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Shift work and working at night in relation to breast cancer incidence

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Abstract

Background: Night shift work has been classified by the International Agency for Research on Cancer (IARC) as a probable carcinogen in humans. Several studies have assessed night shift work in relation to breast cancer risk, with inconsistent results.

Methods: In the prospective Sister Study cohort, current and past occupational history was collected for 48,451 participants. We used Cox proportional hazards models to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between baseline work schedule characteristics and incident breast cancer.

Results: During follow-up (mean=9.1 years), 3,191 incident cases were diagnosed. We observed little to no increase in risk associated with work schedule characteristics (ever working rotating shifts: HR=1.04, 95% CI: 0.91–1.20; ever working rotating night shifts: HR=1.08, 95% CI: 0.92–1.27; ever working at night: HR=1.01, 95% CI: 0.94–1.10; ever working irregular hours: HR=0.98, 95% CI: 0.91–1.06). While short-term night work (>0 to 5 years vs. never, HR=1.12, 95% CI: 1.00–1.26) or rotating shift work at night (>0 to 5 years vs. never, HR=1.30, 95% CI: 1.05–1.61) were associated with increased breast cancer risk, working nights for more than 5 years was not associated with risk.

Conclusions: Overall, we observed little evidence that rotating shift work or work at night was associated with a higher risk of breast cancer, except possibly among those who participated in such work for short durations of time.

Impact: This study indicates that if night shift work is associated with breast cancer, the increase in risk is small.

Introduction

In 2019, the International Agency for Research on Cancer classified night shift work as a probable human carcinogen[1]. Most evidence supporting higher breast cancer risk among

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night shift workers comes from case-control studies; cohort studies have observed largely null associations[2].

Materials and Methods

The Sister Study is a prospective cohort of 50,884 women (2003–2009), aged 35–74 who had a sister with breast cancer but were breast cancer-free themselves[3]. Baseline occupational questionnaires asked about current job and past jobs held for ≥2 years. For each job, women were asked if they worked regular hours (starting/stopping at the same time every day) and if they worked at night (≥1 hour between 12:00–2:00 AM). If they reported not working regular hours, they were asked if they worked rotating shifts (number of shifts, usual start/stop times for each shift) or irregular hours. Rotating shift work (N=3,183) included women who reported ≥1 job with rotating shifts; rotating night shift work (N=2,275) was a subset of those women who also reported night work for the same job. Working irregular hours (N=15,895) could include women who reported night work for ≥1 job. Any work at night (N=13,992) included all women, regardless of schedule type, who met our definition of night work for ≥1 job. Self-reported incident breast cancer, confirmed with medical records[3], was classified as invasive breast cancer or ductal carcinoma *in situ*. Women were followed through September 15, 2017 (data release 7.2). The final sample included 48,451 women who completed the occupational questionnaire and were not missing covariate data.

Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs), with age as the timescale. For each analysis, women who reported never having that work schedule were the referent. Confounders were selected *a priori* and included race/ethnicity, education, marital status, and parity. We explored whether the association differed by time-varying menopausal status, timing of starting work relative to first childbirth, or time since stopping shift work.

Results

Over follow-up (average=9.1 years), 3,191 incident breast cancer*s* were diagnosed. Study population characteristics are available elsewhere[3]. Although ever and never rotating night shift workers were similar, ever workers were more likely to have at least some college (92% vs. 84%), be nulliparous (21% vs. 18%), or have ever smoked (47% vs. 43%).

We observed little association between breast cancer and ever working shifts, night shifts, at night, or irregular hours (Table 1). However, compared to women who never worked rotating night shifts or at night, women who reported working night shifts (HR_{adj}=1.30, 95% CI: 1.05–1.61) and who reported any work at night (HR_{adj}=1.12, 95% CI: 1.00–1.26) for ≤5 years (“short-term”) had a greater risk of breast cancer. Associations were not seen for longer durations.

The association between short-term work at night and breast cancer appeared stronger for premenopausal (HR_{adj}=1.29, 95% CI: 1.02–1.63) than for postmenopausal women (HR_{adj}=1.06, 95% CI: 0.93–1.22) (Table 2). Similar associations were seen for shift and

night shift work. These associations did not differ by age started working (before first childbirth) or time since stopping.

Discussion

Night shift work, classified as a probable carcinogen, is hypothesized to act via light at night (LAN)-related circadian disruption, by decreasing levels of melatonin[2,4]. Melatonin suppresses estrogen production, functions as an antioxidant, and has apoptotic and anti-proliferative effects in breast cancer cells[4]. Other potential mechanisms include oxidative stress and chronic inflammation resulting from disrupted circadian rhythm[2].

Some, but not all, case-control studies have suggested that increasing duration and frequency of night shift work may be associated with an increased breast cancer risk[2]. Although the Nurses' Health Study II observed an increased risk for long-term (20+ years) rotating night shift work[5], results from other cohort studies have been mostly null[2], consistent with our findings. The discrepancy between study types is possibly due to more comprehensive lifetime exposure data in the case-control studies, although retrospective data collection is a limitation. Despite our comprehensive lifetime exposure assessment, we observed that only short-term night shift work and work at night were associated with breast cancer risk. Although we had a wide age distribution and most women (65%) were still working at baseline, we cannot dismiss the possibility of left-truncation or healthy-worker bias in our study. While these could be chance findings, one possibility is that some women who worked shifts or at night short-term may have switched to a daytime schedule sooner because of difficulties adjusting to a rotating or night schedule. There is some evidence that individuals who are "night owls" tend to tolerate shift work better than those who are "early birds"[6] and that early-bird women who work at night short-term have higher odds of breast cancer[7]. We did not assess chronotype in our study.

