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Effects of Pregnancy on Otosclerosis

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Abstract

Objective.—The effect of pregnancy on otosclerosis is controversial. If pregnancy physiologically increases the risk of progression, females with children would be expected to receive stapedectomy earlier than childless females and males. Here, we seek to determine whether sex moderates the relationship between number of children and age at stapedectomy.

Study Design.—Retrospective observational study of national health care claims.

Setting.—2003 to 2016 Optum Clinformatics Data Mart.

Subjects and Methods.—In total, 6025 privately insured US adults (3553 females, 2472 males) who received stapedectomy for otosclerosis were queried for age and number of children at the time of initial surgery.

Results.—The average age at stapedectomy was significantly lower in females than males (46.8 vs 48.1 years; *t* test, $P < .0001$). Females with children had a significantly lower age at surgery compared to childless females (39.3 vs 49.9 years; *t* test, $P < .0001$). Males with children similarly had a significantly lower age at surgery compared to childless males (40.5 vs 51.3 years; *t* test, $P < .0001$). A higher number of children was correlated with lower age for both females (Pearson, $r = -0.3817$, $P < .0001$) and males (Pearson, $r = -0.3675$, $P < .0001$). Linear regression showed that younger age of surgery could be predicted by female sex and number of children ($F(3, 6021) = 336.93$, $P < .001$, $R^2 = 0.1437$) with no significant interaction between sex and number of children ($P = .186$).

Conclusion.—Sex does not moderate the effect of increasing number of children on decreasing age at stapedectomy. Social, rather than biological, factors surrounding parenthood such as

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Author Contributions

Z. Jason Qian, acquisition, analysis, and interpretation of data; drafting of the manuscript; final approval of work; agreement to be accountable for work; Jennifer C. Alyono, conception and design of study; analysis and interpretation of data; critical revision of manuscript; final approval of work; agreement to be accountable for work.

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Supplemental Material

Additional supporting information is available in the online version of the article.

increased overall health care utilization may explain prior associations between pregnancy and otosclerosis.

Keywords

otosclerosis; pregnancy; stapedectomy; claims data

The association between otosclerosis and pregnancy is controversial. Soon after otosclerosis was initially described in 1893, demographic studies revealed its hereditary nature and preponderance for affecting females.[1,2] In the subsequent decades, both European and American physicians described using abortion and sterilization as treatment options, as it was thought that pregnancy was associated with otosclerosis progression.[3–5] With the development of modern surgical techniques, such reproductive-related approaches became obsolete. Yet the effects of pregnancy on otosclerosis remain unclear.

If pregnancy physiologically increases the risk of otosclerosis progression, one might hypothesize that sex should moderate whether having children affects how soon patients experience significant hearing loss and consequently undergo stapedectomy. Accordingly, females with children would be expected to undergo surgery earlier than childless females and males. In addition, males with children would not be expected to have surgery earlier than childless males. In this study, we seek to determine whether sex moderates the relationship between number of children and age at initial stapedectomy using a large, nationally representative insurance claims database.

Methods

A retrospective analysis of insurance claims data documented by the Optum Clinformatics Data Mart (Eden Prairie, Minnesota) from December 31, 2002, to November 30, 2017, was performed. This source includes deidentified administrative claims for over 12 million privately insured patients annually in the United States. The patient population of the database is nationally representative with respect to sex, age, and geographic distribution.[6] These data include diagnoses identified by using *International Classification of Disease, Ninth and Tenth Revisions, Clinical Modification* (*ICD-9-CM* and *ICD-10-CM*) codes; procedures identified by *Current Procedural Terminology, Fourth Edition* (*CPT-4*) codes; and demographic information, such as age, sex, and number of dependent children. This study used deidentified claims data and was exempt from review by the Institutional Review Board of Stanford University.

All patients diagnosed with otosclerosis who underwent stapedectomy were identified using appropriate *ICD* and *CPT* codes (see Supplemental Table S1 in the online version of the article). The first occurring instance of stapedectomy for otosclerosis was selected as the initial surgery date. Demographic factors including date of birth, sex, and the number of dependent children at the initial surgery date were recorded. The age at initial stapedectomy was calculated from the date of birth and surgery date. All patients younger than 26 years were excluded from the analysis, as this was the maximum age an individual could be considered a dependent under the Affordable Care Act passed in 2010.[7] Parallel analyses were conducted between females, where the number of dependent children was assumed to

equate to the number of pregnancies, and males, where the number of dependent children did not equate to the number of pregnancies. Patients with no dependent children were classified as being childless.

Statistical analysis was conducted using Stata 15 (Stata Statistical Software: Release 15; StataCorp LP, College Station, Texas). The age at initial stapedectomy and number of dependent children were compared using *t* tests and Pearson correlation coefficients (*r*). Regression analysis was used to assess how age of surgery is associated with sex and number of children. An interaction term between sex and number of children was included in the regression model. Regression results were reported as regression coefficients (β) and 95% confidence intervals (CIs). Statistical significance was determined at a threshold of $P = .05$.

