Evaluation of natural growth rate and recommended age for shaving procedure by volumetric analysis of craniofacial fibrous dysplasia

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Abstract

Background: We evaluated the preoperative natural growth pattern of craniofacial fibrous dysplasia and postoperative volume changes in patients undergoing shaving procedures.

Methods: Thirty-three patients who underwent serial computed tomography (CT) preoperatively and/or postoperatively were identified. The natural tumor growth rate was assessed using preoperative CT scans. The postoperative tumor regrowth rates and relevant variables were analyzed.

Results: The preoperative tumor growth rates were significantly lower in patients aged ≥16 years than in those aged <16 years (P < .001). The postoperative tumor regrowth rates were significantly greater when a shaving operation was performed at age <16 years than at age ≥16 years (P = .04). In patients with clinical recurrence, the postoperative remnant tumor volume was inversely correlated with the tumor regrowth rate.

Conclusions: The tumor growth rate of craniofacial fibrous dysplasia significantly decreased after age 16. This should be considered when conducting functional and aesthetic assessments in planning for the shaving of craniofacial fibrous dysplasia.

Keywords: contouring, craniofacial, fibrous dysplasia, recurrence, shaving procedure

1 | INTRODUCTION

Fibrous dysplasia (FD) is a benign bone disease in which the normal bone is replaced by fibro-osseous tissue. It accounts for approximately 5% to 7% of benign bone tumors and can affect one bone (monostotic) or multiple bones (polyostotic).1 Craniofacial involvement is noted in 50 to 100% of the patients with polyostotic FD and in 10% of the patients with monostotic FD.2-4 Among patients with craniofacial involvement, the frontal bones are the most commonly affected, followed by the sphenoid, ethmoid, parietal, temporal, and occipital bones.3

The mainstay of treatment is reconstruction after radical resection and more conservative operations such as the shaving procedure. In adult patients, many surgeons favor radical resection and reconstruction,6 whereas conservative therapy is considered for the tooth-bearing jaw area and skull base.7 Children are usually kept under observation until the disease progression rate is...
decreased, but surgical management can also be performed in younger patients with lesions, which cause functional impairment or severe deformity, or based on the patients’ desire. Generally, conservative therapy is considered more appropriate than radical resection to prevent growth alteration in children, especially in patients with massive bone involvement. The shaving procedure has the advantage of a short recovery time, low incidence of postoperative deformity, and less functional deficit. However, postoperative tumor regrowth is the main disadvantage of a conservative operation.

The natural growth rate and disease course of craniofacial FD remain unclear. To the best of our knowledge, a serial follow-up study with a quantitative analysis of craniofacial FD volume has not been conducted until recently. The progression of FD is believed to stop after adolescence in most cases. However, this assumption is based on clinical implications and is not supported by objective quantitative data. Owing to the lack of quantitative data regarding the natural growth and postoperative regrowth patterns of FD, the timing and extent of surgery remain controversial, especially in children in whom FD lesions tend to be more active. This study aimed to evaluate the natural growth rate of craniofacial FD by performing quantitative analysis of preoperative serial computed tomography (CT) scans to help decide the timing of surgery for children. Furthermore, we assessed the tumor regrowth rate after shaving procedures and associated factors using quantitative data to aid in preoperative counseling and planning for the shaving procedure.

2 | PATIENTS AND METHODS

After obtaining institutional review board approval, we retrospectively reviewed the data from patients who were diagnosed with craniofacial FD between January 2001 and February 2019. Patients were included if they underwent at least two consecutive CT scans preoperatively and/or postoperatively. The patients’ medical records were reviewed for demographic data, surgical history, age at presentation, affected areas, and clinical recurrence after the shaving procedures. Clinical recurrence was defined as a diagnosis of recurrence on clinical examination and assessment of serial medical photographs taken from various angles by the senior author.

