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MAJOR ARTICLE

Evaluating the Diagnostic Paradigm for Group A and Non–Group A Streptococcal Pharyngitis in the College Student Population

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Background. Acute pharyngitis is a frequent illness presenting in outpatient settings. Antibiotics are only recommended for bacterial pharyngitis caused by group A β-hemolytic streptococci (GAS); however, infections with non–group A β-hemolytic streptococci (NGAS) have similar clinical presentations and are common in young adult populations. The objective of this study was to analyze the performance of a current (expert) diagnostic algorithm for GAS pharyngitis, the Centor score, and compare it to alternative models developed to predict GAS and NGAS in a college student population.

Methods. Electronic health records were obtained for all patients who received a streptococcal rapid antigen detection test (RADT) and/or a bacterial throat culture (n = 3963) at a southeastern US university in 2014. Bivariate and multivariable regression models (least absolute shrinkage and selection operator [LASSO] and stepwise-selected) were fitted to assess and compare their diagnostic performances for GAS-positive and NGAS-positive infections.

Results. Prevalence of GAS was 18.8%. In the subset of RADT-negative patients who received bacterial throat cultures (n = 313), growth of NGAS occurred in 34.8%, with group C streptococci the most frequent isolate. Mean Centor score was higher for NGAS (3.2) vs GAS (2.9) infections ($P = .0111$). The area under the curve (AUC) for GAS prediction was 0.64 using the Centor score and 0.70 using the LASSO model. For NGAS, the most important features were cough, pharyngeal erythema, tonsillar exudate, and gastrointestinal symptoms (AUC = 0.63).

Conclusions. GAS and NGAS pharyngitis were indistinguishable among college students in this study utilizing a commonly applied decision score. Alternative models using additional clinical criteria may be useful for supporting diagnosis of this common illness.

Keywords. clinical decision support systems; group A *Streptococcus*; non–group A *Streptococcus*; pharyngitis.

Acute pharyngitis ("sore throat") is a frequent illness that accounts for an estimated 4% of all primary care and emergency department visits annually in the United States (US) [1]. Although the majority of pharyngitis cases are attributed to a viral etiology (requiring no antimicrobial treatment), group A β-hemolytic *Streptococcus* (GAS) is responsible for approximately 5%–10% of these infections in adults and 15%–30% in children in whom antibiotic therapy is indicated [2]. Treatment of GAS pharyngitis with antibiotics is recommended to shorten symptom duration, reduce transmission, and prevent complications that are suppurative (eg, peritonsillar or retropharyngeal abscess, cervical lymphadenitis, mastoiditis) and nonsuppurative (eg, acute rheumatic fever) [3].

The clinical presentation of GAS pharyngitis often resembles other respiratory infections [4] and consequently, a clinical decision-making tool known as the Centor score was developed to help clinicians estimate the probability of GAS and judge whether to proceed with laboratory testing. The Centor score is a 4-point algorithm that predicts the likelihood of a GAS infection based on 4 symptoms: fever, absence of cough, cervical lymphadenopathy, and tonsillar exudate [5]. The American College of Physicians (ACP) recommends performing a streptococcal rapid antigen detection test (RADT) for individuals with Centor scores of 2–3 and empiric antibiotic treatment for individuals with Centor scores of 4 [4]. Among children, a modified version of the Centor score, the McIsaac score, is employed since it assigns an extra point to children aged 3–14 years, who tend to have the highest prevalence of GAS [6].

Both the ACP and the Infectious Diseases Society of America (IDSA) recommend backup bacterial throat cultures for children and adolescents with symptoms of pharyngitis who

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test negative on the RADT, but not adults [7], leading some clinicians to question which recommendation applies best to the college-aged population. Evidence of diminished sensitivity of the Centor score and the acknowledgement of other important bacterial pathogens in this population has led this paradigm to be challenged by several clinicians and researchers [8, 9], including most notably by Robert M. Centor himself [10]. Among college students with pharyngitis, non–group A β-hemolytic *Streptococcus* (NGAS) species, specifically *Streptococcus dysgalactiae* subspecies *equisimilis* (β-hemolytic groups C and G), appear to be endemic [8, 11, 12]. In fact, 1 study reported that the prevalence of group C streptococci was 2-fold greater than GAS in throat swab cultures of college students with acute pharyngitis [12]. Despite that antibiotic therapy is only indicated for GAS [2], NGAS infections have also been reported to cause complications similar to GAS, including acute rheumatic fever and glomerulonephritis [13], though the incidence of such complications is unclear. Furthermore, there is evidence of shared gene content between GAS and NGAS species, including virulence factor genes for superantigens, DNases, proteinases, peptidases, and other immunomodulatory toxins [14], suggesting that some NGAS infections have comparable virulence to GAS infections.

