African American Ethnicity as a Risk Factor for Respiratory Complications Following Adenotonsillectomy

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Objective: To evaluate whether African American ethnicity is a risk factor for major respiratory complications following adenotonsillectomy (T&A).

Design: Retrospective cohort study.

Setting: A Canadian tertiary care center.

Patients: Children aged 0 to 18 years who underwent T&A at our institution from 2002 to 2006 with planned or unplanned postoperative admissions.

Main Outcome Measures: We evaluated the association between ethnicity and our main outcome measure, major perioperative respiratory complications of T&A. Parental report of ethnicity was available for 23% of our cohort. At our institution, African American children undergo a routine preoperative sickle cell test (TestSC). Data on TestSC were included for all children. We established that having a TestSC was an accurate proxy for African American ethnicity (sensitivity, 96%; specificity, 93%; positive predictive value, 77%; negative predictive value, 99%).

Results: Seventy-four of 594 children experienced major respiratory complications (12.5%). Compared with children who did not have major respiratory complications, those who did had a TestSC ($P = .01$), were 2 years or younger ($P < .001$) and had lower weight-for-age $z$ scores ($P = .04$), moderate to severe obstructive sleep apnea ($P = .003$), and comorbidities ($P < .001$). When controlling for these variables in a multivariate analysis, children of African American ethnicity (TestSC used as a proxy) were at higher risk of having major perioperative respiratory complications (adjusted odds ratio, 1.82 [95% CI 1.05-3.14]) ($P = .003$).

Conclusions: Children of African American ethnicity (TestSC used as a proxy) are nearly twice as likely to experience major respiratory complications related to T&A. Ethnicity may be an additional independent risk factor for clinicians to consider when planning for T&A.

formed the basis of this study. The study was approved by the Montreal Children's Hospital (MCH) research ethics board. Data from the MCH Anesthesia Department, Sleep Laboratory, and administrative databases formed the basis of this study.

RESPIRATORY COMPLICATIONS

The MCH Anesthesia Department database, which was reported in a previous study, was the principal database for our study. A total of 594 children had complete perioperative data and met our inclusion criteria (aged 0 to 18 years; underwent T&A at our institution between 2002 and 2006; and were admitted to the hospital postoperatively for a minimum of 1 night). Perioperative respiratory complications were classified as major or minor based on whether they required intervention delivered by a physician or a nurse, respectively. Major interventions were defined as bag-mask ventilation, reintubation, and/or the administration of medication. Minor interventions were defined as supplemental oxygen therapy beyond the usual postoperative period, repositioning of patient for upper airway obstruction, and/or airway instrumentation with an oropharyngeal-nasopharyngeal airway.

The occurrence of a major respiratory complication was our primary outcome, given that these are well documented by hospital staff and of greatest clinical concern and risk to the patient. Secondary outcomes were all perioperative respiratory complications, independent of other known risk factors for surgical morbidity following T&A.

ETHNICITY

Given that our principal database does not contain information on patient ethnicity or race, we sought another available source for these data. The MCH Sleep Laboratory database contains demographic and clinical information on all children who underwent testing for sleep-disordered breathing from 2005 to 2009. Specifically, this database includes parental report of child's ethnicity. Parents are requested to complete a questionnaire as part of their child's clinical evaluation. Parents are asked to report their child's ethnicity by answering the following question: "Some breathing difficulties may occur more in certain cultures or racial groups. Please indicate which of the following best describes your child's origin: Caucasian, Black, Asian, Amerindian, Inuit, Latin American, Other." In addition to selecting 1 of the categories, parents are provided a blank space where they may provide additional details. In cases where parents provided written details only, the child's ethnicity was classified into the named categories. If written information and category selection conflicted, the written information was used for categorization of ethnicity. These ethnicity data were available for only a subset of children in our principal database (139 of 594 [23%]). We therefore considered an alternate source for ethnicity data.

METHODS

The study was approved by the Montreal Children's Hospital (MCH) research ethics board. Data from the MCH Anesthesia Department, Sleep Laboratory, and administrative databases formed the basis of this study.

SICKLE CELL TESTING AS A PROXY FOR AFRICAN AMERICAN ETHNICITY

We used preoperative sickle cell testing (TestSC) as a proxy for children's African American ethnicity following a preliminary statistical analysis that confirmed the validity of the use of this proxy. At our institution, all children who are at risk of sickle cell anemia are screened preoperatively using a serum hemoglobin electrophoresis test. We therefore decided to evaluate the accuracy of preoperative TestSC as a proxy for African American ethnicity. We conducted an extensive review of our hospital's administrative database, as well as patient medical records, to ascertain the status and timing of TestSC for all children in our principal database. Tests performed at any point prior to or on the day of T&A were considered preoperative. For those children with ethnicity data available (n=139), the relationship between parentally reported ethnicity and TestSC status was evaluated. Our analysis showed that the use of TestSC is an accurate proxy for African American ethnicity: TestSC had a sensitivity of 96%, a specificity of 93%, a positive predictive value of 77% and a negative predictive value of 99% (Table 1).

