Annals of Epidemiology 24 (2014) 122–126

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

Uterine leiomyomata and cesarean birth risk: a prospective cohort with standardized imaging

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ARTICLE INFO

Article history:
Received 23 July 2013
Accepted 30 October 2013
Available online 12 November 2013

Keywords:
Leiomyoma
Cesarean section
Epidemiology
Prospective studies

ABSTRACT

Purpose: To determine if women with leiomyomata detected using uniform ultrasound methods are at increased risk of cesarean birth, without regard to indication.
Methods: Women were enrolled in *Right from the Start* (2000–2010), a prospective pregnancy cohort. Leiomyomata were counted, categorized, and measured during first trimester ultrasounds. Women provided information about demographics and reproductive history during first trimester interviews. Route of delivery was extracted from medical records or vital records, if the former were unavailable. Generalized estimating equations were used to calculate risk ratios (RR) and 95% confidence intervals (CIs) for the risk of cesarean birth by leiomyoma presence and characteristics.
Results: Among 2635 women, the prevalences of leiomyomata and cesarean birth were 11.2% and 29.8%, respectively. Women with leiomyomata, compared with those without, had a 27% increase in cesarean risk (RR, 1.27; CI, 1.17–1.37). The association was weaker following adjustment for maternal body mass index and age (adjusted risk ratio [ARR], 1.11; CI, 1.02–1.20). The adjusted risk was elevated for women with a single leiomyoma 3 cm or more in diameter (ARR, 1.22; CI, 1.14–1.32) and women with the largest total leiomyoma volumes (ARR, 1.59; CI, 1.44–1.76).
Conclusions: Women with leiomyomata were at increased risk for cesarean birth particularly, those with larger tumor volumes.

Introduction

During pregnancy, approximately 11% of women have leiomyomata detectable via ultrasound [1]. Black women are disproportionately affected, with a prevalence of 18%, compared with 8% in white women [1]. Estimates of prevalence and risks of pregnancy outcomes vary across studies due to differences in criteria used to define leiomyomata and underlying population characteristics [2–7]. Presence of leiomyomata has been associated with increased risk of cesarean birth [2–7].

Studies retrospectively identifying women with leiomyomata via routine clinical ultrasounds report adjusted odds ratios for cesarean birth ranging from 1.2 to 2.1 [3–5]. Those relying on hospital birth records (i.e., billing codes) to identify these women suggest a six-fold increase in cesarean risk [6,7]. Many studies are biased to detect large or clinically concerning leiomyomata by ascertaining the presence of leiomyomata with medical record coding or at the time of cesarean, potentially inflating effect estimates. Inclusion criteria and adjustment for potential confounders also differ between studies, making comparisons of risk estimates difficult.

Leiomyoma presence may influence route of birth via complications that occur before the onset of labor (placenta previa and malpresentation) or after the onset of labor (dysfunctional labor and obstruction). Each of these indications has been hypothesized to be in the causal pathway between leiomyomata and cesarean birth. However, the research question of most direct relevance to clinical care is: Are leiomyomata, associated with an overall increased risk of cesarean birth? This is of special interest as average maternal age rises and clinicians speculate about the contribution of increasing age and greater likelihood of leiomyomata

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1047-2797/$ – see front matter
http://dx.doi.org/10.1016/j.annepidem.2013.10.017

as a potential contributor to the rising use of cesarean. Currently, leiomyomata during pregnancy are monitored by "expectant management;" there are no practice recommendations for selecting the route of delivery due to their presence.

Clinical instinct produces both the view that leiomyomata are deleterious during pregnancy and a need to parse out any causal pathways leading to cesarean birth. However, risks for cesarean indicators due to leiomyomata presence are generally small and do not suggest intervening action; once placenta previa or breech presentation occurs, management options for leiomyomata are fixed. Treatment or removal of leiomyomata is actionable between pregnancies. Therefore, in general populations of women planning pregnancies, the magnitude of the overall risk of cesarean birth is most informative (inclusive of risk due to complications and patient/clinician preferences). The overall risk is currently the best estimate of the projected maximal reduction of cesarean risk that could be achieved by intervening on leiomyomata. An analysis that excludes or adjusts for casually related indications, such as breech presentation, will underestimate the net effect of leiomyomata. Therefore, to address biases in prior studies and understand the overall influence of leiomyomata on cesarean risk, we sought to determine if leiomyomata increase risk of cesarean birth, without regard to indication, among women with leiomyomata detected using uniform research ultrasound imaging methods in a prospective community-based pregnancy cohort.

Methods

Study population

Right from the Start (RFTS) is a community-recruited, prospective cohort study [8]. Between 2000–2011, the study enrolled women from locations in North Carolina, Texas, Tennessee who were newly pregnant or trying to become pregnant. To be eligible for the study, women were aged at least 18 years, less than 13 weeks pregnant, spoke English or Spanish, planned to carry to term, and did not use assisted reproductive technologies [8].

