Chapter 7

The incidence of venous thrombosis in commercial airline pilots: a cohort study of 2630 pilots

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Submitted for publication
Abstract

Airline pilots may be at increased risk of venous thrombosis because air travel has recently been established as a risk factor for venous thrombosis. The aim of this study was to assess the risk of venous thrombosis in a cohort of Dutch airline pilots.

Methods: Airline pilots who had been active members of the Dutch Airline Pilots Association (ALPA), in Dutch called the Vereniging Nederlandse Verkeersvliegers (VNV), were questioned for the occurrence of venous thrombosis, presence of risk factors for venous thrombosis and number of flight hours per year and rank. Incidence rates among pilots were compared to that of the general Dutch population and to a population of frequently flying employees of multinational companies.

Results: 2630 male pilots were followed up for a total of 20,420 person-years. Six venous thromboses were reported, yielding an incidence rate of 0.3/1000 py. The standardized morbidity ratio, comparing these pilots to the general Dutch population adjusted for age, was 0.8. Compared to the employees, this standardized morbidity ratio was 0.7 when all employees were included and 0.6 when only the frequently travelling employees were included. The incidence rate did not increase with number of flight hours per year and did not clearly vary by rank.

Conclusions: the risk of venous thrombosis is not increased amongst airline pilots.
Introduction

Commercial airline pilots are occupationally exposed to factors that may have a negative impact on their health. Even though their overall mortality is lower than that in the general population\(^1\)-\(^3\), some diseases occur more often in airline pilots. Cohort studies have shown that the incidence rate of malignant diseases is increased in aviation crew members\(^3\)-\(^11\). Especially skin-cancer (both melanoma and non-melanoma), leukaemia and breast-cancer occur more frequently in airline cabin crew than in the general population, possibly due to exposure to cosmic radiation, jet fuel, cabin air pollutants or constant changing of the circadian rhythm. Cosmic radiation may also be responsible for an increased risk of developing cataract later in life\(^12\). Furthermore, the incidence rates of HIV and AIDS, dermatitis and injuries have been shown to be increased in cabin crew members\(^3\),\(^13\),\(^14\) as compared to the general population.

In recent years, it has become clear that long distance air travel increases the risk of venous thrombosis. Case-control and follow up studies have demonstrated that risk of venous thrombosis shortly after long haul travel is approximately 2-4 fold increased\(^15\)-\(^19\). The absolute risk of a symptomatic venous thrombotic event within 8 weeks of flights longer than 4 hours is approximately 1 in 4500 flights\(^17\). The risk increases with duration of travel\(^17\),\(^20\),\(^21\) and particularly when individuals are exposed to several flights within a short time period\(^17\).

Because of their frequent exposure to air travel and because of the higher prevalence of conditions that increase the risk of venous thrombosis (malignant diseases, injuries), commercial airline pilots may be at increased risk of developing venous thrombosis. No large epidemiological studies have so far investigated the incidence of venous thrombotic disease in airline pilots. Knowledge of this incidence rate is needed to provide airline pilots with solid advice regarding the use of prophylactic measures such as exercises or elastic compression stockings. When the incidence rate is indeed increased, venous thrombosis may be a serious occupational health problem for airline pilots, since they are usually not allowed to fly while using anticoagulant drugs.

The aim of the current study was to assess the incidence rate of symptomatic venous thrombosis in commercial airline pilots and to compare this incidence rate to that of the general population as well as to that of a frequently travelling population of employees of international companies and organisations. The employees were used as a second control population in order to take the so-called healthy worker effect into account (meaning that the incidence rate of many diseases is lower in a working population than in the general population). Furthermore, we assessed the effect of number of flight-hours per year and type of most flown airplane on this incidence rate.
Methods

Study design
We performed a cohort study among commercial airline pilots. During a follow up period of 10 years, we assessed the occurrence of venous thrombotic events.

Participants: airline pilots
More than 95% of all commercial airline pilots in the Netherlands are member of the Dutch Airline Pilot Association (APLA), in Dutch called the Vereniging Nederlandse Verkeersvliegers (VNV). All pilots who were a member of the VNV at some point during the follow-up period and who were still alive in March 2003 were included in the study. Only the years that they were employed as a commercial airline pilot contributed to the total number of person years of follow up. The follow-up period started at January 1st 1993 or at start of employment as a commercial airline pilot if this was later. Follow-up ended at January 1st 2003, when venous thrombosis was diagnosed or when the employment as a commercial airline pilot ended, whichever occurred first. The VNV provided us with names and addresses of all possible participants. For the main analysis, only individuals who were still members of the VNV at the time the study was conducted were included. However, airline pilots may have ended their membership of the VNV because of occurrence of disease, such as venous thrombosis. Therefore, we also sent questionnaires to all pilots who had ended their membership of the VNV during the follow up period. Furthermore, the VNV provided us with data (names, birth dates and last known addresses) on pilots that had been a member after January 1993, but who had deceased at the time we performed the study, which made it possible to assess whether any of the deceased pilots had died due to venous thrombosis.