DEFINITION OF ADJUSTMENT VARIABLES

Our adjustment variables in the multivariate regression models were determined based on known risk factors for respiratory complications following T&A and the results of our between-group comparisons.

Moderate to Severe OSA

A subset of children had been assessed for suspected OSA prior to T&A. An objective diagnosis of OSA was made either by polysomnography or by at-home nocturnal pulse oximetry using the validated McGill Oximetry Score (MOS). Classification of OSA severity was based on our institutional diagnostic criteria; there is no consensus regarding the clinical classification of pediatric OSA severity. Our local practice defines moderate to severe OSA as an obstructive apnea-hypopnea index of 10 or more events per hour (evaluation by polysomnography) or a MOS of 2, 3, or 4 (evaluation by home nocturnal oximetry).

Obesity

Obesity was defined based on a BMI in the 95th percentile or higher and, if height data were not available, a weight-for-age profile in the 95th percentile or higher.

<table>
<thead>
<tr>
<th>TestSC Status</th>
<th>African Americans (n = 28)</th>
<th>Non–African Americans (n = 111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TestSC (n = 35)</td>
<td>27</td>
<td>8</td>
</tr>
<tr>
<td>No TestSC (n = 104)</td>
<td>1</td>
<td>103</td>
</tr>
</tbody>
</table>

Abbreviation: TestSC, sickle cell testing.

Table 1. Correspondence Between Preoperative TestSC and African American Ethnicity

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Comorbidities

Comorbidities, as determined by review of patient records, were categorized as asthma, neuromuscular disease, craniofacial conditions, cardiac abnormalities, Down syndrome, and other. Other comorbidities included pulmonary and airway abnormalities other than asthma, genetic/metabolic conditions, gastroesophageal reflux disease, global developmental delay, neurological disease, prematurity, hematologic abnormality, and unclassified.

STATISTICAL ANALYSIS

For the primary and secondary outcomes, we assessed differences between groups with t tests for continuous variables and \( \chi^2 \) tests for categorical variables. We performed a univariate analysis to test the association between TestSC (our proxy for African American ethnicity) and major perioperative respiratory complications. Multivariate logistic regression analysis was also performed, adjusting for known risk factors of respiratory complications of T&A (age \( \leq 2 \) years, weight-for-age \( z \) score, moderate to severe OSA, and comorbidities). For all analyses, statistical significance was set at \( P < .05 \). Version 17.0 of SPSS software (SPSS Inc) was used for database management and statistical analyses.

RESULTS

Our study population included 594 children who met our inclusion criteria.

MAJOR RESPIRATORY COMPLICATIONS

Seventy four children experienced 1 or more major perioperative respiratory complications (12.5%). Table 2 lists the demographic characteristics of our population and compares children with and without a major respiratory complication. Table 3 outlines the interventions provided by health care professionals in response to major respiratory complications. Compared with children who did not have major respiratory complications, children who experienced major respiratory complications were younger \( (P = .02) \) (specifically, age \( \leq 2 \) years \( P < .001 \)) and had a higher percentage of TestSC \( (P = .01) \), lower weight-for-age \( z \) scores \( (P = .04) \), and higher rates of moderate to severe OSA \( (P = .003) \) and comorbidities \( (P < .001) \). Comorbidities among the group who experienced major respiratory complications included asthma (14%), neuromuscular abnormalities (11%), craniofacial defects (3%), cardiac disease (1%), and other conditions (31%).

Univariate analysis showed that among children who had TestSC (our proxy for African American ethnicity), 19% experienced a major respiratory complication compared with 10% of children who did not have TestSC \( (P = .01) \). Thus, children with TestSC were nearly twice as likely to have major perioperative respiratory complications as those who did not have TestSC (odds ratio [OR], 1.96 [95% CI, 1.17-3.28]) \( (P = .01) \). Multivariate analyses included the following adjustment variables: patient age 2 years or younger, weight-for-age \( z \) score, moderate to severe OSA, and comorbidities. As expected, younger children, children with moderate to severe OSA, and children with comorbidities had higher rates of major respiratory complications \( (P < .001, P < .003, \) and \( P < .001, \) respectively). Of note, children with lower weight-for-age \( z \) scores had increased risk of complications \( (P = .04) \). The adjusted OR of having major perioperative respiratory complications if children underwent TestSC was 1.82 (95% CI, 1.05-3.14) \( (P = .003) \).

