Geometrics Morphometrics in Craniofacial Skeletal Age Estimation - A Systematic Review

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KEYWORDS

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ABSTRACT

Geometric morphometrics is a novel statistical shape based technique used as an additional approach to the currently used methods in forensics for the assessment of age. Various craniofacial units are used for the estimation of age using this technique. The aim of this systematic review was to assess if Geometric Morphometrics is an accurate and reliable method in craniofacial skeletal age estimation. A literature search was conducted for cross-sectional studies on geometric morphometrics in craniofacial skeletal age estimation using various search engines such as Pubmed, Google Scholar, and Scopus using specific MESH terms. AQUA (Anatomical Quality Assessment) tool was used for the quality assessment. A total of 4 articles were included for qualitative synthesis as they met the objectives of this review. The results of all the included studies suggested that geometric morphometrics can be used for craniofacial skeletal age estimation. The centroid size calculated using digitized images or CBCT scanned images is said to be the highest predictor of age.This systematic review summarises the merits and demerits of this technique and suggests that it is rapid and accurate method for age estimation even in instances of single skeletal remains of craniofacial units and can be performed on a digitized image or a CBCT scanned images. However, further studies are needed to derive reliable data and meta-analysis can be performed effectively.

INTRODUCTION

Aging is a gradual, continuous and uncertain process of natural change that begins in early adulthood as there are continuous variations occurring in human skeleton, ligaments, muscles, skin etc[1].However, it is been noted that at the end of skeletal development, few features which are age dependent (e.g., ossification centers, bone anatomy and fusion of epiphyses etc) [2] remain unchanged [3]and can be used for skeletal age estimation.

Several studies have utilized various craniofacial units such as frontal sinus [4] palatal sutures[5] sphenooccipital synchondrosis[6] mandible [7] for estimation of age and have shown that these units can be used for better assessment of age. In conventional morphometrics technique size of an object is measured and linear distances are compared and detection of the morphological similarities or differences in a sample is done. However this technique has several disadvantages including size and orientation differences within the sample [8] so a new metrics approach called as geometric morphometrics was developed.

Geometric morphometrics is, "A well-established statistical shape method which can be used to quantify the biological forms in landmark-based analysis."[9-12]

In this technique, landmark points are placed on the images to quantitatively analyze the shape so as to capture the geometry of the morphological structures and to preserve their information for further statistical analysis.[8, 13] Another important contribution of this technique is that it clearly defines the definition of shape and size (centroid size).[13, 14] The centroid size is defined as, "The square root of summed squared distances from each landmark to the configuration centroid." Further the cartesian coordinates of semi landmarks and landmarks are captured in their geometric form.

Landmarks are anatomically recognizable areas which are selected properly to capture the shape and is capable of being replicated. The semi-land marks [15], are used when the location of a landmark along a curvature might not be identifiable or repeatable. Thus, with these landmarks and semi-landmarks, a three-dimensional image can be created which aids in assessment of age.[13-15]

There is no systematic review which evaluates the accuracy of using geometric morphometric method for craniofacial age estimation. Thus, the objective of this review is to summarize the results of the studies done for age estimation by geometric morphometric method using craniofacial units and to assess its accuracy and reliability.

MATERIALS AND METHODS

Protocol and registration

The review is registered in PROSPERO (International prospective register of systematic reviews) with the number CRD42020206250. This systematic review used the Preferred Reporting Items for Systematic Review and Meta Analyses (PRISMA) guidelines.[16]

Search strategy:

The comprehensive data search was performed in 'PUBMED', 'GOOGLE SCHOLAR' and 'SCOPUS' data bases for publications till 1st September 2021. Language restrictions were applied and only studies done in English language were included.