Taken together, further study of the diagnostic paradigm of pharyngitis among college students is warranted. The objectives of this analysis were to analyze the application of current diagnostic guidelines for GAS pharyngitis and evaluate the clinical presentation of NGAS pharyngitis among college students. Specifically, this study evaluated the performance of the Centor criteria (expert model) to identify GAS pharyngitis from other isolates, compared the clinical presentation of GAS vs NGAS pharyngitis, and developed a modified clinical decision tool to predict NGAS infections.

METHODS

Study Design

This was a retrospective analysis of patients who received a streptococcal RADT and/or a bacterial throat culture in an outpatient clinic at a southeastern US university between 1 January and 31 December 2014. Individuals aged 18 years and older were included. In the event a patient received an RADT more than once during the study period, only the encounter closest to the extraction data was included. Data on demographics and clinical characteristics were extracted from the clinic's electronic health records (EHRs). Multiple clinically trained staff (between 10 and 12) served as assessors with oversight by the principal investigator (M. K. T.). Assessors were trained in utilization of the data collection tool with initial medical record reviews being validated by the trainers. Agreement between assessors was not evaluated as data were validated (and checked for errors) independently by a trainer.

Patient Consent Statement

A waiver of informed consent for record abstraction and secondary data analysis was approved as exempt by the Institutional Review Board at the University of Florida (reference numbers IRB201500184 and IRB201802893). The study was performed in accordance with the Helsinki Declaration.

Study Parameters

Patient demographics (age, gender) were collected and EHR data were extracted for components of the Centor score (fever, cough, cervical lymphadenopathy, and tonsillar exudate), as well as other clinical factors, including history of tonsillectomy, sore throat, sore throat onset (days), pharyngeal erythema, temperature, difficulty swallowing, runny nose/nasal congestion, headache, ear pain, and gastrointestinal symptoms (including abdominal pain, nausea, vomiting, and diarrhea). Fever was defined as reported objective measurement either in clinic or at home of 38°C (100.4°F) or greater. Tactile or subjective fever was excluded. Missing categorical data were coded as unknown in the descriptive analysis and handled with multiple imputation—a method to infer the value of missing data points—prior to fitting the multivariable models. This procedure is described in more detail in the Statistical Analysis section. The proportion of missing data ranged from 0 to 0.1% for demographics and 0 to 38.8% for each symptom.

Laboratory Diagnosis

Diagnosis of GAS pharyngitis was determined using the QuickVue In-Line RADT via throat swab. The sensitivity and specificity of the RADT in the general population have been reported as 64.6% and 96.79%, respectively [15]. A subset of RADT-negative throat swab specimens was sent to external laboratories for routine upper respiratory cultures at the clinical provider's discretion. In the event the culture results were found positive for GAS, these patients were grouped into the GAS-positive population. Patients with positive throat culture results for group C or G streptococci were included in the NGAS pharyngitis population. The culture-negative control population included patients with no growth or growth of group B or F *Streptococcus* species (as these species are not known to cause pharyngitis) or non-*Streptococcus* species (*Hemophilus influenzae*, routine upper respiratory flora, or *Staphylococcus aureus*) on the upper respiratory throat culture.

Statistical Analysis

Demographic and clinical characteristics of patients with GAS, NGAS, RADT-negative, and culture-negative infections were compared using χ^2 test for categorical variables. Welch 2-sample *t* test and Wilcoxon rank-sum test were used for normally and nonnormally distributed continuous variables, respectively. Bonferroni *P* value correction was applied to adjust for multiple comparison in the descriptive analysis. Univariable

