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## **Research Article**



# Chronotype Patterns and Circadian Disruption in Cancer Patients: Clinical and Chronobiological Insights

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#### Abstract

**Objectives:** Chronotype, an individual's circadian preference for activity and rest, has been increasingly recognized as a potential factor influencing cancer risk and patient outcomes. However, limited research has explored chronotype distribution among cancer patients and its association with sociodemographic features and cancer types.

**Methods:** This cross-sectional study was conducted in an oncology clinic at a research and training hospital in Turkey and included adults aged 18 years or older with a cancer diagnosis, excluding those with bipolar disorder, psychosis, or intellectual disability. Chronotype was assessed using the Turkish-validated Morningness–Eveningness Questionnaire (MEQ), and participants were categorized into five chronotype groups, with moderate and definite evening types combined into a single evening-type tendency group due to low frequency. Sociodemographic and clinical data were collected through structured forms. Statistical analyses included Fisher's Exact test, ANOVA, and univariate logistic regression, with significance set at p<0.05.

**Results:** Intermediate and morning chronotypes were more prevalent than evening types. Chronotype showed significant associations with gender, education level, and employment status. Definite morning chronotypes demonstrated a substantially lower likelihood of breast cancer compared to evening types (OR = 0.04, p = 0.023), while digestive system cancers were more frequent in morning chronotypes without statistical significance (OR = 0.60, p = 0.136). No significant association was observed with lung cancer.

**Conclusion:** These findings suggest that chronotype may influence cancer risk and patient characteristics. Integrating circadian preference assessment into cancer prevention and supportive care strategies could improve personalized management. Further longitudinal studies are warranted to clarify causal mechanisms and validate these associations..

Keywords: Chronotype, circadian rhythm, cancer risk, morningness-eveningness questionnaire, oncology

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Circadian rhythms, the endogenous timekeeping systems that synchronize behavioral and physiological processes with the 24-hour light–dark cycle, are essential for preserving human health and systemic homeostasis. These biological clocks govern numerous vital functions, including sleep–wake regulation, hormonal fluctuations, metabolic pathways, immune surveillance, and cellular re-

pair mechanisms.<sup>[2]</sup> Central to this system is the suprachiasmatic nucleus (SCN), located in the hypothalamus, which acts as the primary pacemaker. It coordinates the timing of peripheral clocks distributed throughout virtually all organs and tissues, including the liver, pancreas, and adipose tissue, ensuring alignment with environmental cues and exposure to light.<sup>[3,4]</sup> This precise temporal coordination

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enables organisms to adapt to predictable daily ecological changes and optimize internal physiological responses. However, when circadian rhythms become desynchronized—commonly referred to as circadian misalignment—adverse health outcomes may arise, including a heightened susceptibility to chronic diseases such as cancer. The interplay between circadian disruption and cancer development has gained increasing attention, as critical cellular processes such as DNA repair, cell cycle progression, and apoptosis are tightly regulated by clock genes. The interplay between circadian disruption and apoptosis are tightly regulated by clock genes. The interplay between circadian disruption and apoptosis are tightly regulated by clock genes.

Despite this growing body of evidence, the precise mechanisms linking circadian disruption and oncogenesis remain incompletely understood. While some studies suggest that mutations or dysregulation of core clock genes may have a direct role in tumorigenesis, others emphasize indirect pathways, such as metabolic dysfunction, chronic lowgrade inflammation, insulin resistance, and melatonin suppression, as potential mediators of cancer risk.<sup>[7]</sup>