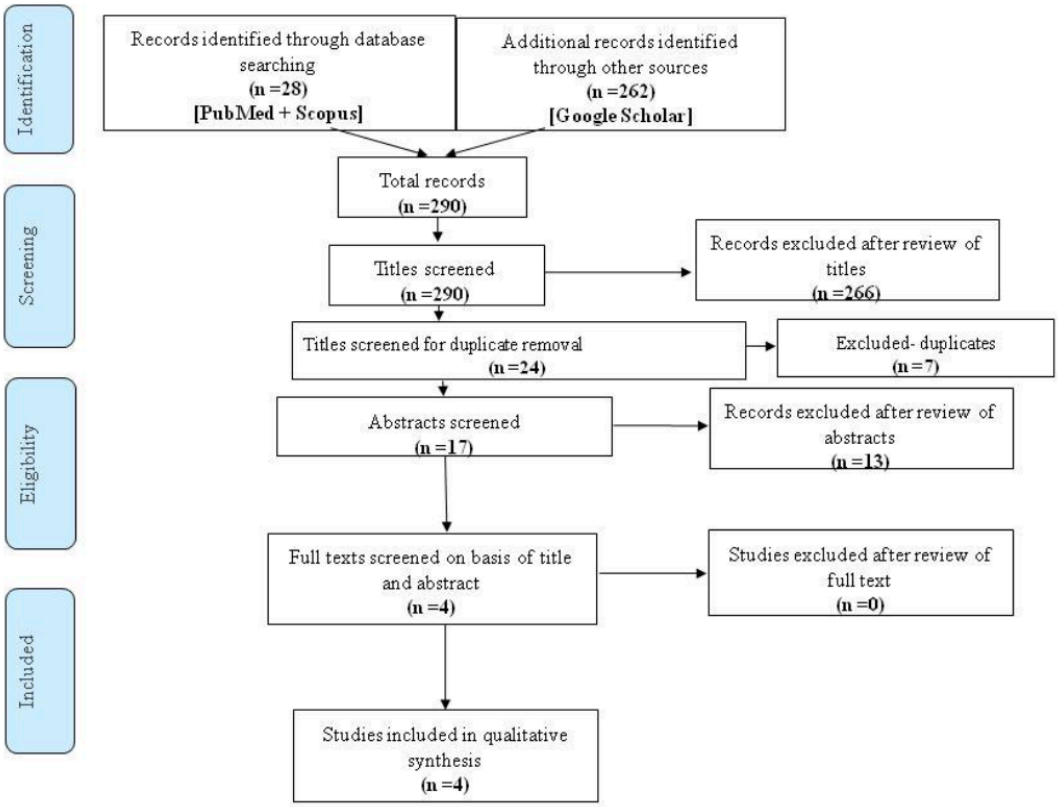
The search strategy used Medical Subject Heading (MeSH) terms like "Geometric Morphometrics AND Craniofacial Skeletal Unit" OR "Skulls, Cranium, Calvaria, Calvarium AND Age Estimation". Original studies done on geometric morphometrics in craniofacial skeletal age estimation were included and Review articles, Case reports & case series, Conference abstracts, Editorials, Commentaries Animal studies, Studies published in other languages were excluded.(Table 1)

Table 1. List of search engines used to retrieve articles along with keywords and search terms

Data base	Keywords and search terms	Number of articles Retrieved
PubMed	(("geometric"[All Fields] OR "geometrical"[All Fields] OR "geometrically"[All Fields] OR "geometrics"[All Fields]) AND ("morphometric"[All Fields] OR "morphometrical"[All Fields] OR "morphometrically" [All Fields] OR "morphometrics"[All Fields]) AND ("humans"[MeSH Terms] AND "english"[Language]) AND ("craniofacial"[All Fields] OR "craniofacies"[All Fields]) AND ("humans"[MeSH Terms] AND "english"[Language]) AND ("skeletal"[All Fields] OR "skeletals"[All Fields])) AND ((humans[Filter]) AND (english[Filter]))	**24**
Google scholar	Geometric morphometrics AND craniofacial age AND skeletal age	**262**
Scopus	(TITLE-ABS-KEY (geometric) AND TITLE-ABS-KEY (morphometrics) AND TITLE-ABS-KEY (cranial) AND TITLE-ABS-KEY (skeletal) AND TITLE-ABS-KEY (age) AND TITLE-ABS-KEY (estimation))	**4**
	Total	**290**

Two review authors screened the titles and abstracts obtained by search strategy and included them if they met the inclusion criteria. Based on this, Full texts of 24 studies were obtained. Finally, the search yielded 4 studies to be included in systematic review. (Fig 1). Any disagreement between the authors was resolved by discussion