Control populations
The incidence rates of venous thrombosis in airline pilots were compared to two control populations. The first control group was the general Dutch population in 1994. Age-specific incidence rates of venous thrombosis were obtained through Prismant, a Dutch institution that keeps statistics on incidence rates according to ICD-9 codes (Prismant, Utrecht, the Netherlands).

As a so-called healthy worker effect (individuals who are employed are generally more healthy than those who are not) is likely to be present when comparing to the general population, we also included a second control group in our analysis. This control group consisted of a cohort of frequently flying employees of international companies and organisations. These employees had
been enrolled in a study on the absolute risk of venous thrombosis after air travel, the results of which have recently been published17. All employees in this cohort received electronic questionnaires on the occurrence of venous thrombosis during a 5-year follow up period. From this cohort of 8755 employees, those who had made at least 5 long haul flights per year on average were selected. Their incidence rate of venous thrombosis during the time they were not exposed to air travel was compared to that of the airline pilots.

Questionnaires and flight data
All pilots were sent questionnaires with questions on general characteristics, such as age and sex, occurrence of venous thrombosis (at any time point during the follow up period), risk factors for venous thrombosis and flight data (number of flight hours per year, employing airline, types of airplanes flown and rank). Questionnaires were sent through regular mail and non-responding pilots received up to 2 reminders with 2-week intervals.

Outcomes
Participants who reported venous thrombosis were asked to fill in a consent form for medical chart review. Only symptomatic first venous thrombotic events that were diagnosed with objective methods were considered. Deep vein thrombosis had to be diagnosed by compression ultrasonography or venography. Pulmonary embolism had to be diagnosed by spiral-CT scanning, high probability ventilation-perfusion scanning or angiography. Superficial thrombophlebitis was not included.

Of the members who were deceased, we obtained causes of death from the central Bureau of Statistics (CBS), where all death certificates are registered.

Statistical analysis
Incidence rates were calculated by dividing the number of events by the total number of person-years the pilots were followed. We calculated both the overall incidence rate as well as incidence rates per category based on age and number of flight-hours per year. In the control-populations, age-specific incidence rates were calculated in the same way. Standardized overall incidence rates in these populations were calculated as the weighted average of the age-specific incidence rates, using the age-distribution of the airline pilots as weights. The ratio of these incidence rates is the standardized morbidity ratio (SMR), which may also be seen as the ratio of the observed over the expected number of cases. Standard errors were calculated based on a poisson distribution of the number of events. All statistical analyses were performed using SPSS version 12.0 (SPSS, Chicago, Illinois, United States).
Protection of privacy
Since the diagnosis of venous thrombosis may have a significant impact on the career of a commercial airline pilot (they are not allowed to fly while they use anticoagulant therapy), we assured extra protection of their personal data: all questionnaires were coded; the key that linked these codes to the names and addresses of the pilots was deposited at a notary public. Only one administrative employee, who was sworn to secrecy, had access to this key, and only in the presence of the notary public.

Results
A total of 3525 airline pilots had been a member of the VNV at some point between January 1st 1993 and January 1st 2003. Of these airline pilots, 3237 were still a member of the VNV at the time they received the questionnaire (active members). A total of 288 pilots were no longer a member of the VNV when they received the questionnaire, but had been at some point during the follow up period (inactive members). Of the active members, 2474 pilots completed and returned the questionnaire, yielding a response of 76%. Of the 288 inactive members, 156 completed the questionnaire (response 54%). General characteristics of all participating active and in-active VNV-members are shown in Table 1.

Table 1: General characteristics of all participating airline pilots

<table>
<thead>
<tr>
<th></th>
<th>Active members</th>
<th>Archive members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range)</td>
<td>30.1 (18-63)</td>
<td>38.0 (19-60)</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>96.1</td>
<td>97.3</td>
</tr>
<tr>
<td>Flight-hours/year, mean (range)</td>
<td>521 (0-1800)</td>
<td>516 (0-1500)</td>
</tr>
<tr>
<td>Rank</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captain (% of py)</td>
<td>46.5</td>
<td>59.6</td>
</tr>
<tr>
<td>First officer (% of py)</td>
<td>46.0</td>
<td>36.1</td>
</tr>
<tr>
<td>Second officer (% of py)</td>
<td>7.5</td>
<td>4.4</td>
</tr>
</tbody>
</table>

The total follow-up time of the participating pilots who were still a member of the VNV at the time the study was performed added up to 20 420 person-years, with a mean follow up time per pilot of 8.3 years (range 0-10 years).