logistic regression was performed to predict GAS infections (vs RADT-negative infections) based on the 4-factor Centor score, which we treated categorically. Multivariable models were fitted to associate uncorrelated variables (ie, with a Pearson correlation coefficient <0.40) with GAS and NGAS infections using 2 feature selection procedures to identify the best model fit: a less restrictive bidirectional (forward and backward) stepwise selection on the basis of Akaike information criterion and least absolute shrinkage and selection operator (LASSO), which is a more restrictive, machine learning–based modeling approach. The RADT-negative population served as the control group in the prediction model for GAS infections, whereas the culture-negative population served as the control group in the prediction model for NGAS infections. Measures of sensitivity, specificity, positive predictive value, and negative predictive value and the receiver operating characteristic (ROC) curves were computed for the multivariable (LASSO and stepwise-selected) models of GAS and NGAS infections and summarized by plotting the area under the curve (AUC). All analyses were conducted using R statistical programming software, version 3.6.0 [16]. The following packages were used: Amelia to perform 5 combinations of multiple imputation for the missing categorical data, MAMI for model selection and averaging over the 5 multiply imputed datasets, and ROCR to compute and visualize ROC curves [17].

RESULTS

Characteristics of Study Population

A total of 3963 patients received a RADT and/or bacterial throat culture at the health care center between 1 January 2014 and 31 December 2014. Of these patients, 18.8% tested positive for GAS. Thirty-four patients who originally tested negative on the RADT were found to be positive for GAS upon bacterial throat culture. Bacterial throat cultures were performed for 407 patients (313 who tested negative on the RADT) in whom growth of NGAS occurred in 34.8% (n = 109). Group C was the most common isolate—attributed to 75.2% of NGAS infections.

Clinical Presentations

In comparing the symptom presentation of patients with GAS-positive vs RADT-negative pharyngitis, we observed symptoms of runny nose/nasal congestion and cough more commonly among RADT-negative patients, whereas pharyngeal erythema, tonsillar exudate, and adenopathy were more common among GAS-positive patients (Table 1). Centor scores tended to be higher in the GAS-positive population, with a mean score of 2.9 in the GAS-positive population compared to 2.3 in the RADT-negative population ($P < .0001$). In the analysis of GAS vs NGAS pharyngitis, patients with NGAS infections were more likely to present with gastrointestinal symptoms and tonsillar exudate. Similarly, patients with NGAS pharyngitis were also more likely to present with tonsillar exudate when compared to culture-negative patients.

Centor Score Prediction of GAS and NGAS

Centor scores between 1 and 4 were associated with increased odds of GAS compared to RADT-negative infections ($P < .05$; Table 2). Increasing Centor scores corresponded to increased odds of GAS pharyngitis, with a Centor score of 4 indicating 4.74 times increased odds of GAS infection compared to a score of 0 (95% confidence interval [CI], 3.21–7.02). Likewise, higher Centor scores (eg, scores of 3 and 4) were also predictive of NGAS-positive compared to culture-negative infections at $P < .05$. A Centor score of 4 was indicative of 4.31 times (95% CI, 1.46–12.71) increased odds of NGAS pharyngitis, compared to a score of 0.

Multivariable Prediction of GAS and NGAS

In the LASSO model comparing predictors of GAS vs RADT-negative infections, the symptoms found to be significantly associated with GAS were absence of cough (odds ratio [OR], 0.70 [95% CI, .59–.85]), adenopathy (OR, 2.35 [95% CI, 1.94–2.85]), pharyngeal erythema (OR, 2.63 [95% CI, 1.97–3.50]), and tonsillar exudate (OR, 1.68 [95% CI, 1.40–2.02]) (Table 3). The stepwise model for GAS additionally found male gender (OR, 1.20 [95% CI, 1.01–1.42]), absence of runny nose/nasal congestion (OR, 0.88 [95% CI, .67–.95]), and absence of gastrointestinal symptoms (OR, 0.76 [95% CI, .58–.99]) to be significantly associated with GAS infections. The LASSO model for NGAS found that tonsillar exudate was significantly positively associated with NGAS compared to culture-negative infections (OR, 2.08 [95% CI, 1.29–3.34]). The results were comparable for the stepwise model. In the analysis of GAS vs NGAS infections, tonsillar exudate was the only symptom found to be significantly associated with the outcome in the LASSO model and it was negatively associated with GAS (OR, 0.45 [95% CI, .30–.68]). Tonsillar exudate was also significantly negatively associated with GAS compared to NGAS pharyngitis in the stepwise model, in addition to gastrointestinal symptoms (OR, 0.57 [95% CI, .34–.97]).