Conclusion

We observed little evidence that either night or shift work was associated with breast cancer risk, except in those who participated in night work for short durations.

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Table 1.

Associations between work schedule variables[1] and breast cancer risk in the Sister Study

		Total (N=48,451)	Cases (N=3,191)	Person-years (N=442,550)	Age-adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)[2]
Rotating shift work[3]	Never	43,771	2,883	400,318	1 (ref.)	1 (ref.)
	Ever	3,183	214	29,042	1.04 (0.91, 1.20)	1.04 (0.91, 1.20)
	>0–5 years	1,548	114	14,172	1.15 (0.95, 1.39)	1.15 (0.95, 1.38)
	>5–10 years	768	48	7,020	0.97 (0.73, 1.30)	0.98 (0.73, 1.30)
	>10 years	867	52	7,850	0.91 (0.69, 1.19)	0.91 (0.69, 1.20)
Rotating night shift work[3]	Never	44,688	2,937	408,668	1 (ref.)	1 (ref.)
	Ever	2,275	160	20,784	1.08 (0.92, 1.27)	1.08 (0.92, 1.27)
	>0–5 years	1,049	88	9,540	1.31 (1.06, 1.62)	1.30 (1.05, 1.61)
	>5–10 years	571	30	5,271	0.81 (0.57, 1.16)	0.81 (0.57, 1.16)
	>10 years	655	42	5,973	0.96 (0.71, 1.30)	0.96 (0.71, 1.31)
Work at night[3]	Never	29,147	1,949	266,951	1 (ref.)	1 (ref.)
	Ever	13,992	914	126,757	1.01 (0.94, 1.10)	1.01 (0.94, 1.10)
	>0–5 years	4,744	334	42,938	1.12 (1.00, 1.26)	1.12 (1.00, 1.26)
	>5–10 years	3,522	230	32,068	1.04 (0.90, 1.19)	1.04 (0.90, 1.19)
	>10 years	5,726	350	51,751	0.92 (0.82, 1.03)	0.92 (0.82, 1.03)
Worked irregular hours[3]	Never	31,312	2,066	285,414	1 (ref.)	1 (ref.)
	Ever	15,895	1,047	146,278	0.99 (0.92, 1.07)	0.98 (0.91, 1.06)
	>0–5 years	6,142	379	56,811	0.96 (0.86, 1.07)	0.95 (0.85, 1.06)
	>5–10 years	3,816	232	35,116	0.93 (0.81, 1.06)	0.92 (0.80, 1.05)
	>10 years	5,937	436	54,351	1.07 (0.96, 1.18)	1.05 (0.95, 1.17)

[1] Rotating shift work and working irregular hours were a specific question on the questionnaire; rotating night shift work is the subset of rotating shift workers who reported working nights as one of their shifts; working at night was defined as working ≥1 hour between 12:00 and 2:00 AM, which includes all of the rotating night shift workers

[2] Multivariable model adjusted for age, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), education (high school diploma or equivalent, some college or technical school, Bachelor's or higher degree), marital status (never married, married or living as married, widowed/divorced/separated), and parity (nulliparous, 1 birth, 2 births, 3+ births)

[3] Some women were missing information on work schedule: rotating shift work, N=94 cases, N=1,497 total women; rotating night shift work, N=94 cases, N=1,488 total women; work at night, N=328 cases, N=5,312 total women; worked irregular hours, N=78 cases, N=1,244 total women

Table 2.

Work schedules and breast cancer risk, stratified by menopausal status at time of diagnosis (N=48,451)[1]

		Premenopausal (N = 5,136)		Postmenopausal (N = 43,179)	
		Cases	Multivariable-adjusted HR (95% CI)[2]	Cases	Multivariable-adjusted HR (95% CI)[2]
Rotating shift work	Never	494	1 (ref.)	2,378	1 (ref.)
	Ever	36	0.99 (0.70, 1.38)	175	1.04 (0.89, 1.21)
	>0–5 years	24	1.25 (0.83, 1.88)	87	1.09 (0.88, 1.35)
	>5 years	12	0.70 (0.39, 1.23)	88	0.99 (0.80, 1.23)
Rotating night shift work	Never	507	1 (ref.)	2,419	1 (ref.)
	Ever	23	0.92 (0.61, 1.40)	134	1.09 (0.92, 1.30)
	>0–5 years	19	1.53 (0.97, 2.42)	66	1.20 (0.94, 1.53)
	>5 years	<5	NE[3]	68	1.01 (0.79, 1.28)
Work at night	Never	320	1 (ref.)	1,622	1 (ref.)
	Ever	173	1.02 (0.85, 1.23)	734	1.00 (0.92, 1.10)
	>0–5 years	87	1.29 (1.02, 1.63)	243	1.06 (0.93, 1.22)
	>5 years	86	0.84 (0.66, 1.07)	491	0.98 (0.89, 1.09)
Worked irregular hours	Never	356	1 (ref.)	1,699	1 (ref.)
	Ever	176	0.95 (0.80, 1.15)	868	0.99 (0.91, 1.08)
	>0–5 years	91	1.04 (0.83, 1.31)	285	0.92 (0.81, 1.04)
	>5 years	85	0.88 (0.69, 1.11)	583	1.03 (0.94, 1.13)

[1] N=136 women missing menopausal status

[2] Multivariable model adjusted for age, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), education (high school diploma or equivalent, some college or technical school, Bachelor's or higher degree), marital status (never married, married or living as married, widowed/divorced/separated), and parity (nulliparous, 1 birth, 2 births, 3+ births)

[3] NE= Not estimated due to cell size <5