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Discrete-time Survival Analysis of Risk Factors for Early Menarche in Korean Schoolgirls

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Discrete-Time Survival Analysis of Risk Factors of Early Menarche in Korean Child

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Abstract

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ABSTRACT

Objectives: To evaluate the effect of body weight status and sleep duration on the discrete-time hazard of menarche in Korean school girls in representative multiple-point prospective panel data.

Methods: The study comprised 914 girls in the 2010 Korean Children and Youth Panel Study who were in the elementary first-grader panel from 2010 until 2016. I used the Gompertz Regression model to estimate the effects of weight status based on age- and sex-specific BMI percentile and sleep duration on an early school child's conditional probability of menarche during a given time interval using general health condition and annual household income as covariates.

Results: The discrete-time survival analysis of time-to-menarche data collected from the Korean Children and Youth Panel Study 2010 suggests that being overweight or sleeping less than recommended duration is related to the increase of hazard of menarche compared to being average weight and sleeping 9 to 11 hours by 1.63 times and 1.38 times respectively while other covariates are fixed. However, the discrete-time hazard of menarche decreases by 66 percent for being underweight.

Conclusion: Weight status based on BMI percentiles and sleep duration of early school years affect the hazard of menarche.

Keywords: Menarche, Survival Analysis, Obesity, Adolescent, Body Mass Index, Sleep

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Chapter 1. Introduction

1.1. Study Background

The importance of age at menarche (AAM) in public health is often overlooked. The timing of menarche, which marks the onset of significant periodic hormonal changes and related physiologic responses, is connected to various health conditions of women. Previous studies have shown the risk of estrogen-dependent tumors such as breast cancer (Collaborative Group on Hormonal Factors in Breast Cancer. 2012), cardiovascular disease (Chen X, et al., 2018), and bone mineral diseases such as osteoporosis are related to age at menarche, specifically. (Zhang Q, et al., 2018)

Though there is various heterogeneity among the results of the above research questions, earlier age at menarche is reported to increase the risk of estrogen-dependent tumors. Meta-analysis of twelve cohort studies showed that each 1-year increase in menarche age decreases the relative risk of cardiovascular disease (RR:0.993, 95% CI: 0.975-1.011) and ischemic heart disease mortality (RR:0.969, 95% CI: 0.947-0.993). The relationship between menarche and bone mineral disease is more complicated. More prolonged estrogen exposure is a protective factor in preventing osteoporosis and bone fracture. However, analysis after controlling estrogen exposure duration showed the harmful effect of earlier menarche. Accelerated menarche causes less circumferential bone growth, making fragile adult bone structures vulnerable to fracture. (Šešelj M, et al., 2012)

Not only limited to these long-term adverse outcomes, but early menarche is also related to public health issues of adolescents, such as unsafe sexual relations, substance use (Johansson T, Ritzén EM, 2005), adolescent depression (Hirtz R, et al., 2022), and suicidal attempts (Kim SR, Lee S, Chung JH, 2021). These relatively short-term adverse outcomes can result in long-hauling negative health impacts.

If we accept the adverse health outcomes of earlier menarches, a downward trend of age at menarche can be perceived as a severe public health problem (Figure 1). Specifically, among developed countries, Korean girls are showing the fastest rate of decline. (Sohn K., 2017, Seo MY, et al., 2020) A downward trend of age at menarche is a global trend, yet the etiology behind this worrisome phenomenon is still a mystery.

Some have argued that earlier menarche is a normal response to improved conditions of childhood, such as better nutrition, so it should not be considered a medical or public health issue (Gluckman PD, Hanson MA., 2006). However, the decline of age at menarche should be understood as a complex phenomenon affected by both positive and negative contributing factors. Herman−Giddens has argued that the acceleration of early menarche in the early 20th century might be due to the advancement of favorable conditions such as better nutrition. In contrast, recent acceleration can be affected by more negative causes. Therefore, careful analyses have been called for to investigate this issue properly, considering the nuances and complexities of genetic, environmental, and social causes of earlier menarche. (Herman−Giddens ME, 2007)

