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Research Paper

Associations between flight time and thyroid nodules in pilots

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ABSTRACT

Pilots have complicated histories of exposure to circadian rhythm disruption and radiation because their occupation has unusual characteristics. Notably however, no study has investigated associations between flight hours and thyroid nodules (TNs) in pilots. The current study was conducted to investigate the incidence of TNs in pilots and assess the influence of flight hours on TNs. We analyzed data from 578 pilots at Shanghai hospital of civil aviation in China. Multiple logistic regression was used to assess associations between TNs and flight time. TN incidence in the 578 pilots was 47.9%, and less total flight hours was associated with a lower risk of TNs rather than less flight hours in the last 12 months, suggesting that flight hours have a significant cumulative effect on TNs. Airlines should consider enforcing the upper limit of flight hours, given the cumulative effects of total flight hours. Further studies such as clinical trials are needed.

Key words: Annual flight time, pilot, thyroid nodule, total flight hours.

INTRODUCTION

Thyroid nodules (TNs) are a common thyroid disease and have been defined by the American Thyroid Association as "discrete lesions within the thyroid gland, radiologically distinct from surrounding thyroid parenchyma" (Haugen et al., 2016). Most TNs are benign and clinically asymptomatic (Haugen et al., 2016). When nodules compress surrounding tissues or organs however, patients can experience trouble swallowing, pain, coughing, voice changes, and lymphadenopathy (Hamming et al., 1990). TNs can also be complicated by other thyroid diseases such as simple goiter, thyroid tumors, thyroid dysfunction, and thyroiditis. Moreover, approximately 5–15% of TNs are malignant (Alexander et al., 2012; Franceschi et al., 1999; Gharib et al., 2006). In a pooled analysis of individual data from 12 case-control studies conducted in seven countries, benign nodules/adenomas were the strongest risk factors for thyroid cancer other than radiation exposure in childhood. Despite the above-described observations, TNs have not been widely studied. The prevalence of TNs has increased worldwide over the past several decades, and it is approximately 19–67% as determined by high-resolution ultrasonography (Hegedus, 2004). Previous studies suggest that many factors such as psychological health, radiation exposure, and circadian rhythm disruption may be associated with the occurrence of TNs (Liu et al., 2018). Airline crews work in conditions that expose them to circadian rhythm disruption and radiation. Moreover, the high work intensity and long-term mental stress experienced by pilots may lead to an increased risk of thyroid disease.

Thyroid disease may potentially reduce the stress capacity and counter-overload capacity of pilots. Pilots with thyroid cancer must be grounded however, minimal research has focused on TNs in pilots, and the factors that influence TNs in pilots are unclear. Flight hours are an important indicator of pilots' work intensity and radiation exposure, but no study has examined the influence of flight hours on TNs. Flight hours may be an important indicator that affects pilots' health, and there may be significant associations between flight hours and TNs in pilots. In the present study 578 pilots were analyzed to determine the incidence of TNs in the cohort and the influence of flight hours on TN incidence was also investigated. The results of the study provide a basis for preventing thyroid diseases and responsibly allocating pilots' flight times, thereby keeping pilots healthy and improving the level of aeromedical support.

MATERIALS AND METHODS

Participants

The current study was conducted at the Aviation Personnel Physical Examination and Identification Center of Civil Aviation East China Area Administration of Shanghai Hospital of Civil Aviation in 2016–2017. Approximately 700 volunteer pilots were initially recruited, but some were not examined for metabolic indicators or TNs. Therefore, 578 pilots were ultimately analyzed in the study. All participants provided informed consent.

Data collection

The data collected included demographic information, physiological parameters, total flight hours, flight hours in the last 12 months (hereafter referred to as "annual flight hours"), and the year of data collection. Total flight hours and annual flight hours were divided into quartiles. Total flight hours was calculated as the total cumulative number of flight hours since beginning employment not including any flight time during training/pre-employment. Annual flight hours are calculated as the number of flight hours in the last 12 months. These data were collected from the 17 airline companies that operate in Shanghai, China, including ChunQiu Airlines and Eastern Airlines.

