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**Incidence of colorectal neoplasms among male pilots**

Moshkowitz M *et al*. Colorectal neoplasms among male pilots

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**Abstract**

**AIM:** To assess the prevalence of colorectal neoplasms (adenomas, advanced adenomas and colorectal cancers) among Israeli military and commercial airline pilots.

**METHODS:** Initial screening colonoscopy was performed on average-risk (no symptoms and no family history) airline pilots at the Integrated Cancer Prevention Center (ICPC) in the Tel-Aviv Medical Center. Visualized polyps were excised and sent for pathological examination. Advanced adenoma was defined as a lesion >10 mm in diameter, with high-grade dysplasia or villous histology. The results were compared with those of an age- and gender-matched random sample of healthy adults undergoing routine screening at the ICPC.

**RESULTS:** There were 270 pilots (mean age 55.2 ± 7.4 years) and 1150 controls (mean age 55.7 ± 7.8 years). The prevalence of colorectal neoplasms was 15.9% among the pilots and 20.6% among the controls (*P* = 0.097, *χ2* test). There were significantly more hyperplastic polyps among pilots (15.5% *vs* 9.4%, *P* = 0.004) and a trend towards fewer adenomas (14.8% *vs* 20.3% *P* = 0.06). The prevalence of advanced lesions among pilots and control groups was 5.9% and 4.7%, respectively (*P* = 0.49), and the prevalence of cancer was 0.7% and 0.69%, respectively (*P* = 0.93).

**CONCLUSION:** There tends to be a lower colorectal adenoma, advanced adenoma and cancer prevalence but a higher hyperplastic polyp prevalence among pilots than the general population.

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**Key words:** Colorectal cancer; Adenomatous polyps; Colon neoplasms; Hyperplastic polyps

**Core tip:**Military and commercial airline pilots are exposed to cosmic radiation and other specific occupational factors. Several epidemiological studies on a possible elevated cancer risk, including colorectal cancer, among flight personnel have yielded contradictory results. We aimed to evaluate the incidence of colorectal neoplasms among Israeli military and commercial pilots and to compare it with the incidence of colorectal neoplasms among the general population. We found that the prevalence of colorectal adenomas, advanced adenoma and cancer is not higher, and tends to be even lower, among aircrew than that of the general population. It seems that ionizing radiation does not constitute a risk factor for colorectal cancer among air crew personal.

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**INTRODUCTION**

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer death among both women and men in the Western countries[1]. It is estimated that up to 90% of CRC cases could be avoided with appropriate screening which allows the detection of asymptomatic cancers that are more amenable to curative therapy as well as the removal of adenomas that could subsequently develop into invasive cancer[2,3]. Several risk factors have been reported to be associated with colorectal adenomas, including obesity, impaired glucose tolerance, hypertension, low high-density lipoprotein cholesterol, and hypertriglyceridemia, as well as lifestyle factors, such as alcohol consumption, cigarette smoking, and lack of physical exercise[4,5]. Airline pilots are recognized as an occupational group at risk for various types of cancers[6].Although they must be physically fit, mentally stabile and lead an appropriate lifestyle in addition to being under closer medical supervision than most other occupational groups, they are subject to several occupational exposures that may pose physiological challenges to their long-term health. The latter include circadian dysrhythmia, mild hypoxia, and exposure to reduced atmospheric pressure, low humi*d*ity, noise, vibration, cosmic radiation and magnetic fields[7-8].

Ionizing radiation in higher doses is known, or suspected, to be a cause of several types of cancer[9], and international recommendations regulate such exposure during flights[10,11]. Chromosomal analyses have showed significantly higher numbers of chromosomal translocations among pilots than among controls, and chromosomal translocation frequency was found to be significantly associated with flight years[12,13]. Health studies that have been conducted on this occupational group over the past three decades usually focused on radiation-associated cancer, and those investigations produced inconsistent results[14-20]. An excess mortality from a variety of lesions that were reported in some of these studies include tumors of brain [14], testis, urinary bladder[15], prostate and acute myeloid leukemia[14]. In addition, an excess risk of breast cancer has been observed among female cabin attendants[18], and several studies reported an increased risk for colorectal tumors with standardized incidence ratios ranging from 1.32 to 1.34[19-21].