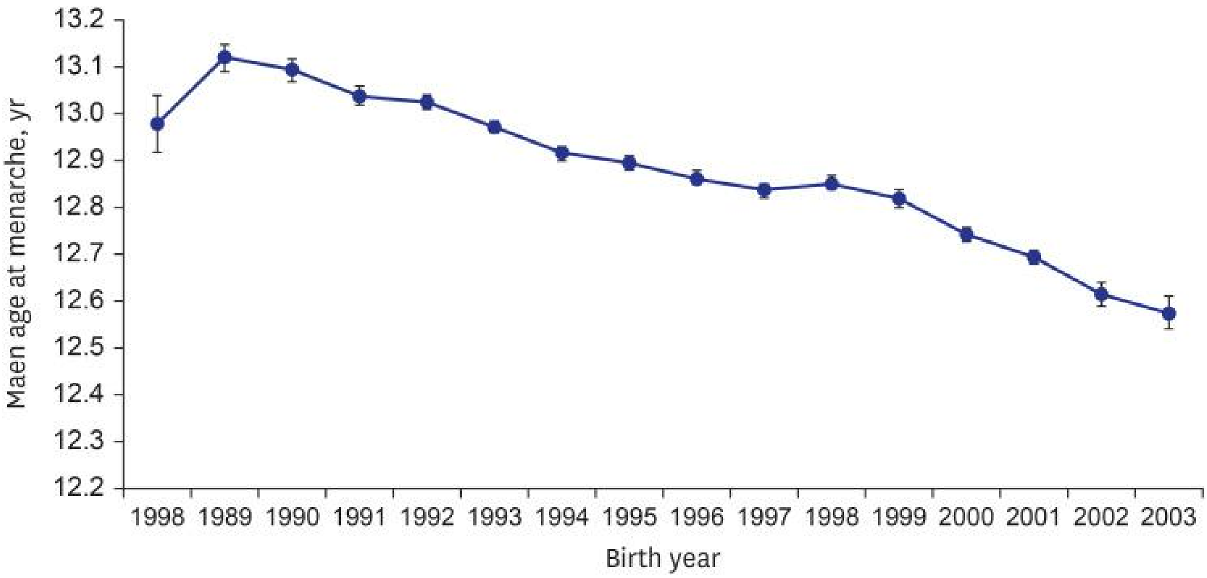

Figure 1. Trends in the age of menarche stratified by birth year in Korean girls.
Adapted from: (Seo MY, et al., 2020)

1.2. Purpose of Research

Investigating the etiology of early menarche can be fruitful, considering its multiple detrimental health impacts and increasing prevalence. Prior studies presented numerous individual-level risk factors related to the improper timing of menarche. Albeit there were some heterogeneities, longitudinal studies suggested the following risk factors of earlier menarches: lower birth weight, higher body weight, and weight gain in infancy and early childhood. (Juul F, et al., 2017)

Not only limited to individual-level biological conditions but socioeconomic conditions have also been suggested to be crucial determinants of age at menarche. Socioeconomic factors at multiple levels, for instance, household income or socioeconomic deprivation of the neighborhood, were also shown to be associated with earlier menarche. On the contrary, being underweight or exposed to strenuous exercise was related to late menarche. For sleep duration, contradictory results have been published suggesting they are both related to early (Murata K, Araki S. 1993) or late menarche (Ku SY et al., 2006).

Fortifying knowledge about risk factors of early menarche can contribute to developing intervention strategies to prevent adverse outcomes associated with earlier menarche. Attention should be drawn to body weight status and sleep duration among suggested risk factors. These amenable variables are relatively easy to monitor, and specific direct interventions can be designed at multiple levels. For example, an intervention targeting school cafeterias can be devised. (Bethmann D, Cho JI, 2022) Moreover, these variables have been collected systematically in various public datasets targeting representative national samples. Utilizing this data can help us to understand the current status of the early menarche problem and its modifiable risk factors. A similar data collection scheme can be further used to monitor a recognized situation's progression or quantify the effect of devised possible interventions.

