Incorporation of a biparietal narrowing metric to improve the ability of machine learning models to detect sagittal craniosynostosis with 2D photographs

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OBJECTIVE Sagittal craniosynostosis is the most common form of craniosynostosis and typically results in scaphocephaly, which is characterized by biparietal narrowing, compensatory frontal bossing, and an occipital prominence. The cephalic index (CI) is a simple metric for quantifying the degree of cranial narrowing and is often used to diagnose sagittal craniosynostosis. However, patients with variant forms of sagittal craniosynostosis may present with a “normal” CI, depending on the part of the suture that is closed. As machine learning (ML) algorithms are developed to assist in the diagnosis of cranial deformities, metrics that reflect the other phenotypic features of sagittal craniosynostosis are needed. In this study the authors sought to describe the posterior arc angle (PAA), a measurement of biparietal narrowing that is obtained with 2D photographs, and elucidate the role of PAA as an adjuvant to the CI in characterizing scaphocephaly and the potential relevance of PAA in new ML model development.

METHODS The authors retrospectively reviewed 1013 craniofacial patients treated during the period from 2006 to 2021. Orthogonal top-down photographs were used to calculate the CI and PAA. Distribution densities, receiver operating characteristic (ROC) curves, and chi-square analyses were used to describe the relative predictive utility of each method for sagittal craniosynostosis.

RESULTS In total, 1001 patients underwent paired CI and PAA measurements and a clinical head shape diagnosis (sagittal craniosynostosis, n = 122; other cranial deformity, n = 565; normocephalic, n = 314). The area under the ROC curve (AUC) for the CI was 98.5% (95% confidence interval 97.8%–99.2%, p < 0.001), with an optimum specificity of 92.6% and sensitivity of 93.4%. The PAA had an AUC of 97.4% (95% confidence interval 96.0%–98.8%, p < 0.001) with an optimum specificity of 94.9% and sensitivity of 90.2%. In 6 of 122 (4.9%) cases of sagittal craniosynostosis, the PAA was abnormal while the CI was normal. This means that adding a PAA cutoff branch to a partition model increases the detection of sagittal craniosynostosis.

CONCLUSIONS Both CI and PAA are excellent discriminators for sagittal craniosynostosis. Using an accuracy-optimized partition model, the addition of the PAA to the CI increased model sensitivity compared to using the CI alone. Using a model that incorporates both CI and PAA could assist in the early identification and treatment of sagittal craniosynostosis via automated and semiautomated algorithms that utilize tree-based ML models.

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KEYWORDS craniosynostosis; machine learning; artificial intelligence; sagittal craniosynostosis; posterior arc angle
utilize artificial intelligence (AI) algorithms have the potential to augment the physical examination by providing objective, quantifiable metrics to characterize the pattern and severity of a deformity.

Sagittal craniosynostosis is typically characterized by biparietal narrowing, compensatory frontal bossing, and an occipital prominence leading to an elongated and narrow head shape. Historically, sagittal craniosynostosis has been most frequently quantified by obtaining head measurements to determine the cephalic index (CI), defined as the ratio of the maximal width of the head divided by the maximal length. In clinical practice, a CI cutoff of 70%—75% is most frequently used; patients with a CI below this value are evaluated more closely. However, not all patients with sagittal craniosynostosis can be segregated from normal cohorts by CI alone. Some patients demonstrate biparietal narrowing without significant compensatory elongation of the skull; therefore, automated screening algorithms that rely on the CI alone risk missing these variant sagittal craniosynostosis phenotypes.

Our group has previously quantified the degree of biparietal narrowing using a novel metric termed the posterior arc angle (PAA). However, to our knowledge the synergistic discriminative power of anteroposterior elongation (CI) and biparietal narrowing (PAA) as components of the sagittal craniosynostosis phenotype. Our findings have implications for standardized screening practices for craniosynostosis and inform factor selection for the development of automated sagittal craniosynostosis ML diagnostic algorithms.