Figure 1. Flow diagram depicting the process of selection and exclusion of articles at each step



Risk of bias assessment

AQUA (Anatomical Quality Assessment) tool.[17] was used to assess the quality of the articles. The tool contains 5 domains and 20 signaling questions. The answers of these signaling questions are, "Yes", "No" or "Unclear". These answers indicate Risk of bias which is Low, High and Unclear, respectively. "Low", Risk of bias was judged when all the signaling questions were answered as "Yes". A consensus point was met by the authors when an answer was obtained as "No" as it indicated potential bias. Indication of "High" risk of bias suggested that the data obtained from the studies was insufficient and the "Unclear" option was used.

Among these 20 signaling questions 2 questions were eliminated as they were not applicable for the study design. (DOMAIN 4 and 5 the 4th signaling question)

RESULTS

Study selection

262 records were identified through data search using search strategy in google scholar, 24 records from PubMed and 4 records from Scopus. Finally, 4 articles were selected for qualitative synthesis as they were fitting in the inclusion criteria of the study.

Data Extraction and Study characteristics

A summary of the 4 studies included in the final systematic review is provided in (Table 2). Individual study characteristics and the outcome extracted from each included study are given below:

Table 2. Individual study characteristics and the outcome extracted from each included study are given below

Author	Jose Braga et al[18] 2007	Antoine Saade et al[8] 2018	Melissa Niel et al[19] 2019	Danniel Franklin et al[20] 2007
Title	Estimation of pediatric skeletal age using geometric morphometrics and three-dimensional cranial size changes	Predictability of Craniofacial Skeletal Age with Geometric Morphometrics	Maturation of the human foetal basioccipital: quantifying shape changes in second and third trimesters using elliptic Fourier analysis	Mandibular morphology as an indicator of human subadult age: geometric morphometric approaches
Location and race	France and North Africa, Toulouse,	lebanon	Marseilles, France	South African Bantu and African American
Study design	Cross sectional	Cross sectional	Cross sectional	Cross sectional
Imaging technique	CBCT	CBCT	CBCT	CBCT
Craniofacial skeletal unit	SKULL	SKULL	Basico occipit- CT-Skull	MANDIBLE
Age	Females- 3days to 17.67 yrs, Male- 3 to 16.5 yrs	7 - 15 yrs	Foetus between 18 - 41 Gestational weeks	1- 17 yrs
Sample size	127	48	221	79
Landmarks / location	supraorbital canal, supraorbital fissure,infraorbital canal ,round foramen and mental foramen and basicranial skeleton	Right and left supraorbital foramina , right and left superior orbital fissures, right and left foramen rotundum canals, oval foramina . Right and left infraorbital foramina . right and left mental foramina	Basico occipit	Coronion, Mandibular notch, Condyle, Posterior ramus. GonionMandibular body. Lateral gnathion infradentaleMentale, Posterior alveola Anterior ramus,Gnathion,Pogonio.symphysis Infradentale
Software used	Gamme Cépha © http://cepha.free.fr/gammecepha.php)	AVIZO 3D analysis software (version 8.1.1; FEI Visualization Sciences group, Merignac, France)	AVIZO Standard Edition software (v.7.0.0, Visualization Sciences Group, SAS)	Microscribe G2X portable digitizer running Inscribe-32 software
3D coordinates For calculating centroid size	Morphologika © (http://www.york.ac.uk/res/fme/resources/software.htm)	MorphoJ Software, version 1.06d	Morpho, Geomorph, TPSDIG2 v.2.17 digitization Programme., Elliptic Fourier analysis	Morphologika2, NTSYS-pc 2.2f
Statistical tests for Removal of shape variations	Generalized Procrustes analysis	Generalized Procrustes analysis	Generalized Procrustes analysis, Principal component analysis,	Generalized Procrustes analysis, Principal component analysis