Therefore, elucidating factors associated in a causal manner with menarche can help us to develop effective public health interventions to lower the burden of various diseases and conditions associated with early menarche.

Chapter 2. Literature Review

2.1. Age at Menarche

There is a global decreasing trend of median and mean age at menarche. (Ibitoye M, et al., 2017) Previous studies showed that in the case of developed countries, in the 19^{th} century, for most ethnic groups, the mean AAM was 17 years of age, while it decreased to 12.5 years of age in the 20^{th} century. The rate of decline has stabilized in countries such as the United States of America, the United Kingdom, Italy, and Greece. Countries including China, Columbia, Denmark, and the Netherlands showed continued downward trends while the rate slowed down. Especially, Asian countries, including the Republic of Korea, showed a fast decline in a relatively short period suggesting the change of environmental factors beyond genetic factors or interaction between these two. (Kim H, et al., 2021) Tiziana Leone and Laura J Brown analyzed World Fertility Survey and Demographic and Health Surveys to show the decline of age at menarche among low-income and middle-income countries, possibly at a quicker pace than a high-income country. (Leone T, Brown LJ., 2020)

The consensus about the reference range of AAM is still being challenged by several researchers. Classical textbooks about juvenile endocrinology or gynecology suggest a reference range of 9.5 to 12.5 years of age. (Mark Sperling, 2014) A group of Korean researchers suggested 10.5 years of age. They argued that 12 years of age, which is a conventional cut-off age to demarcate early menarche among researchers, is too late. Twelve years of age corresponded to about the 3rd to 6th percentile of age at menarche for Korean girls in the 1990s. In 2015, it was compared to the 24th percentile. However, this perspective is not yet widespread. This is because the 12-year of age cut-off value was used frequently among public health researchers to elucidate the adverse health effects of earlier age at menarche. This presence of good research outcomes of these researchers shows that hastening the cut-off range would result in a loss of chance to detect these problems related to earlier age at menarche. Therefore, rather than recalibrating the cut-off age based on percentile, the current phenomenon should be interpreted as an increase in the prevalence of early menarche.

2.2. Risk factors of Early Menarche

Many studies investigated relationships between various risk factors and early menarche. Age at menarche is a complex phenotype affected by genetic, environmental, nutritional, and socioeconomic factors and interactions among these factors.

Studies employing twin and familial structures to study variance decomposition or narrow−sense heritability of age at menarche show that 57 to 82% of the variance can be attributed to heritable factors. (Volodymyr Dvornyk & Waqar−ul−Haq, 2012) Prior heritability studies show that even though a fast rate of declination is shown in Asian countries, we could still postulate that genetic factors can play an essential role in regulating the timing of menarche.

Along with genetic factors, general anthropometric variables such as weight and height were suggested to be associated with the age at menarche. Maternal or perinatal environmental factors were also presented to be related to the age at menarche. Maternal weight gain, gestational diabetes, pre−and postnatal energy availability, micro− and macronutrient intake, environmental hazards such as tobacco smoke or psychosocial stressors, and socioeconomic status. (Volodymyr Dvornyk & Waqar−ul−Haq, 2012)

As summarized in the study background section, a systematic review of longitudinal studies with early menarche as a response variable showed that lower birth weight, higher body weight, and weight gain in infancy and early childhood were suggested to be associated with earlier menarche. (Juul F, et al., 2017)

However, there are several limitations of previous studies. Several studies modeling the relationship between sleep duration and body weight status with early menarche did not include time−varying aspects of those variables. Instead, studies chose the value of specific predetermined critical periods to represent its effect on early menarche. (D' Aloisio AA, et al., 2013) For example, previous studies dealing with BMI−based weight status included the variable as a single variable, such as BMI at age 8−9 years old, or focused on the difference of BMI z−score in a pre−defined interval. (Maisonet M, et al., 2010), Considering the volatile nature of BMI and sleep duration due to growth in childhood, the natural trend or change of those variables over time should be regarded to measure their effect correctly.