The recognition that normal colorectal epithelium progresses to adenomas of increasing degrees of dysplasia and then to invasive cancer has been termed the “adenoma–carcinoma sequence”, and it has proved to be an excellent model of human cancer[22]. According to this model, it can be assumed that an increased incidence of colorectal tumors would be associated with an increased incidence of adenomas.

This study aims to evaluate the incidence of colorectal neoplasms among Israeli military and commercial pilots and to compare it with the incidence of colorectal neoplasms among the general population.

**MATERIALS AND METHODS**

***Study design***

We performed a retrospective case–control study at the Tel-Aviv Sourasky Medical Center from 2003 to 2011. During this period, a total of 270 colonoscopies were performed on military and commercial pilots. All of these individuals were at average-risk for colorectal cancer and underwent colonoscopy for the first time and had all been referred for screening colonoscopy as a primary prevention procedure. Individuals were excluded if they reported a personal history of colorectal adenoma or carcinoma at any time; if they had a family history of colorectal adenoma or carcinoma (one first-degree relative aged < 70, or two or more family relatives at any age); if they had a personal history of inflammatory bowel diseases; if they reported symptoms suggestive of neoplasia (rectal bleeding, change in bowel habit, abdominal pain, or unexplained weight loss during the previous 6 months); or if they had a positive fecal occult blood test (FOBT), or laboratory abnormalities such as iron-deficiency anemia. A comparison group was randomly selected from an average-risk, age- and sex-matched control group (*n* = 1150) from the same institution who underwent colonoscopy during the same time period for similar indications.

***Endoscopic procedures***

All participants were interviewed and examined by a gastroenterologist. Colonoscopy was performed according to the usual protocol in our institute by experienced gastroenterologists using high-resolution Pentax endoscopes. It was complete to the cecum in 98.7% of patients, and the present analyses were restricted to subjects who underwent a complete colonoscopic examination. All the lesions that had been found during colonoscopy were sampled, removed and sent for pathological examination. The size of the polyp was estimated with the use of open-biopsy forceps. If more than one lesion was detected, the colonoscopic findings were classified according to the most advanced lesion. Advanced adenomas were defined by the presence of any of the following adenoma characteristics: size ≥ 10 mm, any villous histology, high-grade dysplasia or colorectal cancer that was either invasive (through the muscularis mucosa) or in-situ. For analyses of advanced adenoma, the subjects were classified according to their most advanced pathological finding.

***Statistical analysis***

The proportion of individuals with polyps in the pilot and control groups was compared using the chi-square and Fisher’s exact tests. A *P* value less than 0.05 was considered statistically significant, and the SPSS (Chicago, Illinois, United States) for Windows software, version 13.0 was used for the analysis.

**RESULTS**

The pilot group was comprised of 270 males whose average age was 55.2 years at the time of the index screening colonoscopy. They were compared to an age-matched control group of 1150 males (average age 55.7 years at time of the index screening colonoscopy) who were also undergoing routine colonoscopy**.**

***Polyp, adenoma and advanced lesion detection***

Eighty-three (30.7%) pilots were found to have polyps of any type (hyperplastic and/or adenomatous) compared to 342 (29.7%) controls (*P* = NS). There was a significant difference in the number of pilots and controls who had hyperplastic polyps [*n* = 42/270 (15.5%) *vs* *n* = 108/1150 (9.4%), respectively; *P* = 0.004]. Adenomas were detected in 41 (14.8%) pilots compared to 234 (20.3%) controls (*P* = 0.06). Similarly, the number of detected advanced adenoma was not significantly different between pilots and controls [*n* = 16/270 (5.9%) *vs* *n* = 54/1150 (4.7%); *P* = 0.49] (Table 1).

***High-grade dysplasia and carcinoma detection***

A total of 16 advanced lesions was detected in 270 pilots, 2 (0.7%) of which were carcinomas and 2 were high-grade dysplasia (0.7%). The control group had similar rates of advanced lesions: 8 of the 1150 subjects had carcinomas (0.69%) and 9 (0.78%) had high-grade dysplasia (*P* = 0.93) (Table 1).