Model Performance

The models for GAS outperformed all the models for NGAS (Figure 1). The area under the ROC curve (AUC) for the bivariable Centor score model prediction accuracy was 0.64 for GAS and 0.59 for NGAS. The mean AUC for the LASSO model prediction accuracy of GAS on all 5 imputed datasets was 0.70 whereas for NGAS it was 0.59. The stepwise model prediction accuracy was comparable for both outcomes (mean AUC = 0.71 for GAS and 0.63 for NGAS), again on all 5 imputed datasets.

DISCUSSION

In this study, we evaluated the diagnostic paradigm for acute bacterial pharyngitis in a population of college students from a university in the southeastern US who presented with symptoms of pharyngitis. The proportion of individuals with acute

Table 1. Characteristics of Patients Who Presented With Symptoms of Pharyngitis Stratified by Diagnosis

Characteristic	RADT-Negative Population[a] (n = 3219)	GAS-Positive Population[b] (n = 744)	*P* Value for Difference: RADT-Negative vs GAS-Positive	NGAS-Positive Population[c] (n = 109)	*P* Value for Difference: GAS-Positive vs NGAS-Positive	Culture-Negative Population[d] (n = 203)	*P* Value for Difference: NGAS-Positive vs Culture-Negative
Age, y, mean (SD)	20.5 (2.9)	20.4 (2.8)	.3481	20.9 (3.0)	.7642	21.1 (3.7)	.1666
Gender			.1633		.2646		1.0000
Female	1958 (60.9)	432 (58.1)		70 (64.2)		129 (63.5)	
Male	1256 (39.1)	312 (41.9)		39 (35.8)		74 (36.5)	
Symptoms							
History of tonsillectomy	208 (6.5)	30 (4.1)	.0162	7 (6.4)	.3863	12 (6.0)	1.0000
Fever	1490 (47.0)	361 (49.3)	.2762	60 (55.0)	.3109	99 (49.0)	.3697
Difficulty swallowing	355 (11.0)	108 (14.5)	.0172	18 (23.7)	.6665	27 (19.9)	.6319
Runny nose/nasal congestion	1563 (48.6)	272 (36.6)	**<.0001**	37 (38.5)	.4566	89 (49.7)	.0996
Cough	1356 (42.1)	208 (28.0)	**<.0001**	21 (21.6)	.0646	65 (34.9)	.0298
Headache	966 (30.0)	213 (28.6)	.6989	38 (45.8)	.1383	67 (43.2)	.8090
Ear pain	366 (11.4)	73 (9.8)	.4745	14 (19.4)	.2967	27 (18.0)	.9403
Gastrointestinal symptoms	434 (13.5)	74 (9.9)	.0286	23 (25.6)	.0023	28 (17.0)	.1404
Pharyngeal erythema	2340 (72.8)	683 (91.9)	**<.0001**	103 (95.4)	.2865	178 (87.7)	.0473
Tonsillar exudate	666 (20.7)	304 (41.0)	**<.0001**	66 (60.6)	**.0002**	86 (42.6)	.0037
Adenopathy (any)	1549 (48.2)	562 (75.6)	**<.0001**	87 (79.8)	.4034	161 (79.3)	1.0000
Sore throat onset, d, mean (SD)	3.9 (4.6)	3.4 (3.6)	.0030	3.6 (3.7)	.7365	4.6 (7.6)	.1206
Temperature, °C, mean (SD)	37.0 (1.5)	37.0 (3.6)	.9600	37.3 (0.7)	.0554	37.2 (0.8)	.5468
Centor score			**<.0001**		.1066		.0707
0	687 (21.3)	79 (10.6)		8 (7.3)		32 (15.8)	
1	1280 (39.8)	202 (27.2)		23 (21.1)		52 (25.6)	
2	816 (25.3)	248 (33.3)		33 (30.3)		58 (28.6)	
3	326 (10.1)	155 (20.8)		31 (28.4)		48 (23.6)	
4	110 (3.4)	60 (8.1)		14 (12.8)		13 (6.4)	
Centor score (continuous), mean (SD)	2.3 (1.0)	2.9 (1.1)	**<.0001**	3.2 (1.1)	.0111	2.8 (1.2)	.0044

Data are presented as No. (%) unless otherwise indicated. Missing values were retained as unknown for this table and therefore, not all proportions and inverse proportions add up to 1. *P* values are for χ^2 test (categorical variables), Wilcoxon rank-sum test (age, sore throat onset), or Welch 2-sample *t* test (temperature, Centor score). Only *P* values significant after Bonferroni correction (at $P < .00098$) are shown in bold.