Chapter 3. Methodology

3.1. Study hypothesis

BMI–based weight status and sleep duration after school entrance are related to the hazard of menarche in a statistically significant way.

3.2. Data Source and Study Subjects

3.2.1. Data Source

The 2010 Korean Children and Youth Panel Survey (KCYPS) is a survey directed by the National Youth Policy Institute (NYPI). The research protocol of this survey was assessed and approved by the Institutional Review Board (IRB) associated with the National Institute of Youth Studies, Korea.

This specific study utilized only the part of KCYPS data on "the elementary first–grader panel" from 2010–2016. KCYPS 2010 data include "the elementary fourth–grader panel" or "the middle first–grader panel." By limiting the study population to a single cohort, we can overcome the heterogeneity problem and potential bias it can introduce.

To consider the effects of time–varying variables such as BMI on the age at menarche, I selected the youngest panel, which allows the most extended investigation of time–varying variables before the onset of menarche. Moreover, using the youngest cohort that did not experience menarche at the beginning of observation guarantees exposures preceding the outcome of interest, menarche.

Due to the multiple–point prospective panel design of KCYPS, a probability sample (N=2,342) representing all elementary school first–year students in Korea was chosen and surveyed every year from 2010 until 2016. A stratified multi–stage cluster sampling method was used. Seventy–eight schools were selected using the probability proportional to size (PPS) sampling method. Then, for each selected school, a class was chosen again, and all students and their legal guardians of that class responded to the survey questionnaire. Individual longitudinal weights were calculated to account for the data representativeness and potential bias resulting from sample attrition and follow−up losses. Additional study details can be viewed on the official website of NYPI. (National Youth Policy Institute (NYPI), 2010)

Since the age at menarche was investigated in Wave 7, the study population was limited to the subgroup of female students who responded appropriately to the age at menarche question.

Because the first year of the panel study did not ask for the height and weight of students used to calculate BMI, I analyzed the data from the second year until the seventh year of follow−up. The observed data was then transformed into a person−period data format of 4469 discrete time intervals of binary observations of 914 students until the event of interest (i.e., menarche) occurs or is censored to calculate the hazard.

3.2.2 Defining Variables

(1) Age at menarche

In the Wave 7 of the panel study, students were asked, "In what grade did your menarche happen?" Students were required to answer in 6 levels [Not Yet, Before 3rd grade, 4th grade, 5th grade, 6th grade, or 7th grade].

Those who responded "Not Yet" were considered right-censored, while those who answered "Before 3rd grade" were supposed to experience menarche during 3rd grade considering possible left censoring.

Since data collection was implemented discretely every year, age at menarche was estimated to happen during the typical age interval of school grades in Korea. For example, those who responded to experienced menarche during 5th grade were estimated to experience menarche between 11 to 12 years old. Interval censoring was considered in the main statistical analysis using the Gompertz regression.

(2) Exposures and covariates

All variables included in the model are time-varying variables collected from the multiple-point prospective panel data. To evaluate the effect of BMI, I classified the BMI status according to age- and sex-specific BMI percentiles according to the 2017 Korean National Growth Charts for children and adolescents: underweight (< 5th percentile), normal (≥ 5th percentile and < 85th percentile), overweight (≥ 85th percentile and < 95th percentile), and obesity (≥ 95th percentile). Exact weight cut-off values for defined percentiles are based on the reference growth table developed by the 'Committee for the Development of Growth Standards for Korean Children and Adolescents' using the 6th month of the specific age interval of the measured grade. (Kim JH et al., 2018)

To evaluate the effect of sleep duration, I calculated the exact duration in minutes based on the response to the questionnaire asking about weekday sleep onset time and wakeup time. Then, sleep duration was classified into short, adequate, and long based on the age group-specific recommendations from the National Sleep

Foundation, which was 9 to 11 hours. (Hirshkowitz M et al., 2015)

A self-reported general health condition answered in 4 levels [Very good, good, poor, very poor] was used as a covariate. Health condition was classified into two categories by merging the first and last two levels.

