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SHORT COMMUNICATION

Rotating night shift work, sleep, and colorectal adenoma in women

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Abstract
Purpose This study aims to investigate the associations of rotating night shift work history and sleep duration with risk of colorectal adenoma.
Methods We evaluated 56,275 cancer-free participants of the Nurses' Health Study II, who had their first colonoscopy or sigmoidoscopy between 1991 and 2011; rotating night shift work and sleep duration were reported by mailed questionnaire. Multivariable-adjusted logistic regression was used to estimate relative risks (RR) of colorectal adenoma, with 95% confidence intervals (CI), across categories of rotating night shift work history (none, 1–4, 5–9, and ≥10 years) and sleep duration (≤5, 6, 7, 8, and ≥9 h/day).
Results We found no association between duration of rotating night shift work and occurrence of colorectal adenoma (p-trend across shift work categories = 0.5). Women with the longest durations of rotating night shift work (≥10 years) had a similar risk of adenoma compared to women without a history of rotating night shift work (multivariable-adjusted RR = 0.96, 95% CI = 0.83–1.11). Similarly, there were no associations of shorter or longer sleep durations with adenoma risk (p-trend = 0.2 across sleep durations of ≤5 through 7 h/day and p-trend = 0.5 across sleep durations of 7 through ≥9 h/day). Results were similar when we examined associations according to adenoma location and subtype.
Conclusions Our results do not support an association between rotating night shift work or sleep duration and risk of colorectal adenoma in women.

Keywords Rotating night shift work · Sleep · Colonoscopy · Polyps · Adenoma · Women

Introduction

The World Health Organization classified shift work as a probable carcinogen, largely based on studies of breast cancer [1]. However, evidence for colorectal cancer is increasing, and a recent meta-analysis suggested that longer durations of shift

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work might also be associated with a higher risk of colon cancer [2]. Sleep disturbances may mediate this association or act independently to increase risk of this outcome [3]. An important precursor for most colorectal cancers is adenomatous polyps (i.e., adenoma), making them an appealing target for interventions [4, 5]. Yet, to date, only one hospital-based case-control study has examined night shift work and sleep characteristics in relation to colorectal adenoma [6]. We hypothesized that longer duration of rotating night shift work and extreme sleep durations might be associated with greater risk of adenoma in the Nurses' Health Study II (NHS II).

Methods

Study population

The NHS II began in 1989, when 116,430 female registered nurses, aged 25–42 years, and living in the United States, completed a mailed questionnaire about lifestyle factors and medical history. Similar questionnaires updated this information biennially; response rates have been ≥90% for every questionnaire cycle. Information on shift work history was collected at baseline and repeatedly throughout follow up, and sleep duration was assessed once in 2001. Women began reporting lower endoscopy procedures and findings of colorectal polyps in 1991, which was considered "baseline" for our analyses.

We identified 56,275 women without a diagnosis of cancer (excluding non-melanoma skin cancer), inflammatory bowel disease, ulcerative colitis, familial polyposis, or colorectal polyps by 1991, who reported first-time lower gastrointestinal endoscopy (colonoscopy or sigmoidoscopy) between 1991 and 2011. We excluded women without an initial report of shift work history ($n = 286$) and information on sleep duration ($n = 7044$), leaving 55,989 women for analyses of shift work history and adenoma risk and 49,231 women for analyses of sleep duration and adenoma risk. The Institutional Review Boards of the Brigham and Women's Hospital and the Harvard T. H. Chan School of Public Health approved this study.

Ascertainment of colorectal adenoma

Women who reported a new diagnosis of colorectal polyps on cohort questionnaires were asked for permission to obtain their medical records. Study investigators, who were blinded to participants' exposure status, reviewed medical records and pathology reports to confirm adenoma cases; they also extracted information on anatomic location, size, number, and histological type of adenoma. For our analyses, we considered adenoma cases that were diagnosed on first lower endoscopy and confirmed by pathology report.