Laboratory analysis

Metabolic indices such as dyslipidemia are reportedly significantly correlated with TN prevalence (Zheng et al., 2015; De Pergola et al., 2007) therefore biochemical indicators were included in the current analysis. All examinations were performed at the Aviation Personnel Physical Examination and Identification Center of Civil Aviation East China Area Administration of Shanghai Hospital of Civil Aviation. The metabolic indices included levels of alanine aminotransferase, creatinine, blood urea, glucose, blood lipids, uric acid, total cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein. Thyroid ultrasonography was performed and serum triiodothyronine, tetraiodothyronine, thyroid-stimulating hormone, free triiodothyronine, and free tetraiodothyronine were examined. The diagnostic criteria for TNs were those described in the American Thyroid Association guidelines (Haugen et al., 2016). Normal volume of thyroid lobe was defined as ≤ 18 ml for women and ≥ 25 ml for men (Haugen et al., 2016). All indicators were classified as normal or abnormal.

Statistical analysis

The risk (odds ratio) of thyroid nodules and associated 95% confidence intervals were estimated via logistic regression analysis performed using SPSS 23 (SPSS Inc., Chicago, IL, USA). Multivariate logistic regression was used to analyze associations between TNs and flight time. The model 1 was used to adjust pilots' age, sex and metabolic indicators including alanine aminotransferase, creatinine, blood urea, uric acid, glucose, high-density lipoprotein, low density lipoprotein, total cholesterol and triglycerides with thyroid nodule. In addition, we also entered age, sex, metabolic indicators, total flight time and annual flight time respectively in the model 2. $P< 0.05$ was deemed to indicate statistical significance.

RESULTS

Demographic characteristics of pilots

The demographic characteristics of the pilots (n = 578) are shown in Table 1. Briefly, 541 (93.6%) were men and 37 (6.4%) were women, and their mean age was 32.83 ± 9.75 years (range 21–59 years). In this study 277 pilots (47.9%) were diagnosed with TNs. The prevalence of TNs in women was 27.0% and in men it was 49.4%. Of the total of 578 pilots, 283 (28.9%) had at least one metabolic index abnormality. The mean total flight hours was 5,925 ±6,826 and the mean annual flight hours was 616 ±309. The shortest total flight time was 10 h, and the longest was 35,500 h. The shortest annual flight time was 10 h, and the longest was 1,000 h. Associations between pilot characteristics and the risk of TNs are shown in Table 1. In the simple logistic regression analysis more total flight hours and more annual flight hours were significantly associated with an increased risk of TNs (both $P< 0.001$). Older age was significantly associated with a higher risk of TNs, with an odds ratio for subjects aged over 45 years of 7.879 (95% confidence interval: 4.215, 14.730; $P< 0.001$) relative to those aged under 25 years. Gender was significantly associated with TNs (P = 0.011) but metabolic indicators were not.

Associations between flight hours and TNs are shown in Table 2. In multiple logistic regression analysis more total flight hours was significantly associated with an increased risk of TNs. In comparison with pilots whose total flight hours were in the first quartile, those whose total flight hours were in the fourth quartile were more than four times as likely to have TNs. Annual flight hours was also associated with an increased risk of TNs. Pilots with more annual flight hours were approximately 1.5 times more likely to have TNs than those with less annual flight hours,

Table 1: Demographic Characteristics and Thyroid Nodule Prevalence in Pilots (N = 578).

	All		No. of thyroid nodules		Odds ratio	95% confidence interval
	No.	%	No.	%		
Gender						
Male	541	93.6	267	49.4	2.631	
Female	37	6.4	10	27.0	1.00	1.249, 5.541
					P^a= 0.011	
Age (year)						
≤ 25	148	25.6	47	17.0	1.00	
26~30	171	29.6	59	21.3	1.132	0.709,1.808
31~35	97	16.8	57	20.6	3.062	1.799, 5.214
36~40	31	5.4	16	5.8	2.292	1.046, 5.025
41~45	47	8.1	32	11.6	4.584	2.267, 9.271
≥ 45	84	14.5	66	23.8	7.879	4.215, 14.730
					P< 0.001	
Metabolic indicators [b]						
Abnormal blood glucose	12	2.1	8	2.9	0.453	0.135, 1.521
					P = 0.200	
Abnormalblood lipid	180	31.1	90	32.5	0.886	0.625, 1.261
					P = 0.502	
Abnormal uric acid	91	15.7	46	16.6	0.883	0.564, 1.381
					P = 0.585	
Total flight hours (100 h)						
Quartile 1(median, 2.36)	146	25.3	42	15.2	1.00	
Quartile 2(median, 16.00)	145	25.1	44	15.9	1.079	0.652, 1.785
Quartile 3(median, 50.00)	143	24.7	84	30.3	3.525	2.162, 5.750
Quartile 4(median, 160.00)	144	24.9	107	38.6	7.161	4.267, 12.018
					P< 0.001	
Annual flight hours(100 h)						
Quartile 1(median, 1.99)	155	26.8	50	18.1	1.00	
Quartile 2(median, 6.00)	135	23.4	61	22.0	1.731	1.074, 2.791
Quartile 3(median, 8.50)	209	36.2	128	46.2	2.144	2.144, 5.137
Quartile 4(median, 9.51)	79	13.7	38	13.7	1.117	1.117, 3.391
					P< 0.001	