Categorized annual household income was also included in the model as a covariate. Considering the right-skewed distribution of the household income variable, I cut ten intervals having equal length, then assigned 'Low' for the lowest interval. The second and the third lowest interval was assigned 'Middle,' and others were assigned 'High.' (Behie AM & O'Donnell MH., 2015)

3.3. Statistical analysis

Survival analysis is a method commonly used to analyze time-to-event data. It aims to model event transition and the time it takes for the event transition. The method can model the effects of time-varying and time-fixed variables on the outcome. The method can also deal with the right censoring issue in the data, which means that for some observations, the time when an event transition occurs is unknown.

One can employ discrete-time survival analysis methods to extend the usability of survival analysis techniques, which usually assume continuous time measurement. In practice, data are often collected in discrete-time intervals. For example, the current data (KCYPS2010) is collected annually in a discrete manner. Therefore, methods that do not require the assumption of continuous time measurement are needed. The fundamental measure used to evaluate the risk of event occurrence in a discrete-time period is a discrete-time hazard. It is the conditional probability that an individual will experience the target event in the time period, given that they did not experience it in earlier time periods.

The quantity used to evaluate the risk of event occurrence in a discrete-time period is a discrete-time hazard which can be denoted by h_{is}. Discrete-time hazard is the conditional probability that individual i is expected to experience the event of interest in a given time period s, given that one did not experience it before time period s. This can be formalized as $h_{is}=P(T_i=s|T_i \geq s)$. T_i represents a discrete random variable indicating the time period s when individual i experiences the event of interest.

Therefore, the hazard function formalized above shows the probability that the event will occur in the current time period s, given that it must occur now or later. The value of discrete-time hazard in the given time period s can be estimated as the division of the number of events at time s by the number at risk at time s.

This study modeled discrete hazards using the Gompertz model or the grouped proportional hazards model. Discrete hazard models can be embedded into the generalized linear model (GLM) framework with an appropriate link function. There are multiple discrete hazard models, such as the logistic model, the probit model, the Gompertz model, or the Gumbel model.

More specifically, a general representation of the hazard function that links the hazard h_{is} with a linear predictor η can be formalized as follows: $\eta = g(h_{is}) = \gamma_{0s} + x_{is}\gamma$. g( ) is called a link function because this links the hazard with the linear predictor. Multiple link function options are available for discrete-time survival analysis, as mentioned above. Among these models, the Gompertz model using a clog-log link is favorable because of its interpretability. The exponential term of a parameter estimate can be used directly to quantify the difference in the hazard value per unit difference in the predictor. (G. Tutz and M. Schmid, 2016)

The current data was processed into the person-period format by assigning separate row for each individual and each period when the person is observed until the event occurs or be censored, eventually turning them into multiple binary observations. Since discrete-time survival analysis describes the conditional probability of event occurrence, the records of the person-period data need only assume conditional independence. It means that multiple observation from the same individual does not harm the validity of estimates due to violation of independence among observations.

The current model includes weight status based on BMI, sleep duration, self-reported general health condition, and income as a categorical variable, as discussed earlier. The 'Exit' is additionally included in the model. The 'Exit' is a variable indicating discrete time intervals when data are observed. In this case, it is represented as the age at the time of the survey. We conducted analyses using R version 4.2.0, and package 'lme4' was used.

Chapter 4. Results

4.1. Descriptive analysis of at-risk population

Table 1 presents the essential characteristics and distribution of covariates for each at-risk population at consecutive time intervals. The hazard increases as individuals reach the next time interval. It is noteworthy that the proportion of overweight participants decreases as they enter the next at-risk population without experiencing menarche in the earlier time intervals. Meanwhile, the proportion of underweight shows an increasing trend, though not monotonously. For sleep duration, the proportion of those who sleep recommended hours decreases as they reach the following time intervals.

