ORIGINAL ARTICLE

Breast cancer risk in airline cabin attendants: a nested case-control study in Iceland

V Rafnsson, P Sulem, H Tulinius, J Hrafnkelsson

Occup Environ Med 2003;**60**:807–809

See end of article for authors' affiliations

Correspondence to: Dr V Rafnsson, Department of Preventive Medicine, Soltun 1, 105 Reykjavik, Iceland; vilraf@hi.is

Accepted 16 August 2002

Aims: To investigate whether length of employment as a cabin attendant was related to breast cancer risk, when adjusted for reproductive factors.
Methods: Age matched case-control study nested in a cohort of cabin attendants. The cases were found from a nationwide cancer registry (followed up to end of year 2000) and the reproductive factors (age at first childbirth and number of children) from a registry of childbirth, in both instances by record linkage with the cabin attendants' identification numbers. The employment time of the cabin attendants at the airline companies and the reproductive factors had been systematically recorded prior to the diagnosis of breast cancer in the cohort. A total of 35 breast cancer cases and 140 age matched controls selected from a cohort of 1532 female cabin attendants were included in the study.
Results: The matched odds ratio from conditional logistic regression of breast cancer risk among cases and controls of cabin attendants was 5.24 (95% CI 1.58 to 17.38) for those who had five or more years of employment before 1971 compared with those with less than five years of employment before 1971, adjusted for age at first childbirth and length of employment from 1971 or later.
Conclusions: The association between length of employment and risk of breast cancer, adjusted for reproductive factors, indicates that occupational factors may be an important cause of breast cancer among cabin attendants; the association is compatible with a long induction period.

Six studies of airline cabin attendants, one each from Finland, Denmark, Iceland, and Norway, and two from the USA have all found an increased incidence of breast cancer among them compared with the general female population, with standardised incidence ratios ranging from 1.1 to 2.0.[1–7] The cause of this excess has not been identified, but occupational factors have been suggested, in addition to conventional risk factors for breast cancer such as those of social and reproductive origin.

In the previous cohort study on cancer of cabin attendants in Iceland, the standardised incidence ratio was 1.5 for breast cancer.[5] The Icelandic situation, where the employment of the cabin attendants at the airline companies and the number of children borne by women and their ages at childbirth has been systematically recorded prior to the diagnosis of breast cancer in the cohort, provided us with an opportunity to compare cases with matched controls.

Our objective was to determine whether length of employment as a cabin attendant was related to breast cancer risk, after adjusting for reproductive factors.

METHODS

This was a matched case-control study nested in a cohort of cabin attendants (n = 1532, all female) which served as a study base and was collected from the union of Icelandic cabin crew and two airline companies, as described previously.[5] Record linkage, using the personal identification number, with the Icelandic Cancer Registry provided information on breast cancer in the cohort. Similarly, record linkage with the registry of childbirth at the Genetical Committee of the University of Iceland provided the information on reproductive factors (age at first childbirth and number of children). The cohort was then subsequently record linked to the Icelandic Cancer Registry in order to extend the follow up and include breast cancer cases accumulated up to the end of year 2000.

Altogether 35 histologically confirmed cases of breast cancer were found, including four cancers in situ and two women who each had two breast cancers. In the previous cohort study[5] involving 26 of the cases, all but one of the breast cancers were of ductal type where the pathology reports decided whether the histology showed lobular or ductal types. All 35 cases were included in the study, assuming that they shared aetiological factors; this has been the procedure in other studies dealing with aetiology of breast cancer.[8] Each of the cases was individually matched by year of birth with four controls from the cohort of cabin attendants. The controls had to have entered the cohort at least in the year the respective case was diagnosed.

