resistance, despite an increase in myocardial oxygen demand, has been reported as a result of acute cigarette smoking [80]. The authors suggested that such ongoing effects with prolonged smoking may well contribute to the adverse cardiovascular consequences of cigarette smoking, such as myocardial infarction and cardiac failure [80].

There are not many studies on the effects of vaping on exercise tolerance or cardiovascular function, but Polosa *et al*. [70] reported no significant changes in BP and HR in regular e-cigarette users. However, results of Polosa *et al*. [70] should be considered with caution, because of the small sample size (9 vapers *vs* 12 cigarette smokers). A meta-analysis that included 11 studies with a total of 283 participants concluded that vaping does acutely increase resting HR and diastolic BP [81], similar to the effects of cigarette smoking, but perhaps less pronounced [82]. These effects combined with the associated increased myocardial demand for oxygen and nutrients and vasoconstriction may lead to myocardial ischemia [83, 84]. Part, or perhaps even most, of these effects may be caused by nicotine [85], where nicotine increases the HR and BP primarily by sympathetic neural stimulation and systemic release of catecholamines [84]. Nicotine-free vaping does not impair vasodilation, increase BP or HR [85], increase arterial stiffness [86, 87], or cause palpations at rest [63]. The absence of a cardiovascular stimulus from nicotine-free vaping is significant, as people using other forms of nicotine delivery (smokers, NRT, dual use vapers and smokers) all had similar levels of circulating nicotine compared to nicotine-free vapers [88], though others report higher levels in smokers than vapers [82]. However, nicotine cannot be the sole culprit as vaping non-nicotinic aerosols also caused impaired femoral artery flow-mediated dilation [89]. Based on the culmination of acute responses, this suggests that a chronic e-cigarette user has an increased risk of increased arterial stiffness and associated adverse cardiovascular outcomes and comparative studies are required to assess whether the effects of smoking on cardiovascular health are more severe than those of vaping. Based on the acute impact of vaping on resting cardiorespiratory and vascular function, we expect that vaping will impair endurance exercise capacity. At this point however, more research is required to determine whether the impact of vaping on endurance exercise capacity, both in the short and long term, is significant and less than that from smoking.

Effects of vaping and cigarette smoking on muscle function and muscle size

Many studies have described the negative effects of smoking on skeletal muscle function and morphology, specifically, the thigh muscles [90]. One aspect is decreased muscle fatigue resistance [71] associated with reduced muscle oxidative capacity [91] and a slow twitch to fast twitch fibre type transition [92]. A diminished oxygen delivery due to the interaction of carbon monoxide (CO) with haemoglobin may hamper the mitochondria to resynthesize Adenosine triphosphate (ATP). The ability of the mitochondria to synthesise ATP can be further aggravated by mitochondrial dysfunction due to interaction of CO and other substances in cigarette smoke with elements of oxidative phosphorylation, and combined with the other changes already discussed, cause a reduction in muscle contractile endurance [93]. Furthermore, smoking could promote skeletal muscle wasting via smoking-induced inflammation that increases protein breakdown and decreases protein synthesis [93,94] and results in a reduced maximal force-generating capacity of the muscles from smokers [95,96].

There are as yet no studies on the effects of vaping on muscle function and/or skeletal muscle size.

Conclusions

In conclusion, despite vaping being marketed as safer and healthier smoking alternative and a smoking cessation technique, vaping has been found to cause similar effects as smoking on lung function and cardiovascular function. There are, however, no studies on the effects of vaping on muscle function and size. To assess whether these effects are less than those seen during smoking, future studies should seek to systematically compare the differences in severity in the smoking- and vaping-induced decrements in humans.

Abbreviations

UK	United Kingdom;
NRT	nicotine replacement therapy;
US	United States;
FDA	Food and Drug Administration;
FEV_1	forced expiratory volume in one second;
FEV_1/FVC	forced expiratory volume in one second/forced vital capacity;
BP	blood pressure;
HR	heart rate;
CO	carbon monoxide.

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