Chronotype, defined as an individual's preference for physical and mental activity at a specific time of day, is a behavioral expression of circadian timing. Sleep is a crucial biological phenomenon that regulates key behavioral and physiological processes, affecting cancer development and progression.[8] Numerous physiological processes, including body temperature regulation, metabolic activity, and immune system function, follow circadian rhythmicity. Sleep itself represents a fundamentally rhythmic behavior tightly governed by the circadian system. Accordingly, disruption of circadian organization can significantly impair sleep architecture. In this context, studies have demonstrated that exposure to light, particularly during the biological night, not only suppresses melatonin secretion but also promotes alertness and diminishes the natural drive for sleep. [9] Chronotype, an indicator of circadian preference, is typically assessed using validated self-report instruments such as the Morningness-Eveningness Questionnaire (MEQ), and allows individuals to be classified into morning, intermediate, or evening types.[10] The Morningness-Eveningness Questionnaire (MEQ) is a commonly used self-report scale that provides this classification.[11] The timing of the sleepwake cycle is a fundamental indicator of individuals' circadian tendencies and is determined by genetic factors. [12] Circadian rhythms are endogenous, approximately 24hour cycles that regulate physiological processes including sleep-wake regulation, cellular metabolism, and immunity. [13] These rhythms are synchronized with external cues, such as light, food intake, and physical activity, forming the basis of chronobiology—a field that has attracted significant attention in cancer research.<sup>[14]</sup> However, individuals may alter these natural rhythms due to lifestyle preferences or environmental factors. At the molecular level, circadian clocks regulate key cellular pathways involved in oncogenesis, and these mechanisms have formed the foundation for chronotherapy. This treatment approach synchronizes therapeutic interventions with the body's internal clock.<sup>[15,16]</sup>

Given the effects of circadian rhythms on processes such as cellular metabolism, transcription, and cell proliferation, it has been suggested that disturbances in these rhythms may contribute to tumorigenesis by altering cell cycle control, DNA repair, and gene expression patterns.<sup>[17,18]</sup>

The circadian clock intricately interacts with cancer-related genes and regulatory networks that influence tumor development and malignancy potential. Rhythmic gene expression patterns, particularly those involved in metabolic and endocrine regulation, play a significant role in tumorigenesis. Disruption of circadian homeostasis not only alters these metabolic axes but also impairs both innate and adaptive immune responses, thereby facilitating malignant transformation and tumor progression. [19]

In certain types of cancer, alterations in the expression of core clock genes have been observed. For instance, malignant thyroid nodules exhibit increased expression of CLOCK and BMAL1, accompanied by decreased levels of CRY2. [19] Similarly, in renal clear cell carcinoma, rhythmic changes in clock gene expression (e.g., BMAL1 and PER) correlate with immune cell infiltration, including macrophages and neutrophils. [20,21] In glioblastoma, CLOCK has been shown to regulate glioblastoma stem cell activity by modulating chemokine expression and microglial content. [22]

Single-cell transcriptomic studies have also highlighted the prognostic significance of circadian rhythm disruption (CRD) in lung adenocarcinoma. Elevated CRD scores are associated with poor clinical outcomes and resistance to systemic therapies, including chemotherapy and tyrosine kinase inhibitors (TKIs).<sup>[23]</sup> In colorectal cancer models using gut organoids, the loss of circadian rhythmicity, particularly through genetic disruption of clock genes, has been shown to drive malignant behavior, a phenomenon also confirmed in patient-derived organoids.<sup>[24]</sup>

The connection between the cell cycle and the biological clock is another key axis of interest. Both function as oscillatory systems and share molecular features, including transcriptional feedback loops, protein post-translational modifications, and proteolytic degradation. The stages of the cell cycle—G1, S, G2, and M—are regulated by the sequential expression of cyclins and the activation of cyclin-dependent kinases (CDKs). Circadian clocks interact with these pathways, influencing the timing of cell

division and potentially contributing to dysregulated proliferation in cancer.

Furthermore, the tumor microenvironment (TME), composed of extracellular matrix components and various immune and stromal cell types (e.g., tumor-associated macrophages, dendritic cells, myeloid-derived suppressor cells, T cells, natural killer cells, and endothelial cells), plays a pivotal role in shaping tumor behavior. [28] Current research is increasingly focusing on the crosstalk between the circadian clock and the tumor microenvironment (TME), particularly on how circadian misalignment modulates the immune response and facilitates metastasis. [29] Given the central role of the immune system in tumor suppression, understanding circadian regulation offers promising therapeutic implications, especially for immunomodulatory treatments.