Table 2 depicts the crude age distribution at menarche of this specific data set. Since the question asking the age at menarche was in a multiple choice style with six options [1: Not yet, 2: Elementary school 1^{st} ~3^{rd} grade, 3: Elementary school 4^{th} grade, 4: Elementary school 5^{th} grade, 5: Elementary school 6^{th} grade, 6: Middle school 1^{st} grade], the answer was modified to age interval of the response given in school years. For example, for those who answered they experienced age at menarche at Elementary school fifth grade, we assigned 11-12 years old for that case.

Table 1. The characteristics of the at-risk population for each time interval, 2011-2016

	Age at the time of survey (years old)					
Characteristic	8-9	9-10	10-11	11-12	12-13	13-14
	N	**N**	**N**	**N**	**N**	**N**
Total	914	886	876	843	675	275
Censor	28	8	1	2	4	108
Event	0	2	32	166	396	167
	%	**%**	**%**	**%**	**%**	**%**
Event Rates	0	0.2	3.7	19.7	58.7	60.7
	N(%)	**N(%)**	**N(%)**	**N(%)**	**N(%)**	**N(%)**
General health condition						
Good	886(96.9)	855(96.5)	855(97.6)	822(97.5)	654(96.9)	261(94.9)
Poor	28(3.1)	31(3.5)	21(2.4)	21(2.5)	21(3.1)	14(5.1)
Weight status						
Underweight	100(10.9)	95(10.7)	90(10.3)	110(13.0)	79(11.7)	32(11.6)
Normal	681(74.5)	670(75.6)	694(79.2)	663(78.6)	552(81.8)	225(81.8)
Overweight	77(8.4)	72(8.1)	53(6.1)	43(5.1)	20(3.0)	8(2.9)
Obese	56(6.1)	49(5.5)	39(4.5)	27(3.2)	24(3.6)	10(3.6)
Sleep duration						
Short	171(18.7)	256(28.9)	408(46.6)	475(56.3)	499(73.9)	253(92.0)
Adequate	732(80.1)	623(70.3)	457(52.2)	364(43.2)	167(24.7)	22(8.0)
Long	11(1.2)	7(8)	11(1.3)	4(0.5)	9(1.3)	0(0.0)
Annual income						
Low	308(33.7)	248(28.0)	233(26.6)	208(24.7)	139(20.6)	49(17.8)
Middle	576(63.0)	612(69.1)	608(69.4)	600(71.2)	503(74.5)	206(74.9)
High	30(3.3)	26(2.9)	35(4.0)	35(4.2)	33(4.9)	20(7.3)

Table 2. The at menarche of Korean Youth and Child Panel Study 2010 of Elementary 1st grader panel

	Age at menarche (years old)				
	10-11	11-12	12-13	13-14	Not Yet
	N	**N**	**N**	**N**	**N**
Count	43	185	430	186	118

4.2. Gompertz regression of discrete time-to-event data.

Table 3 depicts the results of the Gompertz regression of discrete time-to-event data. Exponentials of coefficients of the variables are considered as relative hazards of a unit change of the variable while other variables are fixed. For example, the advancement of a 1-time interval, which in this case is a year, increases the conditional probability of the individual experiencing menarche in the present time interval 2.84 times, given that the individual did not experience menarche up to this point.

Based on the statistically significant coefficients of our model, being overweight or sleeping less than recommended duration is related to the increase of hazard of menarche compared to being normal weight and sleeping 9 to 11 hours by 1.63 times and 1.38 times, respectively, while other variables are fixed. On the other hand, the hazard decreases by 66 percent by being underweight.

Table 3. Gompertz Regression Analysis: Effects of weight status and sleep duration on hazards of menarche

Exposure	Number of Events[a]	Exponential of estimated coefficients[b]	Standard Error	95% Confidence Interval	P-value
Exit[c]		2.84	0.04	2.60 - 3.09	0.00
General health condition					
Good	746	1.00			
Poor	17	0.70	0.32	0.37 –1.31	0.26
Weight status					
Underweight	38	0.34	0.20	0.23 – 0.51	0.00
Normal	657	1.00			
Overweight	41	1.63	0.23	1.03 – 2.57	0.04
Obese	27	0.90	0.29	0.50 – 1.60	0.72
Sleep duration					
Short	593	1.38	0.11	1.11 – 1.72	0.00
Adequate	164	1.00			
Long	6	1.54	0.49	0.59 – 4.03	0.38
Annual income					
Low	172	0.98	0.18	0.69 – 1.39	0.91
Middle	553	0.84	0,16	0.62-1.14	0.26
High	38	1.00			

[a]Represents the number of individuals that have gone through event transition (menarche) with given exposure at the time interval of transition.