ALL (MINOR AND MAJOR) RESPIRATORY COMPLICATIONS

One hundred and seventy five (29.5%) children experienced a perioperative respiratory complication of T&A (both major and minor). Compared with those children who were without surgical morbidity, children who experienced perioperative respiratory complications were younger \( (P = .03) \) (specifically, age \( \leq 2 \) years \( P < .001 \)), male \( (P = .03) \), and had moderate to severe OSA \( (P < .001) \) and comorbidities \( (P = .005) \).

Our univariate analysis showed that children who underwent TestSC were about twice as likely to have perioperative respiratory complications as those who did not have TestSC (OR, 1.89 [95% CI, 1.28-2.80]) \( (P = .001) \). After adjusting for age 2 years or younger, weight-for-age \( z \) score, moderate to severe OSA, and comorbidities, the adjusted OR of having perioperative respiratory comp-

Table 2. Characteristics of the Study Population With and Without Major Respiratory Complications

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 594)</th>
<th>Major Resp Cx (n = 74)</th>
<th>No Major Resp Cx (n = 520)</th>
<th>P Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>TestSC performed</td>
<td>145 (24)</td>
<td>27 (37)</td>
<td>118 (23)</td>
<td>.01</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>4.0 (2.6)</td>
<td>3.3 (2.3)</td>
<td>4.1 (2.7)</td>
<td>.02</td>
</tr>
<tr>
<td>Age ( \leq 2 ) y</td>
<td>77 (13)</td>
<td>21 (27)</td>
<td>56 (11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>384 (65)</td>
<td>53 (72)</td>
<td>331 (64)</td>
<td>.18</td>
</tr>
<tr>
<td>Weight-for-age ( z ) score, mean (SD)</td>
<td>0.14 (1.5)</td>
<td>-0.21 (1.7)</td>
<td>0.19 (1.5)</td>
<td>.04</td>
</tr>
<tr>
<td>Obese</td>
<td>93 (16)</td>
<td>11 (15)</td>
<td>82 (16)</td>
<td>.84</td>
</tr>
<tr>
<td>Moderate to severe OSA</td>
<td>273 (46)</td>
<td>46 (62)</td>
<td>227 (44)</td>
<td>.003</td>
</tr>
<tr>
<td>Comorbidity present</td>
<td>155 (26)</td>
<td>34 (46)</td>
<td>121 (23)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: Major Resp Cx, major respiratory complications; OSA, obstructive sleep apnea; TestSC, sickle cell testing.
aUnless otherwise noted, data are reported as number (percentage) of patients.
bP values reported are for the comparison between the Major Resp Cx and No Major Resp Cx groups.
plications if children underwent TestSC was 1.70 (95% CI, 1.13-2.57) (P = .001).

COMMENT

To our knowledge, this is the first published study evaluating ethnicity as a risk factor for perioperative respiratory complications of T&A in children. We found that children who underwent TestSC (used as a proxy for African American ethnicity) were nearly twice as likely to experience major perioperative respiratory complications of T&A compared with children who did not undergo this hematologic testing. This relationship between African American ethnicity and major perioperative respiratory complications remained significant even after adjustment for known risk factors of complications (ie, young age, obesity, moderate to severe OSA, and other comorbidities).

A similar relationship was found between TestSC and all perioperative respiratory complications of T&A, both minor (nurse-led interventions) and major (physician-led interventions). The propensity for African American children to experience perioperative respiratory complications of T&A is likely multifactorial and may include biological/physiologic and environmental/socioeconomic factors.

AIRWAY MORPHOLOGIC CHARACTERISTICS

Using acoustic pharyngometry, Patel et al showed that the cross-sectional area of the airway of African American children tends to be smaller than that of white subjects. Also worth noting, among airway measures, minimal cross-sectional area best discriminated between children with and without OSA, and this airway characteristic was highly heritable between family members. Small airway dimensions may be a genetically transmitted morphologic characteristic that places African American children undergoing T&A at risk of adverse respiratory events.

INCREASED TENDENCY FOR CODEINE ULTRARAPID METABOLISM

Since in our study, the respiratory complications occurred most frequently on the inpatient ward (47%) and least often in the operating room (11%), oral codeine may have played a role in these adverse events. With the exception of only a few children, codeine was prescribed for pain postoperatively. In the general population, there exists a small subset of codeine ultrarapid metabolizers who, owing to a duplication of the CYP2D6 allele, will convert codeine to morphine in the liver at a significantly increased rate. Ultrarapid metabolism of codeine may lead to respiratory depression and was linked to the death of a young patient with OSA following T&A. The frequency of the ultrarapid metabolizer genotype varies among ethnic groups, and compared with northern Europeans (about 3%), it is found in increasing frequencies in the southern European (5%-10%) and Arab and northeast African populations (10%-30%). Current practice in our institution is that codeine is no longer given to T&A patients postoperatively, but the present study used data from procedures performed from 2002 to 2006 when this phenomenon was less well understood. It is thus plausible that some of the respiratory complications experienced by our patients may have been linked to the effects of codeine metabolites, and we would expect this occurrence to be more likely in our African American patients.