Employment time in the cohort study was recorded without taking into account any part time job, or sick or maternity leave. The length of employment was calculated for the cases from the first year of employment as a cabin attendant to the last year of employment or the year of diagnosis of breast cancer, whichever occurred first. The length of employment was calculated for the controls from the first year of employment to the last year of employment or the year of pseudo-diagnosis—that is, the year of diagnosis for the respective case. The Icelandic airline companies introduced jet aircraft on all international routes in the year 1971[5]; jets are flying at higher altitude and faster than non-jets. Therefore, the length of employment was divided by whether it occurred before 1971 and in the year 1971 or later. The cruising altitude difference between non-jet aircraft and jet is about threefold, hence greater exposure to cosmic radiation.

A multivariate case-control analysis was performed by a conditional logistic regression.[9] The adjusted odds ratio and exact computation of 95% confidence intervals (CI) were calculated using STATA software. Case-control status was the dependent variable. Length of employment was treated as a continuous variable expressed in years. In a different analysis the length of employment was treated as a dichotomous

variable, classified either as five or more years or less than five years. Five years were chosen as the cut off for the duration of employment as the annual exposure to ionising radiation sustained by aircrew is low,[10] and five year employment was considered a minimum exposure time. Length of employment, both as continuous and dichotomous variables, was also calculated according to the cut off in year 1971. Age at first childbirth was classified in five categories, including one category for nulliparous. The number of children was classified in six categories (0, 1, 2, 3, 4, and 5 or more). In yet another separate analysis we counted the remaining length of employment 20 and 30 years before the date of diagnosis (or pseudo-diagnosis) (subtracting 20 and 30 years from the date of diagnosis) and in that way implemented 20 and 30 years lag time.

The National Bioethics Committee and the Data Protection Commission approved the study.

RESULTS

The odds ratio for breast cancer associated with continuous length of employment, adjusted for age at first birth, was 1.00 (95% CI 1.00 to 1.05). The odds ratio for those who had five or more years of employment compared with those with less than five years of employment, adjusted for age at first childbirth, was 2.10 (95% CI 0.93 to 4.73).

Table 1 shows the adjusted odds ratio, taking into account two periods of length of employment according to the division in year 1971. The odds ratio was 5.24 (95% CI 1.58 to 17.38) for those who had five or more years of employment before 1971 compared to those with less than five years of employment before 1971, adjusted for age at first childbirth and length of employment 1971 or later. The corresponding odds ratio was 0.82 (95% CI 0.34 to 1.97) for those who had five or more years of employment after 1971 compared to those with less than five years of employment after 1971, adjusted for age at first childbirth and length of employment 1970 or earlier. When adjusted for number of children instead of age at first childbirth, the odds ratio was 4.31 (95% CI 1.33 to 14.00) for those who had five or more years of employment before 1971 compared with those with less than five years of employment before 1971, adjusted for number of children and length of employment 1971 or later.

When excluding the two second breast cancers (and their controls) from the analysis the odds ratio was 4.30 (95% CI 1.26 to 14.64) for those who had five or more years of employment before 1971 compared to those with less than five years of employment before 1971, adjusted for age at first childbirth and length of employment at 1971 or later. Similarly when the four breast cancers in situ (and their controls) were excluded from the analysis the odds ratio was 4.42 (95% CI 1.09 to 18.02) for those who had five or more years of employment before 1971 compared to those with less than five years of employment before 1971, adjusted for age at first childbirth and length of employment at 1971 or later.

When taking 20 years lag time into consideration, the odds ratio was 3.42 (95% CI 1.05 to 11.20) for those who had five or more years of employment compared to those with less than five years employment, adjusted for age at first childbirth. When applying 30 years lag time the odds ratio was 3.51 (95% CI 0.75 to 16.50) for those who had five or more years of employment compared to those with less than five years of employment, adjusted for age at first childbirth.

The mean age of the breast cancer cases at year of diagnosis was 47 years (range 28–72).