Tumor volume was measured using CT images by two different physicians, using the Invesalixus version 3.1.1 software (https://www.cti.gov.br/invesalixus). The threshold was adjusted to the predetermined bone threshold for all CT scans because the threshold can affect the tumor volume measurements. Thereafter, we outlined the tumor borders in the axial scans and performed three-dimensional reconstruction of the tumor. The tumor volume was automatically measured by the program. The preoperative tumor growth rate was calculated using the tumor volume data from two consecutive CT scans performed preoperatively. The specific formula used to measure the tumor growth rate is given below:

\[
\text{Tumor growth rate (\% per year)} = \frac{\text{Mass volume 2} - \text{Mass volume 1}}{\text{Age 2} - \text{Age 1}} \times 100
\]

The postoperative tumor regrowth rate was calculated using data from two consecutive CT scans performed postoperatively. The above-described formula for the preoperative measurements was also used for the postoperative measurements.

The preoperative tumor growth rates were analyzed to evaluate the natural growth pattern of craniofacial FD. A scatter plot was created, and the change point was determined as the candidate point corresponding to the reduced model with the highest likelihood. The patients were divided into two groups according to this change point, and the tumor growth rate was compared between the two groups. For the postoperative data, the patients were divided into two groups according to age at operation by using the same change point as that used for the preoperative data. Data were excluded after the second operation if the patient underwent two or more operations for FD, considering that the number of operations might act as a confounder. The tumor regrowth rate was compared between the two groups, and other variables, such as preoperative tumor volume and tumor resection rate when shaving procedures were performed, were evaluated. Quantitative data recorded when patients were diagnosed with clinical recurrence were also assessed to evaluate the association between the tumor regrowth rate and clinical recurrence. Figure 1 shows an example case with both preoperative and postoperative serial CT scans. Subgroup analyses were also performed in each age group to assess the differences in the tumor growth rate between the male and female patients using the preoperative and postoperative data.

2.1 | Statistical analyses

Spearman’s correlation coefficient was used to assess the relationship between age and the tumor growth rate. Segmented linear regression models were used to identify the change point in the growth rate using the preoperative CT data. The R package “Chngpt” for threshold regression model estimation and inference of threshold
linear regression models with a segmented-type change point was used for the analysis. By using the threshold as a reference value, the preoperative and postoperative CT data were separately analyzed using linear mixed-effects models to evaluate the differences in the natural growth and postoperative regrowth rates of FD and associated factors. A $P$ value of $<.05$ was considered statistically significant. All analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina) and R 3.4.3 (Vienna, Austria; http://www.R-project.org/).

### RESULTS

Among 54 patients who were diagnosed as having FD with craniofacial involvement, we identified 33 patients who met the inclusion criteria at our institution during the 19-year study period, and their demographic characteristics are shown in Table 1. The mean number of CT scans was $3.70 \pm 1.90$ for each patient. The preoperative indications for CT scans included surgical planning, evaluation of optic nerve compression, and development or aggravation of symptoms, such as visual acuity changes, diplopia, headache, nasal obstruction, purulent nasal discharge, auditory canal obstruction, trigeminal neuralgia, and severe deformity. The postoperative indications included evaluation of the extent of surgical resection, breakdown of the surgical incision, hematomas, and development of neurological symptoms or prolonged pain, especially when the symptoms developed in patients in whom the neurosurgical or otolaryngological procedures were performed simultaneously. Preoperative CT scans for another shaving procedure or other surgical procedures, such as canaloplasty or decompression procedures, were also included in the postoperative CT scans when these scans were taken consecutively to the postoperative CT scans. In cases not covered by national insurance or in those with issues regarding the cost of magnetic resonance imaging (MRI) scans, CT scans were used as substitutes after the risks of CT irradiation were explained to the patients and their parents.

Eight patients had polyostotic FD (24.2%), and 25 patients had monostotic FD (75.8%). The mean age of the patients at diagnosis was $15.0 \pm 9.6$ years (range, 5.0 to 48.7 years). The mean follow-up period was $78.2 \pm 39.5$ months.