Since there were only very few female pilots (n=100, 3.8%) none of whom had experienced venous thrombosis, we decided to restrict all further analyses to male airline pilots only. The total follow up time of male airline pilots who were active members of the VNV when they received our questionnaire was 19 719 person-years.
Venous thrombosis
During the total follow up time, 6 objectively confirmed events of deep vein thrombosis or pulmonary embolism occurred. All patients were men and active members of the VNV. Three pilots had developed a deep vein thrombosis of the leg, two suffered from both deep vein thrombosis of the leg and pulmonary embolism and one airline pilot was diagnosed with a deep vein thrombosis of the arm. None of the inactive members of the VNV reported occurrence of venous thrombosis. During the follow-up period, 54 pilots or ex-pilots died, but in none of these pilots venous thrombosis was reported as the primary cause of death.

Incidence rates and standardized morbidity ratios
The overall incidence rate of venous thrombosis in the cohort of active members of the VNV was 0.3/1000 person-years (CI95 0.1-0.6 per 1000 person-years). Age-specific incidence rates of the airline pilots and both control populations are shown in Table 2. Although the incidence rate was highest in the oldest age category, the occurrence of venous thrombosis did not clearly increase gradually with age.

<table>
<thead>
<tr>
<th>Age</th>
<th>PY</th>
<th>Cases</th>
<th>IR* pilots (CI95)</th>
<th>IR population**</th>
<th>IR employees#</th>
<th>IR employees##</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>19 719</td>
<td>6</td>
<td>0.3 (0.1-0.6)</td>
<td>0.4</td>
<td>0.4 (0.2-1.8)</td>
<td>0.5</td>
</tr>
<tr>
<td>&lt;20</td>
<td>41</td>
<td>0</td>
<td>0 (0-24.4)</td>
<td>0.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20-25</td>
<td>1404</td>
<td>0</td>
<td>0 (0-0.7)</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25-30</td>
<td>4025</td>
<td>1</td>
<td>0.2 (0-1.0)</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30-35</td>
<td>4465</td>
<td>2</td>
<td>0.4 (0-1.3)</td>
<td>0.3</td>
<td>0</td>
<td>0.5 (0-2.1)</td>
</tr>
<tr>
<td>35-40</td>
<td>3486</td>
<td>0</td>
<td>0 (0-0.3)</td>
<td>0.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>40-45</td>
<td>2578</td>
<td>1</td>
<td>0.4 (0-1.6)</td>
<td>0.7</td>
<td>1.0 (0-4.2)</td>
<td>1.7 (0.4-3.8)</td>
</tr>
<tr>
<td>45-50</td>
<td>2006</td>
<td>0</td>
<td>0 (0-0.5)</td>
<td>0.9</td>
<td>1.0 (0-4.0)</td>
<td>0.4 (0-1.7)</td>
</tr>
<tr>
<td>50-55</td>
<td>1306</td>
<td>2</td>
<td>1.5 (0-4.5)</td>
<td>1.2</td>
<td>2.6 (0.7-7.7)</td>
<td>0.5 (0-2.2)</td>
</tr>
<tr>
<td>&gt;55</td>
<td>408</td>
<td>0</td>
<td>0 (0-2.5)</td>
<td>0.4</td>
<td>0</td>
<td>3.3 (06-8.3)</td>
</tr>
</tbody>
</table>

Overall incidence rates in the general population and employees were standardized for the age of the airline pilots
* IR: Incidence rate per 1000 person-years
** IR population: incidence rate per 1000 person-years in the general male Dutch population
# IR employees1: incidence rate per 1000 person-years in male employees who made at least 5 long haul flights during the follow up period of 5 years, while they were unexposed to air travel
## IR employees1: incidence rate per 1000 person-years in all male employees, while they were unexposed to air travel

The age-standardized incidence rate in the general male Dutch population was 0.4 per 1000 person-years. In employees who made at least 5 long haul flights in their follow up period of approximately 5 years, the standardized incidence rate of venous thrombosis while they were unexposed to air travel was also 0.4/1000 person-years. When all employees were included, regardless of the
number of long haul flights made, the standardized incidence rate while they were unexposed to air travel was 0.5/1000 person-years.

The rate ratio (standardized morbidity ratio) comparing the airline pilots to the general Dutch population was 0.8 (CI95 0.7-1.0), i.e. the pilots experienced 0.8 times the number of events that would have occurred in the cohort if the morbidity rates of the population had applied. The standardized morbidity ratio comparing the airline pilots to the employees who travelled at least 5 times during the follow up period was 0.7 (CI95 0.6-0.9), and it was 0.6 (CI95 0.5-0.7) when we compared airline pilots to all male employees that were included in that study.