CI, confidence interval; OR, odds ratio
[a]*P* value across categories calculated using continuous variables.
[b]Metabolic indicators included alanine aminotransferase, creatinine, blood urea, uric acid, glucose, high-density lipoprotein, low density lipoprotein, total cholesterol, and triglycerides.

although the difference was not statistically significant after adjustment for total flight hours.

DISCUSSION

Recent research has shown that the incidence of thyroid cancer is increasing worldwide (Siegel et al., 2016). Notably however, TNs which are significantly associated with thyroid cancer have been largely overlooked, especially in airline crews. To our knowledge the current study is the first retrospective analysis to investigate the prevalence of TNs and parameters associated with TNs in pilots. The incidence of TNs in pilots was 47.9% in the present study, which is higher than that of the general population (Song et al., 2016). In previous studies flight hours were an important indicator affecting pilots' health (Song et al., 2016; Surks et al., 2004; Vigneri et al., 2015), but no previous study has investigated relationships between flight hours and TNs in pilots. In the current study, TNs were significantly associated with flight hours and there was a significant cumulative association between flight hours and TNs. Even after adjustment for annual flight hours in multiple logistic regression analysis, there was still a significant association between total flight hours and TNs. Conversely, there was no significant association between annual flight hours and TNs after adjustment for total flight hours. This suggests that the cumulative effect of total flight hours may be more influential than that of annual flight hours. We also propose that more flight hours may lead to higher work pressure, greater circadian rhythm disruption, and more radiation exposure, and previous studies have

Table 2: Logistic Regression Analysis of Thyroid Nodules and Flight Hours in 578 pilots.

Variables	Model 1		Model 2[c]	
	OR[a]	**95% CI**	***OR***	**95%*CI***
Total flight hours (100 h)				
Quartile 1(median, 2.36)	1.00		1.00	
Quartile 2(median, 16.00)	0.994	0.584, 1.690	0.815	0.372, 1.784
Quartile 3(median, 50.00)	3.173	1.726, 5.834	2.513	1.062, 5.947
Quartile 4(median, 160.00)	5.000	1.768, 14.144	3.960	1.209, 12.968
			P [c]= 0.009	
Annual flight hours (100 h)	OR[a]	95% CI		
Quartile 1(median, 1.99)	1.00	0.581, 1.688	1.00	0.535, 2.307
Quartile 2(median, 6.00)	0.990	1.050, 2.862	1.111	0.731, 3.338
Quartile 3(median, 8.50)	1.734	0.701, 2.346	1.562	0.441, 2.433
Quartile 4(median, 9.51)	1.283		1.036	
			P = 0.113	

CI, confidence interval; OR, odds ratio
[a]Adjusted for age, sex, metabolic indicators, and total flight hours (hundred hours)
[b]Adjusted for age, sex, metabolic indicators, and annual flight hours (hundred hours)
[c]Model 2 included age, sex, metabolic indicators, total flight hours (hundred hours), and annual flight hours (hundred hours).
[d]*P* value based on variable containing median value for each quartile

suggested that these factors can contribute to a rapid increase in TNs incidence (Liu et al., 2018; Horn-Ross et al., 2014; Lim et al., 2017).