Results

The Optum Clinformatics Data Mart identified 6025 adults age 26 years and older who underwent stapedectomy for otosclerosis. Females made up 59% of the sample. The majority of patients (n = 4486, 74.5%) did not have dependent children. Patients with dependent children (n = 1539, 25.5%) had 1 to 8 children. Table 1 details characteristics between sexes in terms of age at initial stapedectomy and number of dependent children.

Overall, the age at initial stapedectomy was significantly lower in females than males (46.8 ± 12.7 vs 48.1 ± 13.0 years; *t* test, $P < .0001$). Females with children had significantly lower age at surgery compared to childless females (39.3 ± 9.9 vs 49.9 ± 12.5 years; *t* test, $P < .0001$; Figure 1). Males with children similarly had significantly lower age at surgery compared to childless males (40.5 ± 10.1 vs 51.3 ± 12.8 years; *t* test, $P < .0001$; Figure 1). Pearson correlation showed a significant inverse relationship between age at surgery and number of children in both females ($r = −0.3817$, P ° .0001) and males ($r = –0.3675$, $P < .0001$).

A linear regression was calculated to predict age at initial stapedectomy based on sex and the number of dependent children. A significant regression equation was found ($F(3, 6021) = 336.93$, $P < .001$), with an $R^2 = 0.1437$. Lower age at surgery was predicted by female sex (β = –1.38; 95% CI,–2.07 to −0.70; $P < .001$) and number of children (β =−5.34; 95% CI, −1.38 to − 4.81; $P < .001$). An interaction term between sex and number of children was included in the linear regression and was not significant (β = −.047; 95% CI, −1.18 to 0.23; $P = .186$), suggesting that number of children affects both males and females similarly.

Discussion

The preponderance of otosclerosis to affect women during childbearing age has led to the hypothesis that endocrine factors may be involved in the etiopathogenesis. While estrogens have an established role in osteoblastic function, the role of osteoblasts in otosclerosis is unclear and no sex hormones have been directly implicated in otosclerosis.[8,9] Associations between pregnancy and otosclerosis progression rely on clinical observations. However, the existing body of work is limited by small cohorts and conflicting conclusions. Here, a unique study design was used to analyze data for a large, nationally representative cohort.

By using the number of dependent children as a proxy for pregnancies in women, a parallel analysis was able to be performed in men. In the current study, the number of dependent children was correlated with younger age of stapedectomy in both women and men, and a theory is offered to reconcile discordant results from prior studies.

Studies that used subjective measures of pregnancy-related hearing deterioration generally report a positive association. For example, Precechtěl[10] reviewed 100 pregnancies in women with otosclerosis and noted subjective aggravation of symptoms in over one-third of cases.[11] Similarly, Gristwood and Venables[12] reviewed 479 women with otosclerosis and reported that of the 309 patients with bilateral otosclerosis, 33% to 66% perceived deterioration of hearing during pregnancy. These studies relied on retrospective survey data, where patients are asked to recall hearing deterioration during pregnancies that may have occurred decades prior and thus may be subject to recall bias.

Vessey and Painter[13] analyzed referral rates for otosclerosis during pregnancy as a proxy for subjective impairment, the timing of which would be less subject to recall bias compared to surveys. The authors analyzed data from 31 women with otosclerosis out of 17,032 in the Oxford-Family Planning Association oral contraceptive pill (OCP) study. While OCP use was not associated with referral rates for otosclerosis, the authors did report a positive relationship between parity and referral rates.

The current study also used a proxy for when subjective severe disease is reached, namely, the timing of stapes surgery. The age at which the threshold for surgery was met was first calculated. Then, the effect of having children on the age of surgery was assessed. Consistent with prior studies, we found an association between younger age at initial stapedectomy and the number of dependent children in women. However, we also find this to be the case in men and to a similar degree, suggesting the historically observed effect may not be modulated by pregnancy physiology.

The relationship between subjective hearing impairment and objective hearing loss is not consistently reliable and is affected by demographic and psychosocial factors. Younger age and a higher burden of psychosocial stressors are correlated with an overestimation of hearing loss.[14,15] Considering that (1) otosclerosis tends to affect women of childbearing age, and (2) parenthood may be considered a psychosocial stressor, one could imagine how pregnancy might be associated with perceived hearing deterioration, even if none were present. When Gristwood and Venables[12] assessed stapes foot-plate pathology, no association with pregnancy was found despite a positive association between subjective hearing deterioration and pregnancy. This is consistent with the present findings, where earlier stapedectomy is associated with parenthood but perhaps not due to a physiologic basis.

Few studies have used objective measures of hearing loss. Podoshin et al[16] studied the association between OCPs and otosclerosis. The authors performed audiograms on 600 nulliparous women who used OCPs and identified 3 patients (0.5%) with conductive hearing loss consistent with clinical otosclerosis, but this prevalence rate was comparable to the incidence in the general population of the time. Most recently, Lippy et al[11] retrospectively

studied audiograms of 94 women with otosclerosis, half with children and half without, and found that having children had no adverse effect on audiometric measurements. As such, the authors concluded that pregnancy was unlikely to cause negative audiometric changes in women with otosclerosis.