Methods

Cranio metric Data set

This study was approved by the Connecticut Children’s Institutional Review Board. An existing retrospective data set of outpatient neonatal craniofacial encounters incorporating the lead authors’ practices was utilized. This data set includes deidentified records from patients treated at Connecticut Children’s that were collected between January 1, 2019, and December 31, 2021, as well as consecutive data collections from Johns Hopkins and the Mayo Clinic during the period from January 1, 2006, to December 31, 2021. Inclusion criteria for the data set can be found in Table 1.

Patient head shapes were recategorized from the data set into three classes: normocephalic, sagittal craniosynostosis, or other (nonsynostotic cranial deformity or nonsagittal form of craniosynostosis) (Table 2). Classifications of cases in the data set were made based on physical examination with or without radiological information and confirmation. While most patients had radiographic confirmation (76%), a small percentage (24%) had only physical examination and gross pathological confirmation (Fig. 1).

The CI and PAA values were calculated using semi-automated software that extracted multiple cranio metric values from orthogonal top-down head photographs that were obtained at each patient’s initial diagnostic encounter. The software-based extraction of metrics has been described previously in Bookland et al. The CI was calculated as the ratio of the medial-lateral width divided by the anterior-posterior length. An illustration of the PAA can be found in Fig. 2A. In brief, the PAA is the angle between two lines defined on the left and right by the posterior point of intersection of the cranial contour and the anterior-posterior line of bisection, as well as the point of intersection along the posterior cranial contour of a 30° line passing through the centroid of the contour.

Statistical Analysis

Descriptive statistics were performed using median and interquartile range (IQR) for continuous variables and frequency and percentage for categorical variables. Further statistical analyses were performed with the R packages Rpart, Mass, ggplot2, and Psych. Distribution densities were used to describe the observed differences in CI and PAA measurements, with statistical significance assessed

### Table 1. Criteria for patient inclusion and exclusion in the craniometrics data set used in this study

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Patient Criteria</th>
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<tbody>
<tr>
<td>Age &lt;1 yr at the time of craniofacial diagnosis</td>
<td>Age &lt;1 yr at the time of craniofacial diagnosis</td>
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<tr>
<td>Craniometric measurements available from orthogonal, top-down patient photos w/o significant obscuration of the cranial equator</td>
<td>Craniometric measurements available from orthogonal, top-down patient photos w/o significant obscuration of the cranial equator</td>
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<tr>
<td>Documentation of age in days at the time of the measurements</td>
<td>Documentation of age in days at the time of the measurements</td>
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<tr>
<td>Documentation of patient sex</td>
<td>Documentation of patient sex</td>
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<tr>
<td>Documentation of neonatal cranial deformity type by an attending craniofacial specialist w/in 30 days of the image used for craniometric measurements</td>
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<th>Exclusion criteria</th>
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<tr>
<td>Disputed or equivocal neonatal cranial deformity diagnosis in the medical record</td>
<td>Disputed or equivocal neonatal cranial deformity diagnosis in the medical record</td>
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<tr>
<td>Patients w/ confirmed or suspected syndromic cases</td>
<td>Patients w/ confirmed or suspected syndromic cases</td>
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<tr>
<td>Patients w/ postintervention cases</td>
<td>Patients w/ postintervention cases</td>
</tr>
<tr>
<td>Patients not meeting inclusion criteria</td>
<td>Patients not meeting inclusion criteria</td>
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</tbody>
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### Table 2. Descriptors for the craniometric data set utilized for model generation and tuning