Research has shown that individuals with an evening chronotype have an increased risk of certain malignancies, such as breast cancer<sup>[30]</sup> and endometrial cancer.<sup>[31]</sup> In an analysis conducted within the Alberta's Tomorrow Project cohort, which included 19,822 participants and identified 1,322 incident cancer cases, it was observed that individuals with a later sleep midpoint—reflecting an evening chronotype—had a significantly higher risk of overall cancer (HR = 1.20, 95% CI: 1.04-1.37) and breast cancer specifically (HR = 1.49, 95% CI: 1.09–2.03), compared to those with an intermediate sleep timing profile.[32] In contrast, the morning chronotype is generally associated with a lower risk of cancer. An extensive analysis from the UK Biobank, which evaluated associations across multiple cancer types, identified that a definite evening chronotype was positively associated with increased incidence of several malignancies, including overall cancer, as well as breast, lung, endometrial, and ovarian cancers. Complementary Mendelian randomization analyses further suggested a potential protective role of the definite morning chronotype, demonstrating a reduced risk for overall cancer (OR = 0.91, 95% CI: 0.85-0.97 per category increase), lung cancer (OR = 0.34, 95% CI: 0.26-0.44), and breast cancer (OR = 0.69, 95% CI: 0.59–0.80). Although the associations were slightly attenuated, protective effects were also observed for ovarian (OR = 0.61, 95% CI: 0.39-0.97) and endometrial cancers (OR = 0.62, 95% CI: 0.43-0.91). These findings were consistent with the observed positive associations between the definite evening chronotype and the risk of these cancer types. [33] Additionally, chronotype variation has been implicated in digestive and prostate cancers, with some studies also indicating increased risk among those with intermediate typologies.[34-36] However, prior research has been limited by methodological variability and an insufficient control for confounders, such as sleep apnea.[36]

This study aims to evaluate the relationship between circadian typologies and different types of cancer at our oncology clinic and to determine which chronotype most cancer patients predominantly belong to. The study aims to contribute to understanding the potential effects of chronotypes on individuals' lifestyles and cancer risk.

#### **Methods**

### **Research Design**

This cross-sectional study was designed. Data were collected at an oncology clinic of a training and research hospital in Turkey. The inclusion criteria for the study included a cancer diagnosis and being at least 18 years old. Individuals diagnosed with bipolar disorder, psychotic disorder, and intellectual disability were excluded from the study.

#### **Data Collection Process**

The sociodemographic and clinical information of the participants was recorded using a data collection form designed by the research team. Chronotype classification was performed using the MEQ scale, which has been validated for reliability in Turkish. The scale consists of 19 questions, and based on the scoring, individuals were classified as follows:

- 16-30 "definite evening"
- 31-41 "moderate evening"
- 42-58 "intermediate"
- 59-69 "Moderate morning"
- 70-86 "definite morning"

### **Statistical Analysis**

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Descriptive statistics for categorical variables are presented as n and %. The mean, standard deviation, and median (min-max) are provided for continuous variables. Fisher's Exact test was used to compare categorical variables, and ANOVA was used to compare two or more groups. A univariate logistic regression analysis was used to assess the relationship between cancer types and chronotypes. Statistical significance was set at p<0.05. Due to the small number of participants in the definite evening and moderate evening chronotype categories, these groups were combined and analyzed as a single group labeled "evening-type tendency" (n=7) for statistical comparisons.

#### Results

A total of 216 patients with cancer participated in the study. The sociodemographic and clinical characteristics of the participants, along with their morningness-eveningness chronotypes, were analyzed in detail. The distribution of these variables is presented in Table 1.

**Table 1.** Distribution of Sociodemographic and Clinical Variables

Variables	n	%
Age		
Mean±SD	57.28±11.47	
Median (min-max)	58.0 (30-85)	
Gender		
Male	141	65.3
Female	75	34.7
Education		
Illiterate	76	35.7
Primary school graduate	49	23.0
High school graduate	17	8.0
University graduate	19	8.9
Marital status		0.5
Single	6	2.8
Married	180	83.3
Widowed	25	11.6
Divorced	5	2.3
	J	2.3
Living arrangement	10	0.0
With parents	19	8.8
With spouse	21	9.7
With spouse and children	156	72.2
Other	20	9.3
Employment status		
Unemployed	174	80.6
Employed	42	19.4
Comorbid medical condition		
Absent	109	50.7
Present	106	49.3
Cancer type		
Lung	21	11.2
Endometrium	9	4.8
Breast	81	43.1
Prostate	9	4.8
Digestive system	42	22.3
Other	26	13.8
Metastasis		.5.5
Present	69	36.5
Absent	120	63.5
Disease duration	120	05.5
Newly diagnosed	33	17.9
	55 79	42.9
0–1 year		
1–5 years	69	37.5
≥5 years	3	1.6
Smoking		
Yes	50	23.1
No	166	76.9
Family history of cancer		
Yes	106	49.1
No	110	50.9
Chronotype		
Definite evening type	1	0,45
Moderate evening type	6	2.75
Intermediate type	113	52.3
Moderate morning type	84	38.9
Definite morning-type	12	5.6
Deminie morning type	12	5.0