[b] Exponential of estimated coefficient of the Gompertz regression model represents the relative hazard by the unit increase of the exposure or compared to the reference group.

[c] Represents the amount of hazard increases as individuals reach the next time interval.

Chapter 5. Discussion and conclusion

5.1. Discussion

This study suggests that being overweight or sleeping less than 9 hours per day was related to the increase in the hazard of menarche. In comparison, being underweight decreased the hazard.

This study agrees with previous studies about the relationship between age at menarche and body weight. (Juul F et al., 2017) However, many previous studies used BMI at fixed age intervals to study its effect on AAM. Behie & O'Donnell reported that a higher BMI at age 8-9 increases the chance of earlier menarche. (Behie AM & O'Donnell MH., 2015) Kelly et al. reported BMI at seven years increases the odds ratio of menarche before reaching 11 years. (Kelly Y et al., 2016) By employing discrete-time survival analysis, I could evaluate the impact of BMI on age at menarche, considering the time-varying nature of variables collected from growing and developing children.

The above studies included BMI as a continuous variable in their model. Yet, it is recommended to use weight status based on BMI-for-age percentile instead because children are growing and developing. Seo MY et al. reported the trends in the prevalence of early menarche stratified by body mass index status of Korean girls. (Seo MY, et al., 2020) The prevalence of early menarche was higher for the overweight and obese group compared to the normal and the underweight group. In some years, the prevalence of early menarche was higher in the overweight group compared to the obese group. This result suggests that the risk of menarche may not increase linearly as BMI increases. (Seo MY, et al., 2020)

Several studies reported a relationship between sleep duration and menarche. Carr R et al., evaluated 44 children with treatment-resistant circadian rhythm sleep disorders and said five children with sleeping disorders developed precocious puberty. Implying that shorter sleep duration may trigger or accelerate menarche, as shown in the current study. (Carr R, et al., 2007) Ku et al. surveyed 411 North Korean refugees and reported that sleep duration was negatively correlated with age at menarche. This result conflicts with our result. However, Ku et al. used a cross-sectional design, and the average age of participants was 31.3 years old. Therefore, they had to assume a consistent lifestyle to infer the impact of sleep duration on AAM. Disruption of temporality might have resulted in different outcomes. (Ku SY et al., 2006) Considering this finding, it would be possible to devise an intervention to induce better sleep hygiene and environment that can allow an overall increase in sleep duration to promote the health of the general student population.

The current result meets biological plausibility criteria. Excess adiposity or overweight status may accelerate pubertal changes through several mechanisms. (Juul F et al., 2017) Adipose tissue produces various adipocytokines that may affect pubertal timing. (Biro FM et al., 2012) Leptin secretion due to energy sufficiency is also suggested to accelerate the process. (Sanchez-Garrido MA & Tena-Sempere M., 2012) The aromatase activity of fat tissue may also induce peripheral conversion of androgens to estrogen. (de Ridder CM, et al., 1990) There is still a lot to understand about the relationship between sleep duration, hormone secretion, and precocious puberty. The timing and duration of sleep can induce or interrupt hormone secretions which may affect the timing of pubertal changes. Hormone secretion with sleep during puberty has been suggested as an essential biological index. Sleep is an important mediator of gonadotropin-releasing hormone (GnRH) secretion, and augmented luteinizing hormone(LH) secretion is proposed to be synchronized with sleep cycles. (Boyar R, et al., 1972) Melatonin plasma levels decrease may also affect puberty onset in children. It is suggested that a physiological decrease in melatonin plasma level induces the activation of the hypothalamus-pituitary-gland axis. (Brezezinski A., 1997)