<table>
<thead>
<tr>
<th>Class</th>
<th>No. of Patients</th>
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<tbody>
<tr>
<td>Normal</td>
<td>314</td>
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<tr>
<td>Sagittal craniosynostosis</td>
<td>122</td>
</tr>
<tr>
<td>Other*</td>
<td></td>
</tr>
<tr>
<td>Plagiocephaly</td>
<td>233</td>
</tr>
<tr>
<td>Brachycephaly</td>
<td>215</td>
</tr>
<tr>
<td>Metopic craniosynostosis</td>
<td>39</td>
</tr>
<tr>
<td>Lt or rt unicoronal craniosynostosis</td>
<td>37</td>
</tr>
<tr>
<td>Bicoronal craniosynostosis</td>
<td>3</td>
</tr>
<tr>
<td>Lt or rt lambdoid craniosynostosis</td>
<td>2</td>
</tr>
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* Nonsynostotic cranial deformity or nonsagittal form of craniosynostosis.
by using Wilcoxon rank-sum tests. Receiver operating characteristic (ROC) curves were generated to describe the relative predictive utility of each method in detecting sagittal craniosynostosis. Patient craniometrics (CI and PAA) were then used to design classification and regression tree models for the detection of sagittal craniosynostosis using sensitivity and specificity optimized CI and PAA cutoffs, as well as a more conventional optimized CI cutoff of 74% based on historical cutoffs for normocephaly.\textsuperscript{5,7,18} Models were constructed using Rpart and a custom script in R that runs a 5-fold cross-validation with 80–20 training-testing sets.

Results

Data set Composition

Of the 1013 unique sets of craniofacial patient craniometric data, 1001 had paired CI and PAA measurements, as well as a clinical diagnosis regarding the head shape (sagittal craniosynostosis n = 122, other cranial deformity n = 565, normocephalic = 314). Overall, 67.6% of the patients were male patients and the average age at the time of the diagnostic encounter recorded in the data set was 171.2 ± 72.7 days. Within the sagittal craniosynostosis cohort, 80.3% of patients were male and the average age at the time of the encounter was 26.9 ± 55.0 days. In 93 of 122 (76.2%) sagittal craniosynostosis cases, the diagnosis was verified with imaging (ultrasound, radiograph, or CT) and via gross pathologic confirmation, and in 29 cases (23.8%) the diagnosis was verified only via gross pathologic confirmation (Fig. 1). Among the cases that were not sagittal craniosynostosis, 314 cases (31.4%) were diagnosed as normal, 251 (25.1%) as deformational brachycephaly, and 233 cases (23.3%) as deformational plagiocephaly. Among the remaining cases, 3 (0.3%) were diagnosed as bicoronal craniosynostosis, 39 (3.9%) as metopic craniosynostosis, 37 (3.7%) as unicoronal craniosynostosis, and 2 (0.2%) as lambdoid craniosynostosis.

Distribution of CI and PAA Across the Craniofacial Cohort

There were no differences in CI or PAA distributions between radiographically confirmed sagittal craniosynostosis cases and those confirmed by clinical examination and gross pathologic confirmation alone (mean CI\textsubscript{sagittal-radiograph} = 70.6% ± 4.7% vs mean CI\textsubscript{sagittal-clinical} 70.8% ± 4.4%, p value not significant [NS]; mean PAA\textsubscript{sagittal-radiograph} = 2.25 ± 0.18 radians vs mean PAA\textsubscript{sagittal-clinical} = 2.24 ± 0.13 radians, p value NS).

There were, however, significant differences in CI and PAA metrics when sagittal craniosynostosis cases were compared to nonsagittal craniosynostosis cases. Compared to both normocephalic patients and those with other cranial deformities, patients with sagittal craniosynostosis had significantly lower CI values (median CI\textsubscript{sagittal} 71%, IQR 67.9%–73.2%; median CI\textsubscript{normocephalic} 84.2%, IQR 80.3%–96.2%; median CI\textsubscript{other} = 93.5%, IQR 87.3%–98.7%; p < 0.001) (Fig. 2B). Additionally, patients with sagittal craniosynostosis demonstrated lower PAA values than normocephalic patients and those with other cranial deformities (median PAA\textsubscript{sagittal} 2.23 radians, IQR 2.14–2.33 radians; median PAA\textsubscript{normocephalic} 2.62 radians, IQR 2.51–2.69 radians; median PAA\textsubscript{other} 2.72 radians, IQR 2.60–2.81 radians; p < 0.001) (Fig. 2B). PAA and CI used together clus-
tered patients with sagittal craniosynostosis in contrast to those with other head shapes, with good correlation ($R^2 = 0.66$) between the two measurements (Fig. 2C). In 6 of 122 (4.9%) cases of sagittal craniosynostosis, the PAA was abnormal while the CI was normal. Furthermore, among all patients with an abnormal PAA and a normal CI, 20% were diagnosed with sagittal craniosynostosis. Conversely, among all patients with an abnormal CI and a normal PAA, 22.7% were diagnosed with sagittal craniosynostosis ($p = 0.001$, chi-square test).