The mean age of the participants was 57.28±11.47 years, with a median of 58.0 years (range: 30–85 years). The majority of the participants were male (65.3%), while females accounted for 34.7% of the sample.

Regarding educational status, 35.7% of the participants were illiterate, 23.0% had completed primary school, 8.0% were high school graduates, and 8.9% had a university degree. In terms of marital status, most individuals were married (83.3%), followed by widowed (11.6%), single (2.8%), and divorced (2.3%).

Regarding living arrangements, a large proportion of the participants lived with their spouse and children (72.2%), while 9.7% lived only with their spouse, 8.8% with their parents, and 9.3% with others. The majority were unemployed (80.6%), and 19.4% were employed at the time of the study.

Half of the participants (50.7%) reported no comorbid medical conditions, while 49.3% had at least one additional illness. The most common type of cancer among participants was breast cancer (43.1%), followed by cancers of the digestive system (22.3%), lung (11.2%), other types (13.8%), prostate (4.8%), and endometrium (4.8%). Metastasis was present in 36.5% of patients.

Regarding disease duration, 42.9% of the participants had been diagnosed within the last year, 37.5% had been diagnosed for 1 to 5 years, 17.9% were newly diagnosed, and 1.6% had been living with the disease for 5 years or more.

When assessing lifestyle factors, 23.1% of the patients reported smoking, while 76.9% were non-smokers. A family history of cancer was present in 49.1% of the participants.

Finally, based on chronotype classification, the majority of individuals were identified as having an intermediate chronotype (52.3%), followed by those with a moderate morning type (38.9%) and a smaller group with a definite morning type (5.6%). Evening chronotypes were less common, with 2.75% identified as moderate evening type and only 0.45% as definite evening type.

Table 2 presents a comparison of various sociodemographic and clinical variables according to morning and evening chronotypes. Although the difference was not statistically significant, individuals with an evening-type tendency had the lowest mean age (52.85±6.86). In contrast, those with a moderate morning type had the highest mean age (59.50±11.21) (p=0.055). Gender distribution significantly differed among chronotypes (p=0.001), with males predominantly found in the intermediate (72.6%) and moderate morning types (63.1%), while females were more common in the definite morning type group (83.3%). Educational level also showed a statistically significant difference (p=0.003), with university graduates most frequently