**Effect of number of flight hours per year and rank**

Table 3 shows the incidence rate of venous thrombosis per category of flight-hours per year. For the cases of venous thrombosis, the number of flight hours in the year preceding their thrombotic event was considered, since they probably flew less hours after their event in the year they developed venous thrombosis. There was no association between flight-hours per year and the incidence rate of venous thrombosis. In the same table, the effect of rank of the airline pilots is shown. The incidence rate of venous thrombosis was highest in second officers (0.7/1000 person-years, CI95 0-2.6/1000 person-years), but the numbers were too small to draw solid conclusions regarding the effect of rank on the occurrence of venous thrombosis.

<table>
<thead>
<tr>
<th>Flight-hours per year</th>
<th>Person-years</th>
<th>Cases</th>
<th>IR* (CI95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-300</td>
<td>5856</td>
<td>1</td>
<td>0.2 (0-0.7)</td>
</tr>
<tr>
<td>300-600</td>
<td>6526</td>
<td>5</td>
<td>0.8 (0.2-1.6)</td>
</tr>
<tr>
<td>&gt;600</td>
<td>3912</td>
<td>0</td>
<td>0 (0-0.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rank</th>
<th>Person-years</th>
<th>Cases</th>
<th>IR* (CI95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captain</td>
<td>9462</td>
<td>3</td>
<td>0.3 (0.1-0.8)</td>
</tr>
<tr>
<td>First officer</td>
<td>9306</td>
<td>2</td>
<td>0.2 (0.01-0.6)</td>
</tr>
<tr>
<td>Second officer</td>
<td>15723</td>
<td>1</td>
<td>0.7 (0-2.6)</td>
</tr>
</tbody>
</table>

* IR: Incidence rate per 1000 person-years and corresponding 95% confidence intervals

**Discussion**

In this follow up study among 2630 commercial airline pilots, with a total of 20 420 person years of follow up time, the incidence rate of venous thrombosis was 0.3/1000 py (CI95 0.1-0.6). This incidence rate was slightly lower than in the general population and also than in a population of frequently flying employees.
of international companies and organizations. Compared to the general Dutch population, the age-adjusted relative risk for venous thrombosis was 0.8 (CI95 0.7-1.0). Compared to healthy employees, it was 0.7 (CI95 0.6-0.9). The incidence rate of venous thrombosis in the airline pilots did not increase with number of flight-hours per year, nor was it associated with the rank of the pilots.

The low incidence rate of venous thrombosis in commercial airline pilots may be explained by the fact that pilots in general are healthier than the general population: the so-called healthy worker effect. Several epidemiological studies have shown that overall mortality rates are lower in airline pilots than in the general population. However, these epidemiological studies also showed that the incidence rate of cancer is increased in airline pilots. This may be caused by exposure to carcinogenic substances (jet fuel, cabin pollution, cosmic radiation). Despite exposure to these flight-related factors, or the higher prevalence of malignant diseases, no increased risk of venous thrombosis was found in this population. The healthy worker effect was countered by contrasting the pilots to another working population, but results were similar and not suggestive of an increased risk of thrombosis.

A surprising finding in this study was that the incidence rate did not clearly increase with age. This may be due to chance, since the number of cases was small. However, in a previous study amongst frequently travelling employees, the incidence rate of venous thrombosis was highest in the lowest age-category as well. In the previous study, this was partly explained by a phenomenon called 'attrition of susceptibles', meaning that susceptible individuals are likely to develop a disease shortly after start of exposure to a risk factor. This may also be the case here, that airline pilots who develop venous thrombosis because of their profession are likely to develop thrombosis shortly after start of exposure (their employment), and subsequently seek different employment.

We may have underestimated the risk of venous thrombosis in airline pilots, because they may have been reluctant to confirm they suffered from venous thrombosis in the questionnaire, due to fear for possible consequences, i.e. losing their job. We tried to avoid non-respondence or misclassification by ensuring and communicating complete protection of privacy in our study. Our finding that the incidence rate of venous thrombosis in pilots is lower than in the general population is supported by the absence of any airline pilots who died of pulmonary embolism during the follow up period. If the risk of venous thrombosis amongst Dutch airline pilots would have been substantially higher than in the general Dutch population, one would also have expected fatal cases. Another finding that supports our conclusion that the risk of venous thrombosis is not increased in airline pilots is that we did not find an association between the
number of flight hours per year and the risk of venous thrombosis, i.e. no ‘dose-
response relation’.

From this cohort study amongst Dutch airline pilots, we conclude that the
risk of venous thrombosis is not increased in commercial airline pilots.
Reference List