Abbreviations: GAS, group A *Streptococcus*; NGAS, non–group A *Streptococcus* (includes groups C and G streptococci); RADT, rapid antigen detection test; SD, standard deviation.

[a]RADT-negative population includes all RADT-negative patients, less those positive for GAS on the throat culture.

[b]GAS-positive population includes patients positive for GAS on the RADT or throat culture.

[c]NGAS-positive population includes patients who tested RADT negative and culture positive for NGAS species.

[d]Throat culture–negative population includes patients who tested RADT negative and had no growth or growth of non-*Streptococcus* species (*Hemophilus influenzae*, routine upper respiratory flora, or *Staphylococcus aureus*) on the throat culture.

Table 2. Prediction of Group A *Streptococcus* and Non–Group A *Streptococcus* Infections Based on the Centor Score

Centor Score	GAS-Positive vs RADT-Negative Infection	GAS-Positive vs NGAS-Positive Infection	NGAS-Positive vs Culture-Negative Infection
1 vs 0	1.37 (1.04–1.81)	0.89 (.38–2.07)	1.77 (.71–4.43)
2 vs 0	2.64 (2.01–3.47)	0.76 (.34–1.72)	2.27 (.94–5.51)
3 vs 0	4.13 (3.06–5.59)	0.51 (.22–1.15)	2.58 (1.05–6.33)
4 vs 0	4.74 (3.21–7.02)	0.43 (.17–1.10)	4.31 (1.46–12.71)

Results are presented as odds ratio (95% confidence interval).

Abbreviations: GAS, group A *Streptococcus*; NGAS, non–group A *Streptococcus* (includes groups C and G streptococci); RADT, rapid antigen detection test.

pharyngitis caused by GAS in this study population (18.8%) reflected estimates more often noted in children (15%–30%) than in adults (5%–10%) [2]. NGAS pharyngitis was present in 34.8% of RADT-negative patients who received bacterial throat cultures. We found that the Centor score (ie, the clinical decision support tool currently recommended by the ACP) was unable to distinguish between GAS and NGAS infections in this population. Tonsillar exudate was indicative of bacterial infection, but it was more strongly associated with NGAS than GAS infections.

The findings of our study were similar to those reported in previous studies. An 8-study meta-analysis from 2017 comparing the sensitivity of individual signs and symptoms of GAS vs NGAS found that clinical presentations of both groups were largely similar [18]. Another study examining acute pharyngitis among college students also found that the presence of tonsillar exudate was predictive of NGAS [12]. This study did not test Centor scores, however. None of the studies included in the meta-analysis considered gastrointestinal symptoms, which were inversely associated with GAS in the current study. Gastrointestinal symptoms, such as diarrhea, are more often a feature of viral pharyngitis than GAS pharyngitis according to IDSA guidelines [7].

The current study has many strengths. To our knowledge, it is the first to examine the efficacy of the Centor score criteria as a clinical decision tool for the diagnosis of GAS pharyngitis specifically in the college student population. The models developed using additional clinical criteria were more predictive of GAS infections than the Centor score alone—though the clinical significance of the modified decision tools needs to be evaluated. These results highlight the need for the development and validation of new clinical decision tools equipped to predict GAS in a prospective cohort of young adults. This study is also the first to evaluate the predictability of NGAS infections using the Centor score compared to a modified score that included other clinical signs and symptoms. These results provide further evidence that NGAS is a prevalent pathogen in the college-aged population in whom the clinical presentation is similar to GAS. The decision to treat NGAS remains a contentious topic in the field today, with limited study of the long-term effects of untreated NGAS infections to support protreatment advocates. A whole genome sequencing study of group C and group G streptococci (ie, NGAS) revealed virulence factor genes that were identical to those in GAS [14], hinting at potential interspecies exchange of virulence genes (ie, horizontal gene transfer). In addition to

Table 3. Prediction of Group A *Streptococcus* and Non–Group A *Streptococcus* Infections Based on Symptom Presentation Using Multivariable Logistic Regression