**Table 2.** Comparison of Various Variables According to Morning-Evening Chronotypes

Variables	Evening-type tendency (definite evening+moderate evening type) N=7	Intermediate type N=113	Moderate Morning- type N=84	Definitely morning- type N=12	р
Age					
Mean±SD	52.85±6.86	56.15±11.66	59.50±11.21	57.33±11.47	0.055ª
Gender					
Male	4 (57.1)	82 (72.6)	53 (63.1)	2 (16.7)	0.001 <sup>b</sup>
Female	3 (42.9)	31 (27.4)	31 (36.9)	10 (83.3)	
Education					
Illiterate	1 (14.3)	17 (15.0)	14 (16.7)	1 (8.3)	0.003b
Primary school graduate	0 (0)	76 (67.3)	56 (66.7)	8 (66.7)	
High school graduate	2 (28.6)	14 (12.4)	11 (13.1)	2 (16.7)	
University graduate	4 (57.1)	6 (5.3)	3 (21.4)	1 (8.3)	
Marital status					
Single	2 (28.6)	1 (0.9)	3 (3.6)	0 (0)	0.236 <sup>b</sup>
Married	5 (71.4)	95 (84.1)	69 (82.1)	11 (91.7)	
Widowed	0 (0)	14 (12.4)	10 (11.9)	1 (8.3)	
Divorced	0 (0)	3 (2.7)	2 (40)	0 (0)	
Living arrangement					
With parents	1 (14.3)	10 (8.8)	7 (8.3)	1 (8.3)	0.875 <sup>b</sup>
With spouse	1 (14.3)	10 (8.8)	8 (9.5)	2 (16.7)	
With spouse and children	4 (57.1)	83 (73.5)	60 (71.4)	9 (75.0)	
Other	1 (14.3)	10 (8.8)	9 (45.0)	0 (0)	
Employment status	, ,,,		, , ,		
Unemployed	6 (85.7)	97 (85.8)	65 (77.4)	6 (50.0)	0.023 <sup>b</sup>
Employed	1 (14.3)	16 (14.2)	19 (22.6)	6 (50.0)	
Comorbid medical condition		(/	. , (==.0)	G (5 5.15)	
Absent	6 (85.7)	62 (54.9)	36 (43.4)	5 (41.7)	0.094 <sup>b</sup>
Present	1 (14.3)	51 (45.1)	47 (56.6)	7 (58.3)	0.051
Cancer type	. ()	5. (.5,	(50.0)	, (55.5)	
Lung	1 (16.7)	9 (9.1)	8 (11.3)	3 (25.0)	0.025 <sup>b</sup>
Endometrium	0 (0)	9 (9.1)	0 (0)	0 (0)	0.023
Breast	4 (66.7)	45 (45.5)	31 (43.7)	1 (8.3)	
Prostate	0 (0)	3 (3.0)	4 (5.6)	2 (16.7)	
Digestive system	0 (0)	19 (19.2)	19 (26.8)	4 (33.3)	
Other	1 (16.7)	14 (14.1)	9 (12.7)	2 (16.7)	
Metastasis	1 (10.7)	11(11.1)	5 (12.7)	2 (10.7)	
Present	2 (28.6)	33 (34.4)	30 (40.5)	4 (33.3)	0.828 <sup>b</sup>
Absent	5 (71.4)	63 (65.6)	44 (59.5)	8 (66.7)	0.020
Disease duration	3 (7 1. <del>1</del> )	03 (03.0)	TT (37.3)	0 (00.7)	
Newly diagnosed	2 (40.0)	16 (16.5)	13 (18.6)	2 (16.7)	0.824 <sup>b</sup>
0–1 year	1 (20.0)	40 (41.2)	32 (45.7)	6 (50.0)	0.024
		40 (41.2)			
1–5 years ≥5 years	2 (40.0) 0 (0)	1 (1.0)	23 (32.9) 2 (66.7)	4 (33.3) 0 (0)	
Smoking	0 (0)	1 (1.0)	2 (00.7)	0 (0)	
Yes	3 (42.9)	25 (22.1)	17 (20.2)	5 (41.7)	0.201 <sup>b</sup>
res No					0.201
	4 (57.1)	88 (77.9)	67 (79.8)	7 (58.3)	
Family history of cancer	6 (OF 7)	F2 (4C 0)	40 (47.6)	7 (50.3)	0.333h
Yes	6 (85.7)	53 (46.9)	40 (47.6)	7 (58.3)	0.223 <sup>b</sup>
No	1 (14.3)	60 (53.1)	44 (52.4)	5 (41.7)	

a: ANOVA test, b: Fisher's Exact test, p < 0.05 statistically significant; † Definite evening and moderate evening types were grouped as "evening-type tendency" due to limited sample size.

observed in the evening-type group (57.1%), while primary school graduates were predominant in the other groups.

No significant difference was observed regarding marital status (p=0.236) or living arrangements (p=0.875). However, living with a spouse and children was the most common arrangement across all groups. Employment status varied significantly among chronotypes (p=0.023); the highest rate of employment was observed in the definite morning-type group (50.0%), while the evening-type group had the lowest rate (14.3%). The presence of comorbidities did not significantly differ between groups (p=0.094), although they were slightly more prevalent in the morning-type categories.

The distribution of cancer types differed significantly across chronotypes (p=0.025). Breast cancer was most common in the evening-type (66.7%) and intermediate (45.5%) groups, while digestive system cancers were most frequent among moderate and definite morning types. Lung cancer appeared more frequently in the definite morning-type group (25.0%). There were no statistically significant differences in metastasis status (p=0.828), disease duration (p=0.824), smoking status (p=0.201), or family history of cancer (p=0.223) across the chronotype groups.