DISCUSSION

Our calculations show a significant association between length of employment, measured as five or more employment years before 1971, and risk of breast cancer adjusted for reproductive factors among cabin attendants. In spite of the small number of cases, the odds ratio was high and the 95% confidence intervals did not include unity. Our observed association is supported by the evidence from the cohort studies,[1–7] suggesting an association of the breast cancer risk with the occupation of cabin attendants.

The results of the present case-control study are not directly comparable to the results of the previous cohort study.[5] In the cohort study an external comparison group was used, but in the present study a type of internal comparison was applied. There are nine more cases in the present study than in the cohort study. The cut off for duration of employment in pre and post 1971 was made differently in the two studies, and in the present case-control study an adjustment was made for reproductive factors.

The possible causal factor or factors in the occupation of cabin attendants have been reviewed recently.[10] They are exposed to cosmic radiation including neutrons and gamma rays, engine exhaust gases, ozone, electromagnetic fields, and radiofrequency radiation.[10] Jetlag and disturbances in the circadian rhythm have also been suggested as possibly playing a part, as well as the previous use of pesticides in aircraft.[4 5 11] The cabin attendants in our study base have all flown on international routes. Keflavik airport (Reykjavik) in Iceland was the hub, cities in Europe and North America were the main destinations; all cabin attendants have therefore sustained disturbances of their circadian rhythms and been exposed to cosmic radiation during northerly flight profiles.[5 12 13] The estimated annual doses received by aircrew

Table 1 Adjusted matched odds ratios from conditional logistic regression of breast cancer risk among cases and controls of cabin attendants according to length of employment and reproductive factors

	Controls (n = 140)	Cases (n = 35)	Matched odds ratio*	95% CI
Length of employment 1947 to 1970				
<5 years	111	21	1	Reference
⩾5 years	29	14	5.24	1.58 to 17.38
Length of employment 1971 to 1997				
<5 years	97	24	1	Reference
⩾5 years	43	11	0.82	0.34 to 1.97
Reproductive factors				
Nulliparous	11	2	0.77	0.14 to 4.10
Age at first birth ⩽24 y	43	16	1.92	0.76 to 4.84
Age at first birth 25–29 y	62	14	1	Reference
Age at first birth 30–34 y	15	2	0.46	0.09 to 2.39
Age at first birth ⩾35 y	9	1	0.44	0.05 to 3.96

*Odds ratios have been calculated in a unique multivariate analysis, taking into account simultaneously all the variables.

are 4–5 mSv[12] for routes between Europe and North America, which may be twofold higher than doses for intracontinental routes.

Exclusion of the second cancers and the cancer in situ did not materially affect the estimates of the odds ratios, which still did not include unity, suggesting that our assumption of shared aetiology was valid.

As far as we are aware, our study is the first published case-control study of breast cancer among cabin attendants adjusting for individual reproductive factors. In previous cohort studies showing an excess of breast cancer among cabin attendants,[1–5 7] the possible confounding of reproductive factors were not directly controlled for. In the Norwegian cohort no association was found between length of employment and the risk of breast cancer after adjustment were made for reproductive factors.[6] In the present study the picture of the relation between breast cancer risk and age at childbirth and nulliparity is the opposite of the findings from most studies on breast cancer and reproductive factors. In the present study the highest risk was found for age at first childbirth $\leqslant 24$ years. It is notable that all confidence intervals for odds ratios of the reproductive factors included unity. However, this relation between breast cancer risk and reproductive factors was also seen in the Norwegian cohort study on cabin attendants.[6] In previous cohort studies of cabin attendants, using the general population as reference, social class differences were considered to be a possible confounder for the breast cancer risk found.[1] Social class is unlikely to be confounding the result of the present study, as the study base is a cohort of cabin attendants belonging to the same social class.

Use of the comprehensive population registers in Iceland strengthens our study. Misclassification of case and control status is unlikely because the recording of cases in the cancer registry is based on histological examination and is independent of occupation. The reproductive factors were also obtained from an ongoing systematic registration of childbirths covering the whole population. The primary data on employment time and reproductive factors were collected prior to follow up and diagnosis of the breast cancer cases, which eliminates the possibility of recall bias. The small size of the study did not allow us to separate out the possible effects of induction period and calendar time.