**DISCUSSION**

Over the last 30 years, studies conducted on airline pilots usually focused on radiation-associated cancer, and their results were inconsistent. Nicholas *et al*[23] reported that US pilots and navigators experienced significantly increased mortality due to cancer of the kidney and renal pelvis, and had a tendency towards increased mortality due to cancer of the prostate, brain, colon, lip, buccal cavity, and pharynx. In their first study which was based on small numbers of subjects, Band *et al*[20] had found excess deaths for brain cancer and for rectal cancer (*n* = 3; SMR = 4.35; *P* = 0.033; 95%CI: 1.20-11.20) and an excess cancer incidence for non-melanoma skin cancer, brain cancer and Hodgkin's disease. In a later study, however, the same investigators found a significantly decreased mortality among pilots for all types of cancers, except for prostate cancer and acute myeloid leukemia, which were significantly increased[21].

Unlike previous studies that examined the presence of CRC or death from CRC, the present study systematically compared the presence of premalignant lesions of CRC among pilots with that of age- and gender-matched subjects randomly chosen from the general population. Our study demonstrated no difference and an even lower rate of polyps and adenomas, regardless of size or polyp pathology, between the two groups. The findings of our study are compatible with those of a recent systematic review of the epidemiological literature on health of aircrew members since 1990, which included 65 relevant publications[6]. It reported that the overall cancer incidence and mortality was generally lower among aircrew members than in the comparison population, however, consistently elevated risks were reported for breast cancer incidence among female aircrew members and for melanoma among both male and female aircrew members. The conclusion of that review was that ionizing radiation was considered to contribute little if anything to elevated risks for cancers among an aircrew, whereas excess ultraviolet radiation was a probable cause of an increased melanoma risk among them.

One explanation for the low incidence of colorectal tumors among the crew members was the relative absence of risk factors among that professional group. Risk factors for colorectal cancer and adenomas have been extensively studied and include nutritional as well as lifestyle habits. Compelling evidence indicates that avoidance of smoking and heavy alcohol use, prevention of weight gain, and maintenance of a reasonable level of physical activity are associated with markedly lower risks of colorectal cancer[24]. The systematic monitoring of the health status of aircrew members presumably contributes to reducing the risk factors and pre-malignant as well as cancer rates.

One interesting finding of the current study is the significantly increased rate of hyperplastic polyps among air crew members compared to controls. Hyperplastic colonic polyps have traditionally been considered to have no malignant potential, and are generally regarded as being of little or no clinical consequence. However, recent evidence has suggested that some hyperplastic polyps may develop into cancer via the serrated or microsatellite instable pathways[24]. Chan *et al*[25] suggested that right-sided or large hyperplastic polyps appear to be the ones of concern. We have no explanation for the greater number of hyperplastic polyps among our cohort of pilots, however, they all were relatively small lesions, and none of them were on the right side of the colon

In conclusion, we found that the prevalence of colorectal adenomas, advanced adenoma and cancer is not higher and tends to be even lower among aircrew than that of the general population. There was an increased number of small, left-sided hyperplastic polyps among the pilots compared to the general population, but the significance of this observation is not clear and further studies are needed to confirm it.

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**COMMENTS**

***Background***

Several occupational exposures may present physiological challenges to the long-term health of airline pilots. These include circadian dysrhythmia, mild hypoxia, exposure to reduced atmospheric pressure, low humidity, noise, vibration, and exposure to cosmic radiation and magnetic fields. Previous studies have shown an excess mortality from a variety of cancers such as brain, testis, urinary bladder, prostate, leukemia, breast and colorectal tumors.

***Research frontiers***

According the “adenoma–carcinoma sequence” model, normal colorectal epithelium progresses to adenomas of increasing degrees of dysplasia and then to invasive cancer. It can be assumed, therefore, that an increased incidence of colorectal tumors would be associated with an increased incidence of adenomatous polyps. In this study, the authors demonstrate that the prevalence of colorectal adenomatous polyps is not increased among male pilots.

***Innovations and breakthroughs***

In contrast to previous studies that examined the presence of colorectal cancer (CRC) or death from CRC among air crew, the present study is the first one that evaluated systematically the presence of premalignant lesions of CRC among pilots. Our study demonstrated no difference and an even lower rate of polyps and adenomas, regardless of size or polyp pathology, between pilots and the general population.

***Applications***

Colorectal cancer screening program among pilots should be equal to that of general population

***Terminology***

Colorectal cancer is the third leading cause of cancer deaths among men and women in the Western world. Colorectal cancer is preventable, and curable, if detected early. Colorectal adenomas are considered as established precursors of colorectal cancers.