### Table 1: Clinical characteristics of the patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>33</td>
</tr>
<tr>
<td>Mean age $\pm$ SD (range), y</td>
<td>$15.0 \pm 9.6$ (5.0-48.7)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
</tr>
<tr>
<td>Type of tumor</td>
<td></td>
</tr>
<tr>
<td>Monostotic</td>
<td>25</td>
</tr>
<tr>
<td>Polyostotic</td>
<td>8</td>
</tr>
<tr>
<td>Number of operations</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Mean follow-up period $\pm$ SD (range), mo</td>
<td>$78.2 \pm 39.5$ (10.2-122.2)</td>
</tr>
</tbody>
</table>
Among the 33 patients, 24 and 20 patients underwent two or more consecutive CT scans preoperatively and postoperatively, respectively. Eleven patients underwent both preoperative and postoperative serial (two or more) CT scans.

3.1 Preoperative measurements

Forty-one calculations of the natural tumor growth rate were obtained from the preoperative measurements in 24 patients. Age and the tumor growth rate were inversely correlated, as determined using a scatter plot (Figure 2). Using the calculations derived from each patient’s initial two consecutive CT scans, the change point was determined to be 16 years of age by segmental linear regression analysis. The mean tumor growth rate was 23.1% per year in the younger age group (<16 years) and 2.7% per year in the older age group (≥16 years), and the difference was statistically significant (P < .001). Patients with polyostotic FD were younger and had larger tumors than those with monostotic FD at diagnosis, but the tumor growth rate was not significantly different between the two groups (15.7% per year and 19.9% per year, respectively; P = .99; Table 2). In subgroup analysis of the younger age group, the tumor growth rates were higher in the male patients than in the female patients, but the difference was not statistically significant (27.6% per year vs 18.3% per year, respectively; P = .65). In the older age group, the tumor growth rates were higher in the female patients than in the male patients, but the difference was not statistically significant (2.1% per year vs 4.2% per year, respectively; P = .45).
3.2 Postoperative measurements

Twenty-eight calculations of the postoperative tumor regrowth rate were obtained from 20 patients. Age and the tumor regrowth rate were inversely correlated, as determined by a scatter plot (Figure 3). The patients were divided into two groups according to the age when the first operation was performed. The change point (16 years of age) obtained from the preoperative measurements was used to divide the postoperative tumor regrowth rate. The younger age group underwent the shaving procedure at age < 16 years, and the older age group underwent the procedure at age ≥ 16 years. For the younger age group, the mean age when the shaving procedure was performed was 12.3 ± 2.5 years (range, 8.3 to 15.4 years), and the mean period of CT follow-up was 52.8 ± 23.8 months (range, 32.5 to 109.5 months). For the older age group, the mean age when the shaving procedure was performed was 23.8 ± 11.1 years (range, 16.0 to 55.0 years), and the mean period of CT follow-up was 33.7 ± 24.4 months (range, 4.7 to 90.4 months). The tumor regrowth rate was significantly higher in the younger age group than in the older age group (17.1% per year and 4.7% per year, respectively; P = .04; Table 3). The preoperative tumor volume was not significantly associated with the postoperative tumor regrowth rate (P = .06). The tumor resection rate and tumor type were also not associated with the tumor regrowth rate (P = .29 and .17, respectively). During the study period, nine patients were diagnosed with clinical recurrence. The mean age at diagnosis of clinical recurrence was 18.1 ± 4.5 years (range, 9.9 to 26.8 years).