Ascertainment of shift work history and sleep duration

Women reported their total duration of rotating night shift work at baseline in 1989 (never, 1–2, 3–5, 6–9, 10–14, 15–19, and ≥20 years), and updated this information on biennial questionnaires in 1991, 1993, 1997, 2001, 2005, and 2007 (for each 2-year period: none, 1–4, 5–9, 10–14, 15–19, and ≥20 months). Because the 1995, 1999, and 2003 questionnaires did not include this question, retrospective assessments of rotating night shift work were included on the 2001 and 2005 questionnaires. We assigned participants the value of the midpoint of their response category and summed these values across all questionnaires through the year of first lower endoscopy.

Women reported their usual sleep duration in a 24-h period on the 2001 questionnaire; response categories were <5, 5, 6, 7, 8, 9, 10, and ≥11 h.

Statistical analysis

Age- and multivariable-adjusted logistic regression models were used to estimate odds ratios (OR), approximating relative risks (RR), and 95% confidence intervals (CI) for overall colorectal adenoma and adenoma by location and subtype across categories of rotating night shift work history (none, 1–4, 5–9, and ≥10 years) and sleep duration (≤5, 6, 7, 8, ≥9 h/day). Non-cases were women without adenoma (or with hyperplastic polyps only) detected at first lower endoscopy; women with no history of rotating night shift work and sleep durations of 7 h/day comprised the reference categories, respectively. Linear trends were evaluated using the midpoint of each rotating night shift work category and separately for sleep durations of ≤5, 6, and 7 h/day and sleep durations of 7, 8, and ≥9 h/day. We utilized a Bonferroni correction to determine the threshold at which p values would be considered significant; therefore, we divided the p value of 0.05 by 33 (the number of comparisons for which a p value was calculated in our main analyses) and considered $p < 0.002$ as indicating statistical significance.

In secondary analyses, we evaluated associations among women who underwent lower endoscopy for screening purposes only and restricted to adenoma cases occurring after women reported sleep duration in 2001. We also evaluated effect modification by body mass index and joint effects of rotating night shift work and sleep duration by adding interaction terms to our models.

Results

After adjusting for potential confounding factors, we found no association between rotating night shift work history and overall risk of colorectal adenoma (p-trend = 0.5) and similar

Table 1 Relative risks of colorectal adenoma, overall and by location and subtype, across categories of rotating night shift work history and sleep duration in the Nurses' Health Study II

		Rotating night shift work history (in years)				
	None	1–4	5–9	≥10		p-trend[a]
Overall adenoma[b]						
Number of cases	936	1425	409	244		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.93 (0.85, 1.01)	0.98 (0.87, 1.11)	0.96 (0.83, 1.11)		0.5
Proximal colon						
Number of cases	427	653	210	115		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.93 (0.82, 1.05)	1.08 (0.91, 1.28)	0.95 (0.77, 1.18)		0.9
Distal colon						
Number of cases	430	680	196	122		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.96 (0.85, 1.08)	1.02 (0.86, 1.21)	1.04(0.85, 1.28)		0.7
Rectum						
Number of cases	177	241	65	43		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.83 (0.69, 1.01)	0.85 (0.64, 1.13)	0.93 (0.66, 1.30)		0.3
Large (≥1 cm)						
Number of cases	220	316	105	60		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.87 (0.73, 1.04)	1.07 (0.85, 1.36)	1.00 (0.74, 1.33)		0.8
Small (<1 cm)						
Number of cases	670	1039	282	169		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.94 (0.85, 1.04)	0.94 (0.82, 1.09)	0.92 (0.77, 1.10)		0.3
Advanced (large, villous histology, or high-grade dysplasia)						
Number of cases	267	396	122	74		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.90 (0.77, 1.06)	1.03 (0.83, 1.28)	1.01 (0.77, 1.31)		0.9
Non-advanced (small and tubular)						
Number of cases	496	751	211	116		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.91 (0.81, 1.02)	0.94 (0.80, 1.11)	0.85 (0.69, 1.05)		0.1
Multiple (≥2 polyps)						
Number of cases	180	292	111	57		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.97 (0.80, 1.16)	1.32 (1.04, 1.68)	1.09 (0.80, 1.47)		0.1
High risk (advanced or ≥3 polyps)						
Number of cases	297	438	140	82		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.90 (0.77, 1.05)	1.06 (0.86, 1.30)	1.01 (0.78, 1.29)		0.7
Low risk (non-advanced and 1–2 polyps)						
Number of cases	476	722	194	113		
Multivariable-adjusted RR (95% CI)[c]	1.00 (Reference)	0.91 (0.81, 1.03)	0.90 (0.76, 1.07)	0.86 (0.70, 1.07)		0.1
		Sleep duration (in hours/day)				
	p-trend[a]	≤5	6	7	8	≥9	p-trend[a]
Overall adenoma [b]						
Number of cases	–	124	672	1242	672	141	–
Multivariable-adjusted RR (95% CI)[c]	0.2	0.83 (0.69, 1.01)	1.00 (0.90, 1.10)	1.00 (Reference)	1.00 (0.90, 1.10)	0.91 (0.76, 1.09)	0.5
Proximal colon							
Number of cases	–	59	313	599	294	56	–
Multivariable-adjusted RR (95% CI)[c]	0.2	0.83 (0.63, 1.10)	0.96 (0.83, 1.10)	1.00 (Reference)	0.91 (0.79, 1.05)	0.76 (0.58, 1.01)	0.03
Distal colon							
Number of cases	–	58	330	576	319	63	–
Multivariable-adjusted RR (95% CI)[c]	0.4	0.81 (0.61, 1.06)	1.04 (0.91, 1.20)	1.00 (Reference)	1.02 (0.89, 1.17)	0.86 (0.66, 1.12)	0.6
Rectum							