Characteristic	GAS-Positive vs RADT-Negative Infection		GAS-Positive vs NGAS-Positive Infection		NGAS-Positive vs Culture-Negative Infection	
	LASSO Model	Stepwise Model	LASSO Model	Stepwise Model	LASSO Model	Stepwise Model
Age (years)	…	…	…	0.95 (.89–1.01)	…	…
Gender (male vs female)	…	1.20 (1.01–1.42)	…	…	…	…
Symptoms (ref. = no)						
History of tonsillectomy	…	0.82 (.42–1.57)	…	…	…	…
Fever	…	0.98 (.81–1.18)	…	…	…	…
Cough	0.70 (.59–.85)	0.75 (.59–.95)	…	1.38 (.69–2.77)	…	0.91 (.47–1.77)
Adenopathy	2.35 (1.94–2.85)	2.37 (1.96–2.88)	…	…	…	…
Pharyngeal erythema	2.63 (1.97–3.50)	2.58 (1.94–3.44)	…	…	…	2.43 (.89–6.65)
Tonsillar exudate	1.68 (1.40–2.02)	1.69 (1.41–2.03)	0.45 (.30–.68)	0.46 (.30–.71)	2.08 (1.29–3.34)	1.91 (1.17–3.12)
Difficulty swallowing	…	…	…	…	…	…
Runny nose/nasal congestion	…	0.88 (.67–.95)	…	…	…	…
Headache	…	…	…	0.79 (.38–1.65)	…	…
Ear pain	…	…	…	…	…	…
Gastrointestinal symptoms (any)	…	0.76 (.58–.99)	…	0.57 (.34–.97)	…	1.10 (.55–2.17)
Sore throat onset (days)	…	0.98 (.96–1.01)	…	…	…	…

Results are presented as odds ratio (95% confidence interval).

Abbreviations: GAS, group A *Streptococcus*; LASSO, least absolute shrinkage and selection operator; NGAS, non–group A *Streptococcus* (includes groups C and G streptococci); RADT, rapid antigen detection test.