**CI and PAA Have Excellent Predictive Power for Sagittal Craniosynostosis**

Identification of sagittal craniosynostosis in this data set using the CI or PAA method was achieved with comparably high levels of accuracy. The area under the ROC curve (AUC) for CI was 98.5% (95% confidence interval 97.8%–99.2%, $p < 0.001$), with an optimum specificity of 92.6% and sensitivity of 93.4% at an optimized CI cut-off of 0.78% (Fig. 3A). The PAA had an AUC of 97.4% (95% confidence interval 96.0–98.8, $p < 0.001$) with an optimum specificity of 94.9% and sensitivity of 90.2% at a cut-off value of 2.42 radians (Fig. 3B).

Patients with sagittal craniosynostosis comprised 66% of patients with a CI below 78% and 86% of patients with a CI below 74%, while representing less than 5% of patients with a CI above these thresholds (Fig. 4A and B). When adding PAA to these CI thresholds, patients with sagittal craniosynostosis comprised 84% of cases with a CI below 78% and a PAA below 2.42 radians and 96% of cases with a CI below 74% and a PAA below 2.42 radians (Fig. 4A and B).
Addition of the PAA to the CI metrics provided increased sensitivity, with a concomitant decrease in specificity and overall accuracy (Fig. 4C and D). Using a CI cutoff of 78% and adding a PAA cutoff branch to a partition model for the detection of sagittal craniosynostosis increased detection by 4.9% (95% confidence interval 2.6%–7.2%, p < 0.001) while decreasing overall model accuracy by 1.8%, to 92.7% (95% confidence interval 91.1%–94.3%) versus 90.9% (95% confidence interval 89.1%–92.7%, p = 0.029), compared to using the CI alone (Fig. 4C). Using a more conventional CI cutoff of 74% and adding a PAA cutoff branch increased detection by 14% (95% confidence interval 10.5%–17.4%, p < 0.001) while decreasing overall model accuracy by 2.3% (96.3% [95% confidence interval 95.1%–97.5%] vs 94.0% [95% confidence interval 92.5%–95.5%], p = 0.002) compared to a partition model that used the CI alone (Fig. 4D). This partition model is illustrated in Fig. 4E.

Discussion

Image processing augmented by AI algorithms has the potential to enhance the diagnostic acumen of craniofacial specialists and nonspecialists alike. While intricate convoluted neural networks may one day offer the most powerful models for neonatal cranial deformity detection and classification, simpler and less computationally intensive ML models have already been shown to provide high levels of accuracy when classifying cranial deformities. These image processing, 2D photograph–based ML systems have immense potential to streamline the evaluation of patients with possible craniofacial abnormalities, particularly through the use of telemedicine to facilitate remote screening. Deploying software armed with automated or semiautomated image processing tools and a reliable, robust AI classification model to a cloud platform may allow providers to screen neonatal patients cheaply and easily for sagittal craniosynostosis even in remote or underserved regions as long as they have a digital camera and internet connection. Such minimum hardware and software requirements now present a low bar to over-

FIG. 3. ROC curve for the specificity and sensitivity of the CI and PAA measurements as an indicator of sagittal craniosynostosis. ROC curves were calculated based on discrimination of sagittal craniosynostosis from the overall cohort for both the CI and PAA. AUC values are provided in the lower right corner of the plots.