***Peer review***

The present study is the first to compare the rates of adenomas among pilots with that of age- and gender-matched subjects in the general population. It is a retrospective study with low number of pilots (*n* = 270), however a large control group (*n* = 1150) helps in the statistical analysis.

**REFERENCES**

1 **Jemal A**, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin* 2010; **60**: 277-300 [PMID: 20610543 DOI: 10.3322/caac.20073]

2 **Mandel JS**, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM, Ederer F. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med* 1993; **328**: 1365-1371 [PMID: 8474513]

3 **Rex DK**, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol* 2009; **104**: 739-750 [PMID: 19240699 DOI: 10.1038/ajg.2009.104]

4 **Harriss DJ**, Atkinson G, George K, Cable NT, Reilly T, Haboubi N, Zwahlen M, Egger M, Renehan AG. Lifestyle factors and colorectal cancer risk (1): systematic review and meta-analysis of associations with body mass index. *Colorectal Dis* 2009; **11**: 547-563 [PMID: 19207714 DOI: 10.1111/j.1463-1318.2009.01766.x]

5 **Harriss DJ**, Atkinson G, Batterham A, George K, Cable NT, Reilly T, Haboubi N, Renehan AG. Lifestyle factors and colorectal cancer risk (2): a systematic review and meta-analysis of associations with leisure-time physical activity. *Colorectal Dis* 2009; **11**: 689-701 [PMID: 19207713 DOI: 10.1111/j.1463-1318.2009.01767.x]

6 **Hammer GP**, Blettner M, Zeeb H. Epidemiological studies of cancer in aircrew. *Radiat Prot Dosimetry* 2009; **136**: 232-239 [PMID: 19608578 DOI: 10.1093/rpd/ncp125]

7 **Bartlett DT**. Radiation protection aspects of the cosmic radiation exposure of aircraft crew. *Radiat Prot Dosimetry* 2004; **109**: 349-355 [PMID: 15273353 DOI: 10.1093/rpd/nch311]

8 **Vuković B**, Radolić V, Miklavcić I, Poje M, Varga M, Planinić J. Cosmic radiation dose in aircraft--a neutron track etch detector. *J Environ Radioact* 2007; **98**: 264-273 [PMID: 17600597]

9 **Sigurdson AJ**, Ron E. Cosmic radiation exposure and cancer risk among flight crew. *Cancer Invest* 2004; **22**: 743-761 [PMID: 15581056 DOI: 10.1081/CNV-200032767]

10 **Hammer GP**, Zeeb H, Tveten U, Blettner M. Comparing different methods of estimating cosmic radiation exposure of airline personnel. *Radiat Environ Biophys* 2000; **39**: 227-231 [PMID: 11200966 DOI: 10.1007/s004110000071]

11 **Mares V**, Maczka T, Leuthold G, Rühm W. Air crew dosimetry with a new version of EPCARD. *Radiat Prot Dosimetry* 2009; **136**: 262-266 [PMID: 19608574 DOI: 10.1093/rpd/ncp129]

12 **Yong LC**, Sigurdson AJ, Ward EM, Waters MA, Whelan EA, Petersen MR, Bhatti P, Ramsey MJ, Ron E, Tucker JD. Increased frequency of chromosome translocations in airline pilots with long-term flying experience. *Occup Environ Med* 2009; **66**: 56-62 [PMID: 19074211 DOI: 10.1136/oem.2008.038901]

13 **Nicholas JS**, Butler GC, Davis S, Bryant E, Hoel DG, Mohr LC. Stable chromosome aberrations and ionizing radiation in airline pilots. *Aviat Space Environ Med* 2003; **74**: 953-956 [PMID: 14503673]

14 **Blettner M**, Zeeb H, Auvinen A, Ballard TJ, Caldora M, Eliasch H, Gundestrup M, Haldorsen T, Hammar N, Hammer GP, Irvine D, Langner I, Paridou A, Pukkala E, Rafnsson V, Storm H, Tulinius H, Tveten U, Tzonou A. Mortality from cancer and other causes among male airline cockpit crew in Europe. *Int J Cancer* 2003; **106**: 946-952 [PMID: 12918075 DOI: 10.1002/ijc.11328]