These findings suggest that certain sociodemographic and disease-related variables, particularly gender, education, employment status, and cancer type, may be associated with individual chronotype preferences among cancer patients.

Table 3 presents the results of the univariate logistic regression analyses evaluating the association between chronotype and the likelihood of having lung or breast cancer. For lung cancer, no statistically significant association was observed across chronotype categories (p=0.438). Compared to individuals with an evening-type tendency (reference group), the odds ratios (OR) for lung cancer were 0.50 (95% Cl: 0.05–4.76) for the intermediate type, 0.63 (95% Cl: 0.06–6.14) for the morning-type tendency, and 1.66 (95% Cl: 0.13–20.57) for the definite morning type. These results indicate no meaningful difference in lung cancer risk by chronotype.

In contrast, for breast cancer, a notable finding emerged. While the intermediate and morning-type tendency groups showed no statistically significant difference in odds compared to the evening-type tendency (OR = 0.41, p=0.325 and OR = 0.38, p=0.291, respectively), the definite morning-type group had a significantly lower likelihood of having breast cancer, with an odds ratio of 0.04 (95% CI: 0.03–0.64, p=0.023). This suggests a potential protective association between a definite morning chronotype and breast cancer risk in this cohort.

**Table 3.** Results of Univariate Logistic Regression on Lung and Breast Cancer

Diedst Caricei			
Lung Cancer			
Variables	OR (95% CI)	р	
Chronotype		0.438	
Evening-type tendency (definite evening+modera evening type)	Ref. te		
Intermediate type	0.50 (0.05-4.76	6) 0.547	
Morning-type tendency	0.63 (0.06-6.14	4) 0.695	
Definitely morning-type	1.66 (0.13–20.5	57) 0.690	
<b>Breast Cancer</b>			
Variables	OR (95% CI)	р	
Chronotype		0.138	
Evening-type tendency (definite evening+modera evening type)	Ref. te		
Intermediate type	0.41 (0.07-2.38	8) 0.325	
Morning-type tendency	0.38 (0.06-2.25	5) 0.291	
Definitely morning-type	0.04 (0.03-0.64	4) 0.023	
Digestive System Cancer			
Chronotype Group	Digestive Cancer (n)	OR (95% CI)	р
Morning	23	Reference	-
Non-morning	19	0.60 (0.30-1.18)	0.136

Due to the absence of any digestive system cancer cases in the evening-type group, the original logistic regression model failed to converge as a result of perfect separation. To address this, chronotype categories were merged into 'morning' (morning-type and definite morning-type) and 'non-morning' (intermediate-type and evening-type). Logistic regression analysis revealed a non-significant trend (OR = 0.60, 95% CI: 0.30-1.18, p=0.136).

The table compares the prevalence of digestive system cancers between two chronotype-based groups: Morning (morning-type and definite morning-type) and Nonmorning (intermediate and evening-type). Among 216 cancer patients, digestive system cancers were present in 31.5% (23/73) of patients with a morning chronotype, compared to 15.8% (19/120) of those with a non-morning chronotype.

A logistic regression analysis was conducted to assess the strength of this association. The non-morning chronotype group had a lower, but not statistically significant, odds of digestive system cancer compared to the morning group (OR = 0.60, 95% CI: 0.30–1.18, p=0.136). This indicates that while there was an inverse trend, it did not reach conventional thresholds for statistical significance (typically p<0.05).

#### Discussion

This study investigated the distribution of morningness-eveningness chronotypes in cancer patients and explored their associations with sociodemographic variables and cancer type. The majority of patients demonstrated an intermediate chronotype, with morning-oriented types being more common than evening-oriented types. These findings are consistent with prior research suggesting that intermediate and morning chronotypes are more prevalent in general populations, particularly among older individuals and those with structured daily routines, such as patients undergoing cancer treatment.<sup>[13,14]</sup>

Our findings revealed that gender, education level, and employment status were significantly associated with chronotype. Males were more likely to exhibit intermediate and moderate morning chronotypes, while females were significantly more represented in the definite morning type group. Furthermore, university graduates were more frequently observed in the evening-type group, possibly reflecting occupational and lifestyle patterns that align with later sleep-wake preferences. Interestingly, employment was more common among definite morning chronotypes. In contrast, unemployment was most prevalent in the evening-type group, suggesting that circadian preference may influence or reflect functional status in cancer patients.