Women whose information contributed to this analysis were enrolled between December 2000 and June 2010. Women may enroll more than once in RFTS, but only information from the first study pregnancy for each woman was used. During this time, there were 3196 different women who had pregnancies resulting in a live birth after 20 weeks of gestation with documentation of route of delivery. Exclusion criteria for this analysis included multiple gestations ($n = 31$), incomplete first trimester computer-assisted telephone interviews ($n = 90$), and no study ultrasound ($n = 76$). The resulting population of 2999 women had uniform assessment for leiomyomata and was at risk for cesarean birth. Only women identified as non-Hispanic white or non-Hispanic black were included in our final investigation ($n = 2635$). Other racial groups were excluded due to small sample sizes ($n = 364$). The Institutional Review Board of Vanderbilt University approved this study and all participants gave informed consent.

Variable definitions

Route of delivery was obtained from medical and vital records. Our outcome was a dichotomous variable: women having a primary or repeat abdominal surgical delivery were considered to have a "cesarean birth," whereas all vaginal births, with or without forceps or vacuum assistance, were "vaginal" or "non-cesarean births." Information regarding whether a cesarean was planned or performed as an emergency was not available.

To determine the presence or absence of leiomyomata, all women underwent a transvaginal ultrasound in the first trimester. The position, type, and size of each leiomyoma were documented by experienced, research trained, pelvic sonographers and confirmed by a study physician using methods that have been described [1]. RFTS includes leiomyomata as small as 0.5 cm in maximum diameter in their counts [1]. Leiomyoma volume (in cm^3) was calculated from three diameter measures using the formula for an ellipsoid. In our primary analysis, leiomyoma presence was dichotomous. Women in whom no leiomyomata were detected were classified as "without leiomyomata" and those with one or more were classified as "with leiomyomata."

Women join RFTS for many reasons, but recruitment was not targeted toward women with specific concerns about leiomyomata or pregnancy health nor is RFTS advertised as a study of leiomyomata. Participation does not influence clinical care. As a courtesy, ultrasound results are sent to the practice or clinic indicated by each participant. In these materials, the sonographer indicated whether she suspected the presence of a leiomyoma, but the classification, measurements, and diagrams collected by RFTS are not released and the sonographers do not discuss findings with participants.

Women self-reported age (quartiles: <26 [reference], ≥ 26 and <29, ≥ 29 and <32, and ≥ 32 years), race/ethnicity (non-Hispanic white, non-Hispanic black), parity (nulliparous, 1, or 2+), date of last menstrual period (LMP), household income ($\leq$\$40,000, \$40,000–80,000, and $>$\$80,000), and education level ($\leq$high school, some college, and $\geq$4 years of college) during computer-assisted telephone interviews. Race/ethnicity was obtained from vital records if not available from these interviews ($n = 3$). The state (study site) in which a woman received prenatal care was also documented (North Carolina, Texas, Tennessee). Gestational age at birth was determined as follows: from self-reported LMP if pregnancy dating conducted at the first trimester ultrasound was within $\pm$7 days of the self-reported LMP and from ultrasound estimates if gestational age by ultrasound differed by more than 7 days from the self-reported LMP or if self-reported information was missing ($n = 348$ and $n = 7$, respectively). A body mass index (BMI) for each woman was calculated from standardized measures of height and weight obtained at the ultrasound examination or from the first trimester interviews. BMI was classified according to World Health Organization and Institute of Medicine guidelines: underweight (BMI < 18.5), normal weight ($\geq$18.5 and $<$25.0 [reference]), overweight ($\geq$25.0 and $<$30.0), or obese ($\geq$30.0) [9].

Statistical analysis

Descriptive summary data of maternal characteristics and all statistical analyses were generated with Stata/SE 12.0 (StataCorp, College Station, TX). Maternal characteristics were compared between women with and without leiomyomata; Pearson χ^2 test was used for categorical factors and the Wilcoxon rank sum test was used for continuous measures (alpha $= 0.05$). Among women with leiomyomata, tumor characteristics were compared by mode of delivery, using similar tests.

For both unadjusted and adjusted analyses, generalized estimating equations (GEE) were used to calculate risk ratios (RRs) and 95% confidence intervals (CIs) for cesarean birth risk by leiomyoma presence or characteristics (log link function, binomial family). This method was used to control for correlation within the three study sites; we presumed an independent correlation structure. *A priori*, we considered maternal age, race, BMI, and parity to be candidate confounders. A confounder was retained for inclusion in the final model if an adjusted estimate for leiomyoma presence was more than 10% different from the unadjusted estimate. The final GEE models were adjusted for maternal BMI and age, with study site included as a grouping variable. Prior cesarean birth was considered to be an intermediate variable in a noncausal pathway between