Author	Jose Braga et al[18] 2007	Antoine Saade et al[8] 2018	Melissa Niel et al[19] 2019	Danniel Franklin et al[20] 2007
Statistical test used	Conventional least square linear regression analysis	Kolmogorov–Smirnov and Shapiro-Wilk statistics Quartile-Quartile plots. Pearson's coefficient Cook's distances, Mahalanobis distances, Residuals, Multiple regressions using SPSS v22.	Procrustes ANOVA RStudio using the software packages -Momocs, Morpho, Geomorph, factoextra, efourier and iefourier functions	Linear regression analyses Multiple regressions SPSS 11.5.0 TPSSmall 1.20
Outcome results	. Accurate results can be obtained when it is based on 3D facial size changes and study suggested that centroid size of the facial skeleton can be used as an age-related variable without any loss of accuracy with increased age.	. This study developed a new equation for determining craniofacial skeletal age was using the centroid size of the craniofacial frame, gender, and the known chronological age.	The study first quantified overall shape changes of the basioccipital between gestational ages and suggested that the morphological shape changes throughout the foetal period can be useful for anthropological studies and provide new perspectives for immature age estimation methods.	The study results showed that the mandible can be used to predict age in the subadult skeleton with accuracy comparable to standards based on the dentition (standard error rates arebetween ±1.3 and ±3.0 years) and will be accurate when adolescents are Included in the sample.

Jose Braga et al, [18] studied geometric morphometrics and its application on skeletal age using 3D shape changes occurring in the cranium of pediatric samples. The study was conducted on CT scan samples from different geographic locations like North Africa and France, Neuroradiology Unit, the Clinique Pasteur, Toulouse (France). Two major cranial components were considered the i.e, the face and base and were represented by skeletal landmarks. A cross-sectional sample of 73 non-adult females and 54 non-adult males ranging from 3 days-17.67 yrs and 3 days-16.5 yrs respectively were considered. Further using the Gamme Cepha software three dimensional points were marked on the CT scans.

The landmarks were distinguished in two configurations, both representing a major cranial component such as, 1. Facialand 2. Basicranial wire frame. Using the Morphologika software the centroid size was calculated for each wire frame and individual. Conventional least square liner regression and standard error at 95% confidence limit was used to indicate the accuracy. Standard error at 95% confidence level were, lower or equal to 2.1 years i.e., for the facial wire frame-1.27 to 2.09 and for the basicranial wire frame-1.52 to 2.64 years. The study showed more accurate results with the use of 3D facial changes only and the facial wire frame showed more significant and accurate results than the basicranial wire with an increasing age and the study concluded that use of geometric morphometrics gave more accurate results with an increasing age, contrary to most methods used in pediatric age estimation. This method has been reported to be reliable because it has demonstrated greater accuracy in centroid measurements of the facial skeleton with increasing age. This method is applicable from the early post-natal age to the end of adolescence and can be used on cranial remains.

To predict the craniofacial age Antoine Saadé et al,[8] conducted a study using geometric morphometrics technique and CBCT scans of 48

participants, which included 18 males and 30 females. This was further correlated with skeletal age which was obtained from hand and wrist radiograph. Six bilateral anatomical land marks were selected based on the method used by Wilson-Pauwels et al using a AVIZO 3D analysis software on the CBCT scans.The landmark analysis was performed using the MorphJ software and the 3D coordinates were obtained. Further, a Procrustes analysis was performed and the centroid size was calculated for each configuration. Mean skeletal age assessed was 11.9 ± 2.4 years and centroid size 151.5±7.2 was significantly correlated with chronological age and skeletal age. The study further determined a new equation for calculating craniofacial skeletal age using centroid size of the craniofacial frame , gender and craniofacial age . The study also highlighted the use of centroid size of craniofacial frame based on trigeminal landmarks as a good predictor to assess the skeletal age. The study emphasized on adding additional landmarks and a bigger sample size to allow better accuracy and possible results divergence related to gender.

Mellissa Niel et al, [19] conducted a study on shape changes occurring in the basioccipital bone of human fetus during third and second trimesters to understand the maturational changes with the help of geometric morphometrics method. The study identified the precise shape changes between gestational ages that is from 18 to 41 gestational weeks and included 221 foetal CT scans with no pathologies among which 75 were from girls, 110 from boys and 36 unknown sexes.The landmarks were assessed on the Basioccipital bone using ImageJ, AVIZO software and landmark points were further digitized with the TPSDIG2.