Some of these findings are consistent with existing literature, while others diverge and may reflect populationspecific dynamics. In line with previous studies, males were more likely to exhibit intermediate and moderate morning chronotypes, whereas females were more prominently represented in the definite morning type group. This aligns with prior meta-analytic findings showing that, although men tend to lean toward eveningness and women toward morningness, these gender differences often diminish with age.[37] On the other hand, some findings diverged from the expected patterns. For instance, while previous studies frequently report a stronger tendency for males to display evening chronotypes, the predominance of intermediate or moderate morning preferences among men in our cohort may reflect the influence of age or cancer-related treatment routines, which may entrain circadian behaviors over time. Additionally, the relatively high prevalence of definite morning types among unemployed women in our sample contrasts with studies that associate morningness with greater functionality and social integration. This inconsistency could be due to confounding variables such as disease burden, caregiving roles, or cultural factors specific to our population that were not fully captured in the current analysis.

Similarly, our observation that university graduates are more frequently represented in the evening-type group is supported by evidence indicating that individuals with higher educational attainment may have more flexible schedules or lifestyle habits that allow for later sleep-wake patterns.<sup>[38]</sup>

Moreover, our finding that employment was more common among definite morning chronotypes, while unemployment was more prevalent in evening types, is consistent with studies highlighting the challenges evening chronotypes face in aligning with conventional work schedules. This misalignment can lead to reduced occupational functioning and lower work engagement.<sup>[39]</sup>

Taken together, these findings suggest that while chronotype distributions and their associations with sociodemographic variables follow expected trends in some respects, contextual factors related to cancer diagnosis, treatment regimens, and cultural environment may shape circadian behaviors differently in oncology populations. Future studies incorporating longitudinal designs and actigraphybased chronotype measurements could provide deeper insight into these patterns.

The distribution of cancer types across chronotypes also yielded notable results. We observed a higher prevalence of digestive system cancers among patients with a morning chronotype compared to those with a non-morning chronotype. Specifically, 31.5% (23/73) of individuals in the morning group had digestive system cancers, whereas 15.8% (19/120) of those in the non-morning group were affected. Although this difference did not reach statistical significance (OR = 0.60, 95% CI: 0.30-1.18, p=0.136), the trend suggests a potential inverse association between non-morning chronotypes and the risk of digestive system cancers. These findings appear to contrast with existing literature, which generally indicates that a morning chronotype is associated with a reduced risk of various cancers, including those of the digestive tract. For instance, an extensive Mendelian randomization study conducted by Yuan et al. found that genetically determined morningness was significantly associated with a lower risk of stomach and colorectal cancers (OR = 0.94, 95% CI: 0.90–0.98). [40] Similarly, several observational studies have linked evening chronotypes to increased cancer risk, attributing this to lifestyle-related circadian misalignment, such as late-night eating, poor sleep quality, and hormonal disruption.[41]

Lung cancer, although not significantly associated with chronotype overall, appeared more frequent in the definite morning type group. These findings align with growing evidence suggesting that disruptions in circadian rhythms may play a role in cancer development and progression. [16,42] Specifically, the link between evening chronotypes and breast cancer risk has been previously documented, with eveningness being associated with greater circadian disruption, melatonin suppression, and lifestyle factors such as irregular sleep and light exposure at night. [43]

In our study, statistical evaluation demonstrated no significant relationship between chronotype and lung cancer. However, a significant association emerged in the context of breast cancer, where patients with a definite morning chronotype were found to have markedly lower odds of breast cancer compared to those with an evening-type tendency (OR = 0.04, p=0.023). A previous analysis from the UK Biobank, which included 469,691 participants free of lung cancer at baseline and reported 2,177 incident cases, demonstrated that individuals with an evening chronotype had an increased risk of developing lung cancer compared to those with a morning preference (HR = 1.25, 95% CI: 1.07-1.46).[44] A subsequent and expanded analysis from the same cohort, comprising 382,966 participants and 3,664 lung cancer cases, further supported this finding; when individuals with a history of shift work were excluded, both slight and definite evening chronotypes were associated with higher lung cancer risk relative to the definite morning type (HR = 1.17, 95% CI: 1.06-1.28 and HR = 1.37, 95% CI: 1.21-1.54, respectively). [45] In contrast, a smaller case-control study did not find a significant association between chronotype and lung cancer risk, highlighting inconsistency in the literature. [46] The lack of association observed for lung cancer in our study may be explained by its multifactorial origin. This lack of association may be attributed to the multifactorial nature of lung cancer, which is predominantly influenced by strong environmental factors such as smoking, air pollution, and occupational exposures.