15 **Langner I**, Blettner M, Gundestrup M, Storm H, Aspholm R, Auvinen A, Pukkala E, Hammer GP, Zeeb H, Hrafnkelsson J, Rafnsson V, Tulinius H, De Angelis G, Verdecchia A, Haldorsen T, Tveten U, Eliasch H, Hammar N, Linnersjö A. Cosmic radiation and cancer mortality among airline pilots: results from a European cohort study (ESCAPE). *Radiat Environ Biophys* 2004; **42**: 247-256 [PMID: 14648170 DOI: 10.1007/s00411-003-0214-7]

16 **Zeeb H**, Blettner M, Langner I, Hammer GP, Ballard TJ, Santaquilani M, Gundestrup M, Storm H, Haldorsen T, Tveten U, Hammar N, Linnersjö A, Velonakis E, Tzonou A, Auvinen A, Pukkala E, Rafnsson V, Hrafnkelsson J. Mortality from cancer and other causes among airline cabin attendants in Europe: a collaborative cohort study in eight countries. *Am J Epidemiol* 2003; **158**: 35-46 [PMID: 12835285 DOI: 10.1093/aje/kwg107]

17 **Pukkala E**, Aspholm R, Auvinen A, Eliasch H, Gundestrup M, Haldorsen T, Hammar N, Hrafnkelsson J, Kyyrönen P, Linnersjö A, Rafnsson V, Storm H, Tveten U. Cancer incidence among 10,211 airline pilots: a Nordic study. *Aviat Space Environ Med* 2003; **74**: 699-706 [PMID: 12862322]

18 **Pukkala E**, Auvinen A, Wahlberg G. Incidence of cancer among Finnish airline cabin attendants, 1967-92. *BMJ* 1995; **311**: 649-652 [PMID: 7549630 DOI: 10.1136/bmj.311.7006.649]

19 **Band PR**, Spinelli JJ, Ng VT, Moody J, Gallagher RP. Mortality and cancer incidence in a cohort of commercial airline pilots. *Aviat Space Environ Med* 1990; **61**: 299-302 [PMID: 2339962]

20 **Band PR**, Le ND, Fang R, Deschamps M, Coldman AJ, Gallagher RP, Moody J. Cohort study of Air Canada pilots: mortality, cancer incidence, and leukemia risk. *Am J Epidemiol* 1996; **143**: 137-143 [PMID: 8546114]

21 **Grayson JK**, Lyons TJ. Cancer incidence in United States Air Force aircrew, 1975-89. *Aviat Space Environ Med* 1996; **67**: 101-104 [PMID: 8834932]

22 **Cummings OW**. Pathology of the adenoma-carcinoma sequence: from aberrant crypt focus to invasive carcinoma. *Semin Gastrointest Dis* 2000; **11**: 229-237 [PMID: 11057950]

23 **Nicholas JS**, Lackland DT, Dosemeci M, Mohr LC, Dunbar JB, Grosche B, Hoel DG. Mortality among US commercial pilots and navigators. *J Occup Environ Med* 1998; **40**: 980-985 [PMID: 9830605 DOI: 10.1097/00043764-199811000-00008]

24 **Hawkins NJ**, Ward RL. Sporadic colorectal cancers with microsatellite instability and their possible origin in hyperplastic polyps and serrated adenomas. *J Natl Cancer Inst* 2001; **93**: 1307-1313 [PMID: 11535705 DOI: 10.1093/jnci/93.17.1307]

25 **Chan AT**, Giovannucci EL. Primary prevention of colorectal cancer. *Gastroenterology* 2010; **138**: 2029-2043 [PMID: 20420944 DOI: 10.1053/j.gastro.2010.01.057]

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**Table 1 Endoscopic findings in the study *vs* control groups*****n* (%)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Pilots** Total *n* = 270 | **Controls**Total *n* = 1150 | ***P* Value** |
| Age, yr (range) | 55.2 (39-74) | 55.7 (40-75) |  |
| Endoscopic finding  |  |  |  |
| Normal  | 185 (68.5) | 805 (70) | 0.65 |
| Hyperplastic polyps  | 42 (15.5) | 108 (9.4) | **0.004** |
| Adenomatous polyps  | 41 (14.8) | 234 (20.34) | 0.06 |
| Advanced adenoma  | 16 (5.9) | 54 (4.7) | 0.49 |
| > 3 polyps | 5 (1.85) | 32 (2.8) | 0.51 |
| High-grade dysplasia  | 2 (0.7) | 9 (0.78) | 0.94 |
| Cancer  | 2 (0.7) | 8 (0.69) | 0.93 |