DECREASED LUNG FUNCTION, POSSIBLY RELATED TO LOW BIRTH WEIGHT

Studies report that African American children have decreased measures of pulmonary function compared with white children. Birth weight, which is lower in African American than white infants may explain, in part, the difference in lung function between these groups of children. In the present study, we did not include measures of pulmonary function, nor were we able to account for birth weight, so it is unknown to what degree these aspects of African American children’s physiologic characteristics and clinical history may have placed them at risk for respiratory complications following T&A.

ENVIRONMENTAL AND/OR SOCIOECONOMIC VARIABLES

In addition to biological considerations, social factors may underlie the increased susceptibility to respiratory complications in African American children undergoing T&A. Harik-Khan et al showed that decreased lung function in African American children compared with white children was associated with socioeconomic factors such as family head employment status, education, and sex; household size; and poverty index. Environmental factors, including in utero and household smoke exposure, contribute slightly to decreased lung function among African American children. Thus, not only could a number of potential biological/physiologic and environmental/socioeconomic factors be involved, but the unique interplay of these factors may add still another layer of complexity to determining the cause of increased perioperative respiratory complications of T&A in African American children.
LIMITATIONS

A limitation to our study was the use of TestSC as a proxy for ethnicity. However, given that parentally reported ethnicity data were available for a reasonable proportion of our study population (139 of 594 [23%]), we were able to confirm that indeed virtually all African American children (ie, 99%) received TestSC per our institution’s current practice guidelines. Among the 8 children who had TestSC but were classified as non–African American by parental report, 7 were determined to be of Arab, African, or Mediterranean origin based on more detailed chart review. Six of the 7 children underwent hemoglobin electrophoresis for evaluation of anemia and/or thalassemia. For the 1 patient who, by parental report, was classified as African American, it remains unclear after thorough chart review why sickle cell testing was not carried out preoperatively.

Also, not all children underwent testing for OSA; thus, it is not possible to say that untested children did or did not have OSA. Untested children and those with inconclusive oximetry test scores (ie, MOS of 1) were classified as not having moderate to severe OSA in our effort to control for the effect of moderate to severe OSA, which is a well-documented risk factor for respiratory complications of T&A.8 Of note, children who had TestSC (68%) underwent objective OSA testing at a similar rate as children who did not undergo TestSC (62%) (P = .13). Furthermore, although we controlled for OSA, which is associated with African American ethnicity,11–13 we did not control for socioeconomic factors (ie, measures of poverty), which have been associated with OSA diagnosis in children24 and may, in part, mediate the relationship between African American ethnicity and respiratory complications.

Our study population comprised children who had planned or unplanned admissions postoperatively and were therefore more likely to have comorbidities including moderate to severe OSA. This is reflected in both our patient characteristics (ie, 46% had moderate to severe OSA; 26% had comorbidities) and our high rate of major perioperative complications, which was nearly double the previously reported rate.8

Of particular note, our study population was drawn from children living within the city and surrounding areas of Montreal, a metropolitan region with socioeconomic and ethnic characteristics that may be different from other metropolitan regions in other countries, such as the United States. In addition, all Canadians have access to universal health care. These 2 factors (ie, population characteristics and health care systems) may limit the degree to which our results could be extrapolated to children living in other countries.

In summary, our study suggests that African American ethnicity may be a risk factor for increased perioperative respiratory complications in children undergoing T&A. Although we acknowledge that our findings should be confirmed in a prospective study, we believe that our results have important clinical implications. A determination of ethnicity could be considered a part of the preoperative assessment and planning of children undergoing T&A, not only to identify those children with sickle cell disease and related morbidity, but because African American ethnicity appears to constitute an independent risk factor for increased perioperative respiratory complications of this frequently performed childhood surgery. Future work should determine the biological/physiologic and environmental/socioeconomic factors that may place African American children at increased risk for serious surgical morbidity.

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Author Contributions: Ms Horwood and Dr Constantin had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Horwood, Nguyen, Brown, Paci, and Constantin. Acquisition of data: Horwood, Nguyen, Brown, Paci, and Constantin. Analysis and interpretation of data: Horwood, Nguyen, Brown, Paci, and Constantin. Drafting of the manuscript: Horwood, Brown, Paci, and Constantin. Critical revision of the manuscript for important intellectual content: Horwood, Nguyen, Brown, Paci, and Constantin. Administrative, technical, and material support: Constantin. Study supervision: Horwood, Nguyen, Brown, and Constantin.

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