5.2. Limitations

The study has some limitations, as follows. The measurement of the event in this survival analysis was based on self-report, which can result in recall bias. (Must A, et al., 2002) R Cooper et al., evaluated the validity of age at menarche self-reported in middle age compared with that recorded in adolescence and showed moderate agreement. (kappa=0.35, r=0.55)

Other known risk factors suggested being associated with early menarches, such as lower birth weight, weight gain in infancy and childhood, or adherence to a high intake of animal proteins and iron. We did not consider these variables in our analysis because variables were not included in the 2010 KCYPS data.

The potential misclassification of self-reported exposures is a study limitation. Since our study is based on a 7-year follow-up of elementary first-grade students, the accuracy of the answers given by students can be questioned. Due to the young age of the study population, for some variables, answers were asked of the parents instead of students. For example, weight and height data were collected from parents before students reached 4th grade. The potential bias in the data collection step can be a threat due to this heterogeneity.

The study size of our study is not very large. This small size resulted in some categorical variables with relatively small sizes, which deteriorated the quality of estimates coefficients. Especially the proportion of students with long sleep duration was tiny.

The current study has some strengths, as follows. The current study uses the answer from the seventh year of follow-up to measure the age at menarche. We can anticipate better validity due to the shorter timespan between the actual event and recall time.

The temporal relationship between the exposures and the outcome of interest is well established due to the usage of multiple-point prospective data. Using longitudinal data collected every year starting when no one experienced menarche, we can guarantee that exposures preceded the outcome of interest.

Previous studies exploring possible risk factors of early menarche commonly employed logistic regression. To do so, they had to come up with reference values to define normal menarche operationally and define exposures as time-fixed variables of a particular critical timing or change of those variables in designated time intervals. Considering the controversies around the reference values of normal age at menarche, this can result in heterogeneous analyses. Compared to logistic regression, discrete survival analysis using menarche as an event has strength in investigating the effect of time-varying exposures across time intervals without coming up with different age criteria for normal age at menarche.

5.3. Conclusion

This study shows overweight status or sleeping less than 9 hours per day is related to the increase in the hazard of menarche while being underweight reduces it. Our study is the first to analyze their effect on the hazard of menarche in a single-panel study representing the nationwide Korean population.

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국문 초록

한국 여학생의 조기 초경 위험 요인에 대한 이산 시간 생존 분석

연구목적 : 한국 여학생들을 대상으로 하는 중다전망적 패널 자료를 기반으로 체중 상태와 수면 지속 시간이 초경의 위험에 미치는 영향을 분석한다.

방법론 : 본 연구는 2010 한국 아동 청소년 패널 조사를 통해 수집된 2010년 당시 초등학교 1학년 생이었던 914명을 대상으로 비연속시간 생존분석을 수행하였다. 연령과 성별을 보정한 체질량지수(BMI) 기반의 체중 상태와 수면시간이 초등학생들의 초경 위험(Hazard) 혹은 해당 관찰 구간에 초경이 발생할 조건부 확률에 어떠한 영향을 미치는지를 분석하기 위해 주관적인 전반적 건강상태와 연간 가계소득을 보정한 곰페르츠 회귀 (Gompertz Regression) 분석을 수행하였다.

결과: 2010 한국 아동청소년 패널조사 참여자의 초경 연령을 결과 변수로 수행한 곰페르츠 회귀 분석은 과체중 상태에 있거나 권고되는 시간보다 적게 수면하는 경우 보통 체중이거나 권고되는 시간만큼 수면하는 학생들에 비해 각각 초경의 위험이 1.63배 그리고 1.38배 증가하는 것으로 나타났다. 반면에, 저체중 상태에 있는 경우에는 초경 위험이 보통 체중인 경우에 비해 0.34배 였다.

결론: 체질량 지수의 백분위수에 따른 체중 상태와 수면 지속 시간은 초등학생들의 초경 위험을증가시킨다.

Keywords: Menarche, Survival Analysis, Obesity, Adolescent