Table 1 (continued)

		Rotating night shift work history (in years)					
	None	1–4		5–9	≥10		p-trend[a]
Number of cases	–	20	110	211	123	32	–
Multivariable-adjusted RR (95% CI)[c]	0.3	0.78 (0.49, 1.24)	0.96 (0.76, 1.21)	1.00 (Reference)	1.07 (0.86, 1.34)	1.20 (0.83, 1.75)	0.3
Large (≥1 cm)							
Number of cases	–	31	166	264	157	39	–
Multivariable-adjusted RR (95% CI)[c]	0.8	0.92 (0.63, 1.34)	1.13 (0.93, 1.38)	1.00 (Reference)	1.10 (0.90, 1.34)	1.14 (0.81, 1.60)	0.3
Small (<1 cm)							
Number of cases	–	84	481	909	479	95	–
Multivariable-adjusted RR (95% CI)[c]	0.1	0.79 (0.63, 0.99)	0.98 (0.88, 1.10)	1.00 (Reference)	0.97 (0.87, 1.09)	0.85 (0.69, 1.06)	0.2
Advanced (large, villous histology, or high-grade dysplasia)							
Number of cases	–	41	198	330	186	50	–
Multivariable-adjusted RR (95% CI)[c]	0.8	0.98 (0.71, 1.37)	1.08 (0.90, 1.29)	1.00 (Reference)	1.04 (0.87, 1.25)	1.18 (0.87, 1.59)	0.3
Non-advanced (small and tubular)							
Number of cases	–	56	356	670	345	69	–
Multivariable-adjusted RR (95% CI)[c]	0.09	0.72 (0.55, 0.96)	0.99 (0.87, 1.13)	1.00 (Reference)	0.94 (0.83, 1.08)	0.8 (0.65, 1.09)	0.2
Multiple (≥2 polyps)							
Number of cases	–	26	142	262	126	36	–
Multivariable-adjusted RR (95% CI)[c]	0.3	0.77 (0.51, 1.15)	0.97 (0.79, 1.19)	1.00 (Reference)	0.89 (0.72, 1.11)	1.07 (0.75, 1.53)	0.7
High risk (advanced or ≥3 polyps)							
Number of cases	–	44	219	365	216	56	–
Multivariable-adjusted RR (95% CI) [c]	0.8	0.96 (0.70, 1.32)	1.08 (0.91, 1.28)	1.00 (Reference)	1.09 (0.92, 1.30)	1.19 (0.90, 1.59)	0.1
Low risk (non-advanced and 1–2 polyps)							
Number of cases	–	54	340	647	326	63	–
Multivariable-adjusted RR (95% CI)[c]	0.08	0.72 (0.54, 0.96)	0.98 (0.86, 1.12)	1.00 (Reference)	0.92 (0.81, 1.06)	0.80 (0.61, 1.04)	0.07