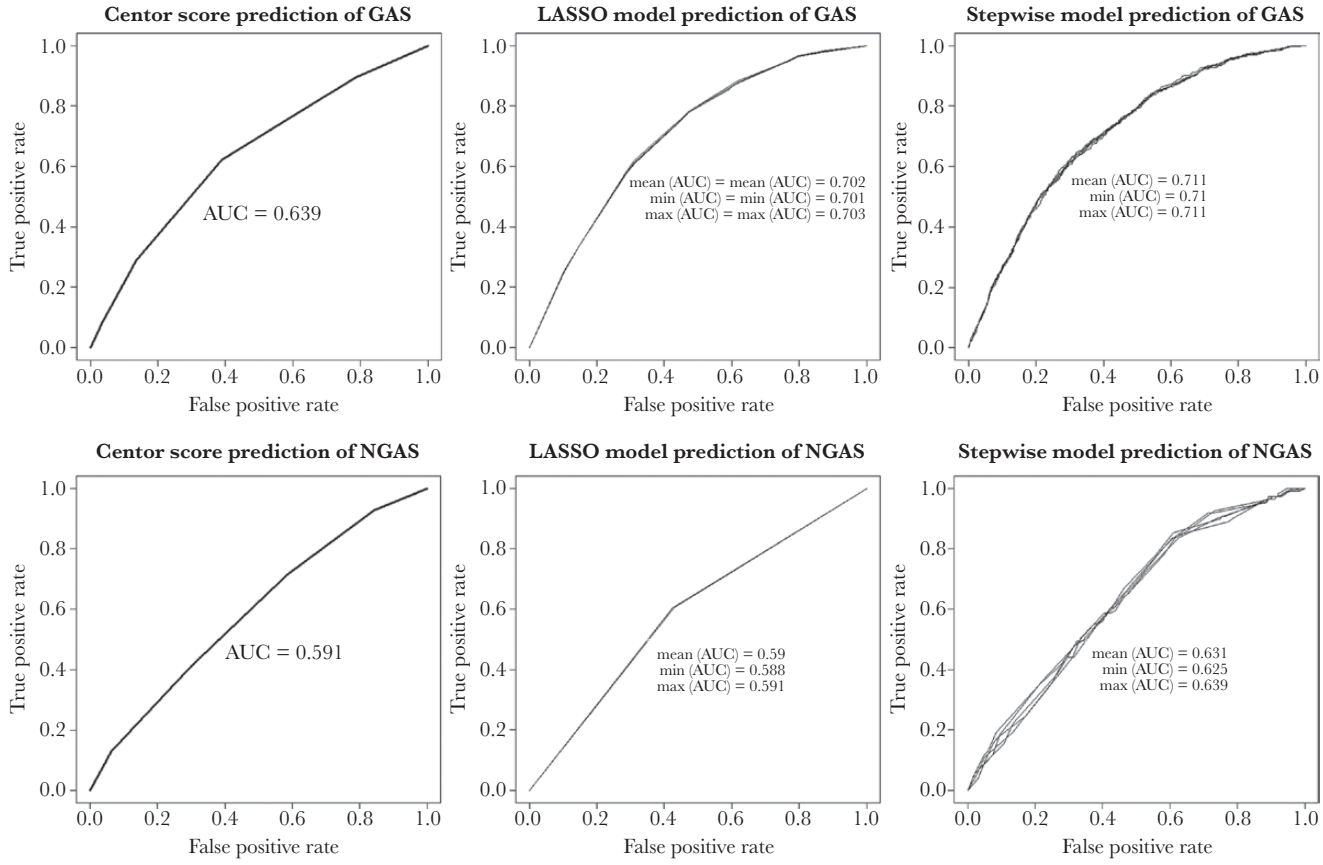

Figure 1. Plots of the area under the curve (AUC) for the univariable Centor score model, least absolute shrinkage and selection operator (LASSO), and stepwise-selected multivariable models for group A *Streptococcus* (GAS) and non–group A *Streptococcus* (NGAS) infections. AUCs were plotted for each of the 5 multiply imputed datasets for the LASSO and stepwise models.

NGAS, *Fusobacterium necrophorum*, an anaerobic bacterial pathogen, has recently been recognized as an emerging pharyngitis pathogen of importance, particularly among young adults and adolescents [10, 19]; however, this bacterium was not tested for in the present study as it is not currently included in the standard upper respiratory culture. Future research should investigate the longitudinal trends and outcomes of pharyngitis infections arising from non–group A streptococcal bacterial pathogens, such as β-hemolytic groups C and G (*S dysgalactiae* subspecies *equisimilis*), and *F necrophorum* to determine whether prevalence of these pathogens is increasing over time and whether treatment should be indicated.

This study also had limitations. Since bacterial throat cultures were ordered on a case-by-case basis, and not for all RADT-negative patients, this study likely suffered from misclassification bias as the number of NGAS infections is likely an underestimation. Furthermore, the number of true GAS infections may have also been underestimated given the relatively low sensitivity of the RADT (64.6%). Although the nonrandom selection of individuals who received cultures reflects current clinical practice, it likely resulted in a study population with more severe illness than would otherwise be expected in the general population as clinicians may have been more likely to order throat cultures for patients with acute or persistent symptoms. This may explain why tonsillar exudate, a Centor score criterion, was associated with higher odds of NGAS than GAS in the study; however, this finding has also been observed in a prior meta-analysis [18]. Future studies should retrieve throat cultures from all RADT-negative patients to eliminate sources of misclassification bias. Additionally, medical record abstraction by multiple assessors can lead to information bias, and therefore, assessor agreement (such as through calculation of κ statistic) should be considered when validating data. Last, this analysis was also limited due to its retrospective nature and the use of incomplete EHR data, which required imputation on multiple variables. Multivariable estimates were averaged across 5 multiply imputed datasets to account for the uncertainty associated with both the imputation process and the variable selection procedures, however, and thus, this source of bias is likely minute.

CONCLUSIONS

In this study, GAS and NGAS pharyngitis were indistinguishable among college students using a commonly applied (expert) decision score, the Centor score. The prevalence of GAS

among college students with symptoms of pharyngitis is more reflective of the expected prevalence in pediatric, rather than in adult, populations. Taken together, closer attention to the diagnostic paradigm and development of new clinical decision support systems, such as those presented in this study, to predict GAS and NGAS pharyngitis in the college student population is warranted. Given the high occurrence of NGAS among college students evidenced in both the current and previous studies, and the potential for shared gene content between *Streptococcus* species, further study of the long-term consequences of untreated NGAS infections is also warranted.

Notes

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