The current study was the first to our knowledge to use men with otosclerosis as a control group. Inclusion of men allowed for differentiation between the psychosocial effects of parenthood from the physiological effects of pregnancy on the perceived disease burden in otosclerosis. This study design revealed that patients with children receive earlier surgery regardless of sex. This may be because parenthood is associated with higher health care utilization. For example, patients with an annual deductible may be more inclined to pursue elective stapes surgery after the deductible has already been met from perinatal or pediatric care. If pregnancy physiology was associated with significant worsening of symptoms, it would be expected that having children would cause women to have disproportionally earlier stapes surgery than men, which was not the case. This finding does not exclude the possibility that some women may indeed experience significant audiometric decline during pregnancy. These women may belong to a subset of otosclerosis that behaves in this manner, but the current data suggest that these cases are relatively rare since no effect was observed on a population level. In addition, given the overlap between the ages at which otosclerosis progression occurs and the ages at which women bear children, some women will inevitably experience hearing loss during pregnancy or nursing.

The main strength of this study is the large sample size and diverse patient characteristics. Using the Optum database allowed for analysis of a nationally representative sample of privately insured patients that was significantly larger than prior studies. Of note, this database does not include uninsured or socially insured patients. Therefore, the generalizability of the results may be limited if confounding factors related to insurance type exist. The major limitation of this study included the assumptions made to proxy clinical information with data captured by insurance claims. First, the number of dependent children is equated to number of pregnancies in females. Such an assumption does not account for adoption, the presence of older children who have aged out of their parents' insurance plans, or other causes of past pregnancies not resulting in dependent children on medical claims. Fortunately, such undercounting of children is likely to have affected both the male and female cohorts in this study. Second, while the age at initial stapedectomy was equated to severity of disease, it is likely that unmeasured extrinsic factors influence age of surgery. However, these effects should also affect male and female cohorts equally.

In conclusion, parenthood is associated with younger age at initial stapedectomy in patients with otosclerosis. However, this effect is seen independent of sex, affecting both males and females, suggesting that social factors surrounding parenthood, such as increased overall health care utilization rather than biological factors due to pregnancy, may be responsible. These findings support a theory for burden of disease in otosclerosis that reconciles prior conflicting results and may be useful in the counseling of otosclerotic patients considering pregnancy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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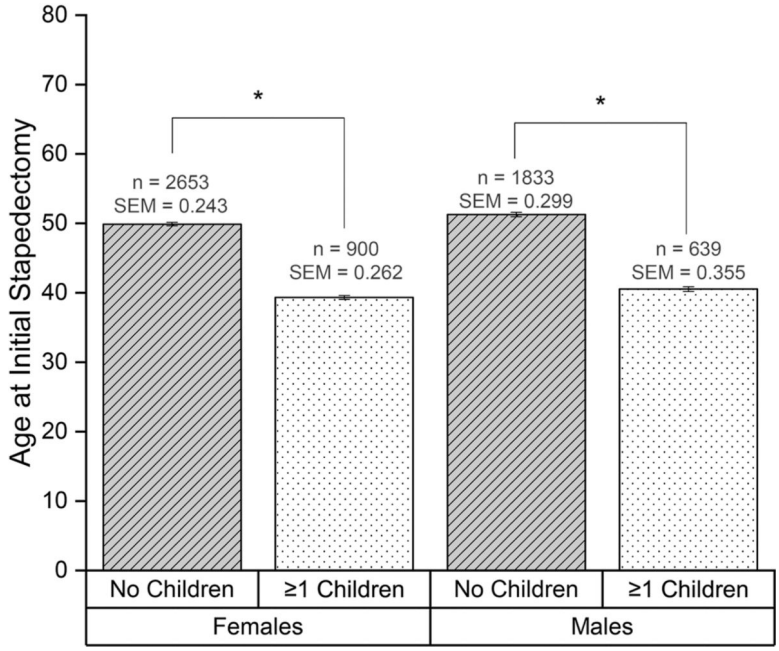

Figure 1.

Age at initial stapedectomy by sex and parenthood status. Error bars represent standard error of the mean (SEM). Asterisks indicate significance on *t* test at $P < .001$.

Table 1.

Characteristics of Individuals with Otosclerosis Who Received Stapedectomies.[a]

Characteristic	Overall, No.	Female, No.	Male, No.
Overall cohort, No. (%)	6025	3553 (58.97)	2472 (41.03)
Age at initial stapedectomy			
26–30	225	162	93
31–40	1183	742	441
41–50	1625	990	635
51–60	1309	769	640
61–70	674	361	313
−70	238	133	105
Number of children at initial stapedectomy			
0	4486	2653	1833
1	785	468	317
2	515	302	213
3	180	101	79
4	46	23	23
5–8	13	6	7

[a]Age at initial stapedectomy was calculated using the date of the first incidence of stapedectomy and date of birth.