CI confidence interval, *RR* relative risk

[a] Due to multiple comparisons, a Bonferroni-corrected threshold of $p < 0.002$ was considered statistically significant

[b] Adenoma found in the proximal and/or distal colon, and/or in the rectum

[c] Models are adjusted for age, time-period of first lower endoscopy, reason for endoscopy, family history of colorectal cancer, height, body mass index, physical activity, pack-years of smoking, alcohol intake, menopausal status, menopausal hormone use, oral contraceptive use, multivitamin use, total calcium intake, supplemental vitamin D intake, red meat intake, aspirin use, non-steroidal anti-inflammatory drug use, and predicted vitamin D score

adenoma risks for women across all categories of rotating night shift work compared to women with no history of rotating night shift work (e.g., RR = 0.96, 95% CI = 0.83–1.11 comparing extremes of ≥10 years of rotating night shift work history versus none) (Table 1). Rotating night shift work was also unrelated to risks of proximal, distal, and rectal adenoma (p-trends were 0.9, 0.7, and 0.3, respectively), as well as large (≥1 cm), small (<1 cm), advanced (large, villous, or high-grade dysplasia), non-advanced (small and tubular), multiple (≥2 polyps), high-risk (advanced or ≥3 polyps), and low-risk (non-advanced and 1–2 polyps) adenoma subtypes.

In addition, there was no overall association between shorter or longer sleep durations and adenoma risk in multivariable models (p-trend = 0.2 across sleep durations of ≤5 through 7 h/day and p-trend = 0.5 across sleep durations of 7 through ≥9 h/day) (Table 1). We did observe a suggestion of a decreased adenoma risk for women with sleep durations ≤5 h/day compared to 7 h/day (multivariable-adjusted RR = 0.83, 95% CI = 0.69–1.01), whereas the adenoma risk was comparable for women with sleep durations ≥9 h/day versus 7 h/day (multivariable-adjusted RR = 0.91, 95% CI = 0.76–1.09). When Bonferroni correction was applied, no significant trends of shorter or longer sleep durations emerged by adenoma location or subtype.

In secondary analyses, results were similar when we restricted our sample to women who underwent lower endoscopy for screening purposes only and to cases occurring after women reported sleep duration in 2001. There was no effect modification by body mass index and no joint effect of rotating night shift work and sleep duration on adenoma risk.

Discussion

We identified no overall association of rotating night shift work history or sleep duration with risk of colorectal adenoma in women. Similarly, these exposures were not related to adenoma risk when considering different anatomic locations or subtypes separately. Thus, our results do not support the hypothesis that longer duration of rotating night shift work or extremes of sleep duration increase the risk of colorectal adenoma.

Our findings are consistent with results from a previous epidemiologic study of night shift work and colorectal adenoma. In that study, there was no difference in the prevalence of adenomas comparing participants with a history of night shift work to those without such a history (OR = 1.16, 95% CI = 0.85–1.59) [6], although information on duration of night shift work was not available. Thus, our study extends these results by suggesting that no association exists even among participants with up to 10 years of shift work history. Given the growing evidence that shift work may be associated with an increased risk of colorectal cancer [2], inconsistent results for colorectal adenoma versus cancer (as occurred in the Nurses' Health Studies) might suggest that circadian disruption acts more as a cancer promoter than initiator.

Few observational studies have examined associations between sleep duration and risk of colorectal cancer [7–9], and the only study that previously examined this association found a 50% increased risk in colorectal adenoma with shorter sleep duration (OR = 1.49, 95% CI = 1.02–2.19) [6]. However, the authors did not account for confounding by important lifestyle factors (e.g., diet and physical activity) in their analyses; therefore, this result could be explained at least in part by residual confounding.

Limitations of our study should be noted. First, rotating night shift work and sleep duration were assessed by questionnaire, which likely resulted in non-differential exposure misclassification. Multiple studies have identified associations of shift work history and sleep duration with chronic disease in this cohort, but such misclassification could still have contributed to our null findings. Second, our study was conducted among women only, and results may not apply to men.

In conclusion, our study does not provide evidence supporting the hypothesis that longer history of rotating night shift work or extremes of sleep duration increase the risk of colorectal adenoma in women.

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Compliance with ethical standards

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Disclosure of potential conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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