Using these landmarks, geometric morphometrics analysis was performed with Elliptic Fourier analysis and Principal components analysis (PCA), Procrustes ANOVA was performed for selection of harmonics and calculation of error, the morphological disparity among the stages were calculated with the individual. The study results showed that the youngest foetuses have the highest intra-stage shape variation.

Thus, the study results showed that the impact of measurement error was very low, indicating that the protocol was reliable and reproducible. The study concluded that the morphological shape changes throughout the foetal period can be useful for anthropological studies and by geometric morphometric method it is possible to quantify shape changes, assess interstage shape variability and precisely identify the shape changes between gestational ages. Daniel Franklin et al [20] studied effectiveness of geometric morphometrics using three dimensional multivariate descriptors of size and shape for subadult forensic age estimation . 79 known age and sex subadult mandibles ranging from 1-17 yrs of age were used. The sample comprised of 43 males and 36 females of South African Bantu and African American origin. The portable Microscribe G2X digitized scanner was used and 38 mandibular landmarks were recorded in three dimensions. The centroid size was calculated for individual configuration and further generalized Procrustes analysis (GPA) was done to standardize each coordinate to remove any size variation. The geometric morphometric analysis was performed with morphologica and NTSYS-pc 2.2f. Linear regression analyses and multiple regressions was performed for shape variations, cross-validate of the regression models was performed using jackknife procedure and TPSS mall 1.20 and SPSS 11.5.0 software's were used for other statistical results. A standard error ±1.3–2.2 years for size and ±1.7–3.0 years for shape, ±1.4– 1.8 and ±2.0–3.0 years for age was noted. The study concluded that mandibular morphology can be used to predict subadult age with a high degree of expected accuracy. Age prediction standards based on geometric morphometric data, are suitable for children (Below 10 years of age) or subadults (1– 17 years of age). It was also noted that prediction accuracy was better when the two populations and/or sexes were treated separately.

Risk of bias

The included studies have shown low risk of bias thus suggesting that the studies have good quality.

DISCUSSION

Skeletal age is considered as the gold standard for assessment of maturation and growth in infants, children and adolescents.[21,22] Geometric morphometrics is a latest approach to shape analysis which enables to visualize and quantify accurate morphological variations.[23-25]

In literature studies have been conducted on geometric morphometrics and its application in skeletal age estimation, sexual dimorphism, shape changes due to growth etc. Geometric morphometrics is a relatively newer technique and this advancement and increased approach the concept of age estimation has provided a new avenue for research and its various stake holders in different fields such as forensic odontology, anthropology, paleontology, law enforcement etc.

Chatzigianni et al [26] conducted a study on the shape of cervical vertebrae using geometric morphometrics and concluded that chronological age and centroid size were better predictors when used as independent variables along with vertebral shape and hand-wrist ossification. Y. Scholtz et al [27] conducted a study on sexual dimorphism of the human scapula and found that use of geometric morphometrics in estimation of sex using the shape of scapula can act as a good indicator and also suggested that better statistical results were obtained when the complete scapula was analyzed. San-Millán et al [28] studied the variability in shape of acetabulum fossa and acetabulum of humans using geometric morphometrics and correlated it with sex and changes related to age.

A preliminary study conducted by Gleim [29] using geometric morphometrics for juvenile dental age estimation demonstrated that tooth shape and size when measured with geometric morphometrics, statistically corelated with the chronological age of individual. Also, principal component analysis reveals that mandibular third molars have the highest correlation between age and shape.

There are a few studies available on application of geometric morphometric method for craniofacial age estimation. Due to lack of consensus in the uniform application of geometric morphometric method for craniofacial age estimation the need to perform this review was percieved. Hence, the review aimed to evaluate the accuracy and reliability of geometric morphometric technique for craniofacial skeletal age estimation.

The four studies included in this review assessed geometric morphometrics and provided a cumulative data with an all-inclusive picture, its applicability, accuracy and reliability in assessment of skeletal age. Two studies included samples from Toulouse [18] and Marseilles, France[19,] other two studies were from Hadath, Lebanon[8] and included collection of skeletons from two different populations. One from the Raymond A. Dart- Bantu tribe of south Africa and second from Todd Osteological collections- Hamann tribe of African American's [20] respectively. As the sample sizes were taken from different genetic groups, which did not include all the 4 major groups, the influence of genetic origin cannot be assessed.