![Figure 3](image-url) Scatter plot showing an inverse correlation (Spearman’s correlation coefficient, r) between the patients’ age and postoperative regrowth rate of craniofacial fibrous dysplasia after the shaving procedure [Color figure can be viewed at wileyonlinelibrary.com]

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of calculations of regrowth rate</th>
<th>Mean age at shaving procedure ± SD, y</th>
<th>Mean growth rate of tumor ± SD, %/y</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16 y old</td>
<td>12</td>
<td>12.1 ± 2.5 (range, 8.3-15.4)</td>
<td>17.1 ± 12.3 (range, 5.4-49.3)</td>
<td>.04</td>
</tr>
<tr>
<td>≥16 y old</td>
<td>16</td>
<td>24.0 ± 11.0 (range, 16.0-55.0)</td>
<td>4.7 ± 4.6 (range, 0.1-14.6)</td>
<td></td>
</tr>
</tbody>
</table>
postoperative remnant tumor volume (on the postoperative CT scan obtained immediately after the shaving procedure) and tumor regrowth rate at the time of diagnosis of clinical recurrence was observed only in patients diagnosed with clinical recurrence. Two different growth patterns were observed in clinical recurrence: a high regrowth rate with a low tumor volume (arrow) and a low regrowth rate with a high tumor volume (asterisk) [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 4 An inverse correlation (Spearman’s correlation coefficient, r) between the immediate postoperative tumor volume after the shaving procedure and the tumor regrowth rate at the diagnosis of clinical recurrence was observed only in patients diagnosed with clinical recurrence. Two different growth patterns were observed in clinical recurrence: a high regrowth rate with a low tumor volume (arrow) and a low regrowth rate with a high tumor volume (asterisk) [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

The present study evaluated the natural growth rate of craniofacial FD and the tumor regrowth rate after the shaving procedure by performing a quantitative analysis of serial CT scans and found inverse correlations between patient age and both the natural tumor growth and postoperative tumor regrowth rates. Sixteen years of age was determined to be the change point of the tumor growth rate based on the analysis of the preoperative serial CT data. When comparing the tumor growth rate of the two groups defined according to the change point, significantly higher natural growth and postoperative regrowth rates were found in the younger age group than in the older age group. These findings were consistent with those of a study by Park et al., who reported an association between incomplete resection of FD at age < 17 years and tumor regrowth. The cut-off age in Park et al.’s study was not derived from objective assessment but from an arbitrary classification. Conversely, in the present study, the cut-off age was calculated by segmental linear regression analysis using quantitative volumetric data. Patients with polyostotic FD had a higher tumor volume and younger age at diagnosis than those with monostotic FD, but the natural growth and postoperative regrowth rates of FD were not significantly different between the polyostotic and monostotic FD groups. In the patients with clinical FD recurrence, the postoperative remnant tumor volume and tumor regrowth rate were inversely correlated. In subgroup analyses, both the preoperative and postoperative data showed that the tumor growth rates were higher in the male patients than in the female patients in the younger age group and that the tumor growth rates were higher in the female patients than in the male patients in the older age group.

Several studies have evaluated the surgical outcomes of craniofacial FD and the relevant factors associated with the recurrence or regrowth of FD. Hence, patients with recurrence or regrowth of FD were identified. However, the definition of recurrence or regrowth was not described in most of these clinical series, indicating that the diagnosis was made according to clinical examination findings or the physician’s judgment based on radiological evaluation, such as a CT scan, rather than by volumetric measurements. To evaluate the differences between the nonvolumetric assessment of recurrence and volumetric regrowth rates, we defined clinical recurrence as the diagnosis of recurrence by clinical examination and assessment of serial medical photographs and identified patients who were diagnosed with clinical recurrence in the study population. We found that the immediate postoperative remnant tumor volume and tumor regrowth rate were inversely correlated in patients with clinical FD recurrence after the shaving procedure, indicating that patients with a larger remnant tumor volume tended to be more frequently diagnosed with clinical recurrence, although the regrowth rate was low. However, patients with a smaller remnant tumor volume were diagnosed with clinical recurrence only when the regrowth rate was high. We believe that a certain increase in the tumor volume is necessary to diagnose clinical recurrence, regardless of the tumor regrowth rate, because the clinical diagnosis of recurrence is generally made based on the clinician’s subjective viewpoint and not on quantitative volumetric measurement. Therefore, we can infer that the clinician’s visual diagnosis of recurrence was made based on the increased amount of bone,
not on the growth rate of bone. Therefore, tumors with a low regrowth rate and large tumor volume and those with a high regrowth rate and small tumor volume were classified in the same category as clinical recurrence (Figure 4). The heterogeneity of the nature of tumor growth in cases of clinical recurrence could make it difficult to investigate the relevant factors and causes of recurrence or regrowth of FD. The definition of recurrence or regrowth of FD needs to be refined, and the quantification of tumor volume and volume changes should be included in the definition of recurrence or regrowth, especially for research purposes. Furthermore, when performing conservative management, such as shaving procedures in patients with a large tumor volume, overcorrection might be considered because clinical recurrence can easily develop even in patients with low regrowth rates.