FIG. 4. Partition of and performance statistics for a model incorporating CI and PAA for diagnosis of sagittal craniosynostosis. Cohort distribution between sagittal patients and other diagnoses based on patients above or below a CI threshold of 78% (A) or 74% (B). Plots on the right represent the addition of a PAA threshold at 2.42 to the CI thresholds. Performance statistics for the diagnostic model when incorporating a CI threshold of either 78% (C) or 74% (D). Bar graphs represent the accuracy, sensitivity, and specificity (95% confidence intervals; *p < 0.05, **p < 0.001, chi-square test). Gray bars represent the model performance when only considering CI thresholds; orange bars represent model performance when combining CI and PAA. Partition tree of the craniofacial cohort classes using indicated CI or PAA cutoffs (E). Pie charts represent the overall makeup of the node (blue = sagittal patients, gray = other patients). Node color is based on the dominant population (blue = sagittal class, gray = other class).
come in most regions of the world.\textsuperscript{19,20} Even for patients and providers in well-resourced communities, ML models of sagittal craniosynostosis or other forms of craniosynostosis could provide an inexpensive means of screening infants at home or in a provider's office without the need for ionizing radiation and potentially lower the mean age at which patients reach specialty care and reduce diagnostic costs.

Our group has previously developed cranial shape classification algorithms with accuracies > 98% for sagittal craniosynostosis deformities.\textsuperscript{7} This level of accuracy is on par with levels for some convolutional neural networks previously used in attempts to model craniosynostosis detection.\textsuperscript{5,21,22} In the present study, however, we demonstrated that the PAA, an automatically calculated metric of biparietal narrowing, can be of particular value in similar ML or deep neural network models by improving sagittal craniosynostosis detection with minimal overfitting costs. Given the favorable synergy between CI and PAA for the detection of sagittal craniosynostosis, we propose that metrics of biparietal narrowing should be included in the construction of any diagnostic ML model for which sagittal craniosynostosis is an output class.

The clinical impact of having accurate head shape classification tools available to medical providers was highlighted by Hughes et al., who recently demonstrated that the severity of the head shape is the most significant factor in determining whether surgeons recommend surgical treatment for a patient with sagittal craniosynostosis.\textsuperscript{23} Historically, CI has been used to quantify the severity of scaphocephalic head shapes, but some groups have noted that the use of CI can lead to underreporting of the severity of sagittal craniosynostosis in some patients due to the anterocephalad displacement of the euryon in these cases.\textsuperscript{24,25} The appropriateness of relying on the CI was also studied by Fearon et al., who determined that although the average preoperative CI was below normal among patients with sagittal craniosynostosis, 87.5% of patients had measurements that fell within 2 standard deviations of the mean.\textsuperscript{26} The authors also found that the CI did not correlate well with subjective assessments of severity and was relatively normal among patients undergoing secondary corrections. Other investigators have described the use of CI alone as a subpar indicator of sagittal craniosynostosis when using ultrasound to diagnose the deformity prenatally.\textsuperscript{27} These findings suggest that other metrics are needed to accurately represent the sagittal craniosynostosis phenotype to optimize the objective evaluation of both pretreatment status and posttreatment outcomes. This need has particular significance when developing ML models for the automated diagnosis of sagittal craniosynostosis, for which descriptive metrics rather than brute-force models based on massive data sets will likely provide clinicians and researchers the fastest path to the development of effective and accurate models.

To that end, several groups have described new metrics to characterize patients with sagittal craniosynostosis. Kronig et al., for example, used an analysis of sinusoid curves (obtained from external landmarks identified on standardized CT slices) associated with different head shapes to generate a diagnostic flowchart for different sub-types of isolated craniosynostosis.\textsuperscript{28,29} In contrast, Blum et al. recently identified a metric, the VNO (vertex, nasion, and opisthocranion), which can be measured using CT scans and used to characterize the anterior-posterior location of the vertex.\textsuperscript{30} In their study Blum et al. noted that a VNO > 50° can be used to reliably diagnose sagittal craniosynostosis with a 99.2% specificity.\textsuperscript{30} Both the sinusoid curve and VNO methodologies, however, rely on CT-based metrics, which require exposure to ionizing radiation. The PAA metric described in the current study is unique in that it can be calculated using top-down 2D orthogonal photographs, thereby eliminating the need for diagnostic testing that involves radiation.