In our study the increased risk of breast cancer among cabin attendants is related to length of employment before 1971, the period before jet aircraft were taken into operation. We cannot conclude that the exposure related to the increased risk of breast cancer is solely confined to the period before 1971, because long lag time may be required for inducing breast cancer. Our analysis with 20 and 30 year lag time is compatible with this view and corresponds to a long induction period between ionising radiation exposure and development of breast cancer.[14]

More detailed information on the different components of the occupational exposure is needed in further studies in order to understand their importance or their possible combined effects.

ACKNOWLEDGEMENTS

We thank Helgi Sigvaldason for statistical advice.

Authors' affiliations

V Rafnsson, P Sulem, H Tulinius, Department of Preventive Medicine, University of Iceland, Soltun 1, 105 Reykjavik, Iceland
J Hrafnkelsson, Department of Oncology, Landspitali-University Hospital, Reykjavik, Iceland

This work was supported in part by University of Iceland Research Fund.

Contributors: HT, JH, and VR were involved in designing the study. VR collected the data. PS and VR performed the analysis of the results. VR wrote the first draft of the manuscript, which was discussed, revised, and accepted by all contributors. VR is the guarantor of the study.

REFERENCES

1 **Pukkala E**, Auvinen A, Wahlberg G. Incidence of cancer among Finnish airline cabin attendants, 1967–92. *BMJ* 1995;**311**:649–52.
2 **Lynge E**. Risk of breast cancer is also increased among Danish female airline cabin attendants. *BMJ* 1996;**312**:253.
3 **Wartenberg D**, Stapleton CP. Risk of breast cancer is also increased among retired US female airline cabin attendants. *BMJ* 1998;**316**:1902.
4 **Wartenberg D**, Stapleton CP. Risk of breast cancer among female airline cabin attendants. *BMJ* 1999;**318**:126.
5 **Rafnsson V**, Tulinius H, Jonasson JG, *et al*. Risk of breast cancer in flight attendants: population-based study (Iceland). *Cancer Causes Control* 2001;**12**:95–101.
6 **Haldorsen T**, Reitan JB, Tveten U. Cancer incidence among Norwegian airline cabin attendants. *Int J Epidemiol* 2001;**30**:825–30.
7 **Reynolds P**, Cone JE, Layefsky M, *et al*. Cancer incidence in California flight attendants (United States). *Cancer Causes Control* 2002;**13**:317–24.
8 **Cutuli B**, Borel C, Dhermain F, *et al*. Breast cancer occurred after treatment for Hodgkin's disease: analysis of 133 cases. *Radiot Oncol* 2001;**59**:247–55.
9 **Breslow NE**, Day NE. *Statistical methods in cancer research, Vol. I. The analysis of case-control studies*. Lyon: International Agency for Research on Cancer, 1980.
10 **Blettner M**, Grosche B, Zeeb H. Occupational cancer risk in pilots and flight attendants: current epidemiological knowledge. *Radiat Environ Biophys* 1998;**37**:75–80.
11 **Mawson AR**. Breast cancer in female flight attendants. *Lancet* 1998;**352**:626.
12 **Nicholas JS**, Lackland DT, Butler GC, *et al*. Cosmic radiation and magnetic field exposure to airline flight crews. *Am J Ind Med* 1998;**34**:574–80.
13 **Wilson JW**. Overview of radiation environments and human exposures. *Health Phys* 2000;**79**:470–94.
14 **Tokunaga M**, Land CE, Yamamoto T, *et al*. Incidence of female breast cancer among atomic bomb survivors, Hiroshima and Nagasaki 1950–1980. *Radiat Res* 1987;**112**:243–72.