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Original article

Determination of Relative Timing of Pubertal Maturation through Ordinal Logistic Modeling: Evaluation of Growth and Timing Parameters

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Abstract

Purpose: (1) To propose a new method using statistical modeling to determine relative timing of pubertal maturation; (2) to validate the new method by evaluating its relationship with pubertal growth and timing parameters, including age at menarche, age onset of areolar maturation, age of peak height velocity, age at attainment of adult height, adult height, peak height velocity, body mass index, and percent body fat; and (3) to contrast the new method with relative timing of menarche on these pubertal parameters.

Background: The timing of puberty has a well-known impact on anthropometric and psychosocial outcomes. Multiple methods have been used to determine pubertal timing, but all with limitations. A uniformly applicable method is needed for different study designs and study populations.

Methods: Using the National Heart Lung and Blood Institute Growth and Health Study data, an ordinal logistic modeling was used to assess relative timing of pubertal maturation.

Results: The proposed method demonstrated good reliability and strong associations with all pubertal timing parameters, also body mass index and percent body fat. Timing was not significantly associated with adult height and peak height velocity.

Conclusions: The proposed method is highly feasible, easy to implement, and valid. The study demonstrated important differences between the relationships of relative timing of secondary sexual characteristics and the timing of menarche on pubertal parameters. The study also demonstrates that individuals with early or late timing at one point of time are likely to maintain the same relative timing throughout puberty.

Keywords: Timing of puberty; Ordinal logistic regression; Statistical modeling; Validation; Generalize estimating equation (GEE)

The pubertal maturation process represents a critical biological and psychological period of the life span. The timing of pubertal maturation has potentially profound implications for multiple health outcomes, including anthropometric and psychosocial parameters [1–4]. Accelerated physical growth, appearance of secondary sexual characteristics, and memorable events such as initiation of menarche or spermarche mark the critical events throughout pubertal maturation. Thus, age at peak height velocity, age at onset of secondary sexual characteristics, and age at menarche or spermarche are often used for determining timing of pubertal maturation. To reliably capture age at peak height velocity or age at onset of secondary sexual characteristics, longitudinal follow-up at least yearly, and preferably every 6 months is required. Age at menarche or spermarche occurred relatively later, and may not be accurately reported because of recall bias [5,6]. A longitudinal study design is often not feasible because of the costs and logistical difficulties, and age at menarche or spermarche is available only for adolescents who had been far enough along in their pubertal development to experience initiation of menarche or spermarche, alternative approaches to the determination of timing of puberty are needed.

Perceived relative timing refers to the relative advance or delay of pubertal development for an adolescent with respect to their gender and age-matched peers. It has been reported typically through responses by parents or adolescents to

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questions in standard formats, such as those in the Pubertal Development Scale (PDS) questionnaire [7]. The PDS is a subjective measure, being influenced by psychosocial characteristics of the individual such as their social norm, self-esteem, and body image. A more objective approach has been utilizing statistical modeling for determining the relative timing of puberty [8,9].

Marshal and Tanner introduced a system of staging pubertal maturation on a 1–5 scale, ranging from ''prepubertal'' to ''mature stage,'' based on the appearance of secondary sexual characteristics. Currently, Tanner maturation stage has been widely utilized in research and clinical studies. Tanner maturation stage assessed by a trained clinician is considered ''gold standard'' [10], and a reliable measure [11,12]. Recently, new approaches have been proposed, including Garn and Falkner [13] areola staging to better determine breast development independently from adiposity, and testicular volume to better determine genital development [14].

By regressing pubertal maturational stage on chronological age within a homogeneous population (same gender and race/ethnicity), statistical modeling provides estimation of the expected mean pubertal maturational stage as a function of age. The regression residuals correspond to the deviation of an adolescent's maturation stage from the expected population mean maturational stage, thus providing relative advance or delay of the adolescent compared to the gender–age-matched peers. Determination of relative timing of pubertal maturation via statistical modeling has many advantages: it is easy to obtain, does not require longitudinal study designs, and is applicable to both genders across all stages of puberty. Currently, linear regression modeling has been used [8,9], but with limitations. First, the linear regression analysis assumes a linear relationship between the chronological age and maturation stage, whereas biologically, a nonlinear S-shape relationship is expected when the maturation stage plateaus at both younger and older ends of age spectrum. Second, it assumes a normal distribution, which may not be reasonable for the ordinal scaled maturation stage. Further, no study has been done to evaluate the validity of the statistical modeling approach for determination of relative timing of puberty.

Ordinal logistic regression is a less commonly used statistical modeling technique than linear regression. It is a specific modeling technique for an ordinal type of outcome, such as pubertal maturation stage. Just like the commonly used binary logistic regression, ordinal logistic regression models the log-odds of cumulative probabilities of the ordinal outcome as a linear regression function of the predictive variables. Mathematically, if a continuous outcome is classified into multiple ordered categories, ordinal logistic regression modeling could obtain unbiased beta estimates as if fitting a linear regression model to a continuous outcome. The ordinal logistic regression maintains an ordinal nature of the outcome, provides estimation of the expected probabilities for each of the ordered categories, and further calculates the mean score of the expected outcome, for a given set of predictive variables.

The literature provides ample evidence that timing of puberty is related to body fat [15]. A recent genetic study suggested that the same gene that regulates pubertal growth may also explain body fat attainment [16]. However, it is less clear whether timing of puberty is related to adult height and peak height velocity. Although some studies noted the relationship between timing of puberty and adult status [17–19], others reported no association [20,21]. Such inconsistency may be due to the different measures used for pubertal timing.

Increasingly, the literature suggest that onset of menarche and onset of puberty may represent distinct biological phenomena [2,22]. Onset of puberty may be driven by an heritable trait such as genetic influence, whereas the onset of menarche is influenced by multiple factors including genes, nutrition factors, and environmental exposure [23]. As suggested by the February 2008 special issue of *Pediatrics* (Vol. 121, Suppl. 3), reanalyzing the same existing study data using different indexes of pubertal timing should help shed light on various issues concerning pubertal development.

We propose that ordinal logistic modeling could be used to provide a valid approach to determination of the relative timing of puberty. To illustrate this new approach, we analyzed the National Heart Lung and Blood Institute Growth and Health Study (NGHS), a large multisite longitudinal study that followed a group of 9- and 10-year-old black and white girls for 10 years annually. We choose to analyze the NGHS study because it provides rich growth and pubertal timing related data, including age at menarche, body mass index (BMI), and percent body fat, and allows for evaluation of age at peak height velocity, age at attainment of full adult height, and final adult height. This is also a reanalysis of a published study by Biro et al [2], using the same dataset and variables. Unlike the previous study, which utilized age at menarche as the pubertal timing measure, this study used the relative time of puberty as determined by ordinal logistic regression modeling. As in the previous study, the analyses were done separately for black and white girls, because of the well-known racial differences in pubertal maturation [2,11].

The specific aims of this study are:

1. to illustrate that ordinal logistic modeling can be used to determine relative timing of pubertal maturation by conducting secondary data analyses using the NGHS study;
2. to validate the newly proposed approach to the determination of relative timing of pubertal maturation by evaluating its relationship with pubertal growth and timing parameters: age at menarche, age at appearance of areolar stage 2, age of peak height velocity, age at attainment of adult height, adult height, peak height velocity, BMI, and percent body fat;
3. to contrast the two pubertal timing parameters, relative timing of breast development versus relative timing of menarche, by comparing the results from this study with the results from the Biro et al [2] study.