Regardless of the inputs and architecture used in their construction, AI models may one day play an important role in supplementing current diagnostic processes. With early intervention being associated with more favorable outcomes for craniosynostosis patients, AI facilitated screening systems could lead to earlier disease diagnosis, improved patient outcomes, and lower screening costs while covering a wider proportion of the at-risk population by leveraging telemedicine and non–craniofacial specialist healthcare providers.\textsuperscript{31,32} The optimal approach to providing these high-fidelity AI detection models has yet to be determined, but there is reason to believe that deep convolutional neural networks may provide the most robust results over the long term.\textsuperscript{6,22} However, with any deep learning model, AI performance is strongly dependent on the quality of the original data used to develop the model. Models based on physician classification can lose stability as a result of interprovider variability. Using independently validated measurements such as the PAA and CI may increase the stability of deep learning models by decreasing classification differences and providing stronger data for the development of such models. The data presented in this study, as well as past work with ML models, suggest that the addition of informed factors such as the PAA and CI to tailored models can produce results that are comparable to, if not better than, the use of unsupervised deep convolutional neural networks.\textsuperscript{7}

Future research opportunities include the development of vector-based and unit-invariant metrics particular to classes of neonatal cranial deformities, as well as exploring the development of 3D metrics, in anticipation of the growing access to 3D scanners within the public domain. The creation of more sophisticated model outputs could also provide greater clinical utility. In the current study, binary outputs were used—sagittal craniosynostosis versus no sagittal craniosynostosis. However, practical applications would benefit from more granular classifications that could include other skull shape abnormalities such as positional dolichocephaly, bathrocephaly, etc. Identifying the potential variant pathologies that are responsible for abnormal CI and/or PAA measurements will be necessary as future ML models are built, and any new models will require thoughtful, unbiased validation studies that include real-world use cases. To that end, community feedback through open distribution and field testing of models over the web may prove useful for future projects, given the relatively small amount of data from craniosynostosis patients available to any one institution.
Study Limitations

As with any data modeling project, this work is confined by the data set available, and the results must be interpreted in light of the biases intrinsic to the training data set. In this case, we used a preexisting data set of labeled craniometric values with unbalanced categories. To recapitulate the relative distribution of positive cases to negative cases that would be expected in a clinical practice, we did not artificially rebalance the data set by using a subset of the whole. This approach can skew classification models to exploit proportional differences in the data. Although the generated partition trees do not, grossly, appear to have leveraged proportional biases between categories in their branch points, the models generated in this exploratory study may lack generalizability. The data set also included data from multiple tertiary referral institutions within the United States, without including encoded geographic or ethnic characteristics of the patients. As such, these data may not be generalizable to populations across diverse geographic, ethnic, and healthcare referral parameters. The retrospective nature of the data set may also introduce unaccounted for selection bias, as could the reliance on images of sufficient quality to allow for inclusion. Last, the optimum cutoff value identified for CI in this cohort was much higher than the value most specialists would use in clinical practice, as many use an abnormal CI cutoff of 71%–75%. This cutoff value finding in the present study may have resulted from inclusion of unbalanced craniofacial classes due to the aforementioned biased patientselection in the data set. A larger, balanced patient cohort could help resolve this incongruence with prior literature. For now, the provided alternate partition model using a CI cutoff of 74% should be interpreted as an approximation of a classification model with more “expected” parameters based on historical reports.

Conclusions

Both CI and PAA are excellent discriminators for identifying sagittal craniosynostosis. Using an accuracy-optimized partition model, the addition of the PAA to the CI increased model sensitivity by 4.9% compared to the use of CI alone and resulted in the identification of patients with sagittal craniosynostosis who had a normal CI. The PAA may be a useful factor in the construction of ML models targeting sagittal craniosynostosis as an output, in addition to conventional factors, such as CI. Using a model that incorporates both CI and PAA could assist in the early identification and treatment of sagittal craniosynostosis via automated and semiautomated algorithms that utilize tree-based ML models.

References


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

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