Additionally, the biological heterogeneity of lung cancer, particularly the presence of distinct molecular subtypes such as EGFR, ALK, and KRAS mutations, may obscure potential associations with circadian regulation. It is also possible that the peripheral circadian regulation in lung tissue is less responsive to chronotype-related mechanisms compared to hormonally driven or immunologically active cancers, such as breast or gastrointestinal malignancies. Furthermore, the tendency for chronotype to shift toward morningness with increasing age may contribute to reduced variability in circadian preference among lung cancer patients, thus limiting the detection of significant differences. Lastly, the relatively small sample size of patients in the evening-type chronotype group may have limited the statistical power to detect subtle associations.

The discrepancy between our findings and previous studies may be attributed to several factors. Firstly, the limited number of patients in the evening-type subgroup may have affected statistical power. Secondly, chronotype classification varies across studies, making direct comparisons difficult. Lastly, confounding factors such as diet, physical activity, or cancer-induced changes in sleep-wake patterns may have influenced chronotype reporting or cancer risk itself.

Future studies with larger and more diverse populations, using standardized chronotype assessments and adjusting for lifestyle and behavioral factors, are warranted to clarify the relationship between circadian typology and digestive system cancer risk.

Taken together, our findings underscore the potential clinical relevance of chronotype assessment in oncology settings. Chronotype may influence not only patients' biological vulnerability to cancer but also their functional status, psychological well-being, and response to therapy. Given that circadian disruption has been proposed as a modifiable cancer risk factor, future interventional studies should investigate whether chronotherapeutic strategies or lifestyle interventions that target circadian alignment can improve outcomes in cancer patients.

However, several limitations must be considered. The sample size in specific chronotype subgroups, particularly the evening-type group, was small, so it was necessary to merge the definite and moderate evening types for statistical analysis. Additionally, the study's cross-sectional design precludes any causal inference. Further prospective studies with larger and more balanced samples are warranted to validate these findings and explore underlying biological mechanisms.

### **Clinical Implications**

The present findings suggest that chronotype assessment may serve as a practical, low-cost tool in oncology settings to inform individualized patient care. Identifying patients with an evening chronotype could help clinicians recognize individuals who may be at greater risk for circadian disruption, reduced functional status, or specific cancer risk profiles, such as higher odds of breast cancer. Integrating chronotype screening into routine assessments may support tailored scheduling of treatments, optimization of supportive care interventions, and targeted behavioral strategies to promote circadian alignment. In the long term, such personalized approaches could contribute to improved quality of life, treatment adherence, and potentially better clinical outcomes for patients with cancer.

#### Conclusion

This study demonstrates that circadian preference is associated with cancer risk profiles and patient functionality. The morning chronotype is linked to a lower risk of breast cancer, indicating a potentially protective role. Incorporating chronotype assessment into oncology practice can enhance individualized prevention strategies and supportive care planning. Regulating circadian rhythms based on individual chronotypes is a promising direction for reducing cancer risk. These findings are grounded in existing scientific evidence and should be expanded upon in future large-scale, longitudinal studies.

#### Limitations

This study has several limitations. First, the sample size within specific chronotype subgroups—particularly the evening-type group—was relatively small, which limited statistical power and necessitated group merging for analysis. Second, the cross-sectional design precludes any inference of causality between chronotype and cancer types. Third, chronotype was assessed through self-report, which may be influenced by subjective perception or illness-related changes in sleep patterns. Additionally, potential confounding variables such as lifestyle habits, comorbidities, and treatment-related circadian disruptions were not fully controlled. Future longitudinal studies with objective chronotype measures and larger, more diverse populations are needed to validate these findings and clarify underlying mechanisms.

### **Disclosures**

**Ethics Committee Approval:** This study was approved by the Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (Approval number: 2024/276; Approval date: 28 August 2024). All participants provided written informed consent to participate.

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