The estimations of age was done using CBCT scan and digital images of males and females using craniofacial skeletal units such as skull and mandible ranging in age from 18-41 Gestational Week to 18 years. The selected units were- CT scan images of Skull- face and base, CBCT scan images of basioccipit and digitized images of the mandible. This poses an advantage as there are no limitations for the age group to be studied on and even one bone from the craniofacial skeleton can be digitized and used.

There were methodological disparities among the included studies which were identified in this review. The software's used among the studies were different. Various analysis software were used like AVIZO 3D analysis software [18] ,Gamme Cepha and Microscribe G2X [20] portable digitizer for procuring the cartesian 3D coordinates.

Morphologika [18,20] and MorphJ [8] software's were used in three studies for obtaining the 3D landmark configurations or wire frames for centroid size calculation. Outline digitization and normalization was done using the TPSDIG2, Morpho and Geomorph software's for centroid size calculation in another study. These software's are technique sensitive, expensive and need prior training. Yet as the technological progress is rapid newer and cheaper options are being explored so that they would sufficiently aid in exploring geometric morphometrics.

AQUA tool [17] is a tool used for quality assessment of anatomical specimens. In our systematic review This tool was modified according to the included studies and applied on the CT scans, digitalized images of various craniofacial skeletal units for risk of bias assessment. The tool has 5 main domains with each domain having their separate signaling questions. One question each, from domain 4 and 5 were excluded for our review as they were not applicable for the study design. It was found that after the quality assessment of the four included studies all the

studies have shown low risk of bias thus suggesting that the studies have good quality.
The Generalized Procrustes analysiss[3] was done in all the studies which superimposes a population of shapes, and removes non-shape related differences like, size, orientation and position. Finally various statistical tests were performed in all the included studies for assessment of skeletal age. Two studies [18,20] performed linear regression analysis and other two studies performed multiple regression analysis[8] and Procrustes ANOVA, Principal component analysis.[19]
Intra and inter-observer agreement and error, were done for the selection of landmarks in two studies [18,20,] one study [8] performed Inter and intra- observer agreement for selection of the radiographs and in another study the error was calculated for the validation of the samples[19]Standard error at 95% confidence interval for estimation of age was reported in three studies [8,18,20] and one study [19] did measurement error for repeatability and reproducibility.
It was necessary to read the papers several times to understand the methodology and how the accuracy was reported. In all the four studies included in this systematic review, geometric morphometric method could accurately estimate age of craniofacial units and reliability was usually associated with highest accuracy in all the studies.
To our knowledge, this is the first systematic review conducted on predicting the accuracy and reliability of using geometric morphometric technique in craniofacial skeletal age estimation. Limitations noted in the included studies were high heterogenicity in craniofacial units used for assesment, age groups analyzed, sample size, approaches in the steps performed in geometric morphometrics method, software's used and statistical tests performed.
We limited our search only to papers published in English language and unpublished studies, Conference abstracts, Editorials etc. were not included in this review so the interpretation and representation of the global literature on geometric morphometric was limited.
Due to varied interpretations and in consistencies of findings between studies included with regard to different age groups and sexes, it was not possible to perform a meta-analysis.
We recommend the future researches to conduct more studies on this technique and report the study results in an elaborate and specific way in terms of sample size and gender, mean, standard error, standard deviation. Also, studies are required to give a steady opinion about the software's used in the methodology, its ease in use and availability. Thus, in order to warrant the technique of geometric morphometrics and to allow its better application in craniofacial skeletal age estimation to obtain accurate and reliable outcomes.

CONCLUSION

This systematic review on geometric morphometrics in craniofacial skeletal age estimation has highlighted all the merits and demerits of this technique. It was noted that this technique is applicable and facilitates rapid, accurate and reliable identifications of a single bone or skeletal remain of the craniofacial skeletal unit, even with a digitalized image or a CBCT scan. The centroid size calculated using these images is said to be the highest predictor of age. However, the reliable data which was necessary for performing the meta-analysis was insufficient. Hence there is a need for conducting more studies that can estimate the craniofacial skeletal age using geometric morphometrics.

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