Pilots experience high work intensity and long-term stress due to long flights, and they report higher levels of stress than those in some other occupations (Ragan, 2011). Previous studies indicate that the prevalence of thyroid disease is related to stress (Ragan, 2011) and it has also been demonstrated that high levels of stress were significantly associated with pilots' health (Omholt et al., 2017); therefore we hypothesized that sustained flight time and cumulative flight hours may cause pilots to experience greater stress, and ultimately cause or aggravate thyroid disease. Circadian rhythm disturbances due to long flight times may contribute to TNs. Pilots often perform long-distance flights, transmeridian flights and night flights which disrupt circadian rhythms. Research has shown that irregular work and rest cycles can cause endocrine disorders and hormonal changes associated with the development of TNs (Gotlieb et al., 2018). In one study the prevalence of thyroid diseases in nurses in intensive care units, operating rooms, and other departments was higher than that of nurses in other departments, and it was suggested that this was due to frequent night shifts and irregular work schedules (Yang et al., 2017). Therefore, longer flight times may increase the irregularity of work performed by air crews and this may contribute to the development of TNs. Ionizing radiation is a well-established risk factor for TNs formation and tumorigenesis (Hatch et al., 2005). Previous studies have shown that the thyroid is susceptible to the effects of radiation. During the course of their work pilots are exposed to strong radiation for long periods at high altitudes, such as cosmic radiation and electromagnetic fields from cockpit instruments and other electronic equipment (Buja et al., 2005). Airline cabin crews are occupationally exposed to ionizing radiation at doses of 2–6 mSv per year (Bartlett, 2004).

This is approximately twice the average annual amount that the general population is exposed to via natural and medical sources. Flight duration is the factor most strongly correlated with radiation, thus longer flight hours expose pilots to more radiation. One study investigating pilots on polar vs. non-polar route flights suggested that the only viable option for limiting radiation doses was to limit flight hours when the average annual effective dose exceeded the standard 5 mSv per year (Fei et al., 2012). This suggests a need to limit flight time if the aim is to reduce risks associated with radiation. Notably, it was reported in one study that pilots were exposed to greater doses of radiation than flight attendants because the passenger cabin provides more of a shielding effect than the cockpit (Cardis and Hatch, 2011). The inclusion of flight crew other than pilots was beyond the scope of the current study however, and further studies that analyze pilots and flight attendants separately are needed. As well as radiation, other factors that have been implicated in the development of TNs include age and sex. In the current study, TNs were more frequent in male pilots than in female pilots and this differs from a previously reported study (Vander et al., 1968). The discrepancy may be because the current study only included a comparatively small number of women. The prevalence of TNs generally increased with age in the present study, and this is concordant with previous studies performed in other populations (Jiang et al., 2016). We surmise that in addition to the established fact that thyroid function decreases as age increases (Huo et al., 2017), the observed association in the current study may be due to the positive association between pilot age and cumulative total flight hours. Endocrine hormone disorders caused by long-term flights in pilots may also contribute to a relationship between age and TNs (Liu et al., 2018). The present study had some limitations. It only included pilots, not other flight crew such as flight attendants; whose annual flight hours tend to be longer due to the different nature of their work. Another limitation was that TNs number, size and malignancy were not evaluated in the study, thus associations between flight hours and TNs could not be analyzed further with reference to these variables. Lastly, temporal relationships could not be investigated because the study was a cross-sectional analysis.

In conclusion, in the current study TNs incidence in pilots was higher than that of the general population and flight hours were significantly associated with TNs prevalence. Thyroid disease is common in pilots and most TNs cause no obvious symptoms but TNs pose a hidden potential threat to pilots' health (Liu et al., 2018). Therefore, we recommend that pilots undergo regular thyroid examinations. Airlines should consider enforcing an upper limit on flight hours and exert reasonable limitations on pilots' overall flight time, given the cumulative effects of total flight time. To improve pilot health and safety, the Civil Aviation Administration stipulated that flight time should be limited to 1,000 h annually in China. Moreover, a new rule has recently been implemented adjusting the annual flight time limit to 900 h. The current regulations do not account for the effects of total cumulative flight time however, but in the current study associations between TNs and total flight hours were stronger than associations between TNs and annual flight hours. Therefore, we strongly recommend paying more attention to total flight hours and customizing flight times with due consideration of thyroid conditions in pilots to enhance pilot health. Further studies such as cohort studies and clinical trials are needed to confirm the results of the present study.

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