Controversy still exists with respect to the best type of surgical management for FD (including conservative

**FIGURE 5**  A, A 9-year-old boy diagnosed with left hemifacial fibrous dysplasia. The tumor volume was 245.5 cm³. B, Preoperative appearance at 12 years of age. The tumor volume increased to 349.1 cm³, and a shaving procedure was planned according to the patient’s desire. C, Clinical photographs taken at 3 weeks postoperatively. The tumor volume decreased to 293.3 cm³ after shaving, as noted on a computed tomography scan taken to evaluate a postoperative hematoma on postoperative day 3. D, Four years after the shaving procedure (16 years of age), the patient was diagnosed with clinical recurrence. The tumor volume increased to 404.3 cm³. The postoperative regrowth rate was 9.5% per year, and the tumor had increased by 111.0 cm³. The patient was diagnosed with clinical recurrence despite the low tumor regrowth rate because of the large remnant tumor volume after the shaving procedure [Color figure can be viewed at wileyonlinelibrary.com]
surgeries and radical excision and reconstruction)\(^\text{15}\) and the timing of surgical management.\(^\text{16}\) Surgeons supporting radical excision and reconstruction have raised issues regarding the high recurrence rates after conservative surgeries.\(^\text{6,8,14,17}\) Although this may be partially true, the main cause of high recurrence rates after a conservative surgery may be the age indication for surgical management, as conservative surgeries are more often indicated than radical excision and reconstruction in younger patients,\(^\text{14}\) and tumor growth rates usually decrease with age. Age should be adjusted for when comparing the postoperative recurrence rates between conservative surgeries and radical excision and reconstruction. According to the results of the current study, quantitative volumetric analysis revealed an abrupt decrease in the growth rate of craniofacial FD, and 16 years of age was determined to be the change point for the tumor growth rate. We believe that the tumor recurrence rates could be decreased when conservative surgeries are performed at \(\geq 16\) years of age.

Pediatric patients are known to be more sensitive than adults to ionizing radiation.\(^\text{18,19}\) Balancing the diagnostic purpose while minimizing the risks of CT imaging is mandatory for patients with craniofacial FD because repeated imaging is usually needed for patients who require neurological, ophthalmological, or otolaryngological evaluation or for those who are undergoing surgical procedures. Despite CT being the “gold-standard” imaging modality for FD, no widely accepted consensus or solid indication has been established regarding serial CT imaging for patients with craniofacial FD.\(^\text{20}\) During the study period, we attempted to reduce the dose of ionizing radiation in CT and the effective dose for each CT examination with the current pediatric dose reduction protocol of less than 1 mSv, which is equal to or less than the most recent protocol of low-dose CT.\(^\text{21,22}\) The risk of carcinogenesis has not yet been confirmed for the current low-dose CT protocol for pediatric patients.\(^\text{21,23}\) However, given the possible risk of ionizing irradiation even with low-dose CT, the number of CT scans must be reduced as much as possible, and other imaging modalities such as MRI or optical coherence tomography,\(^\text{24}\) could be considered when indicated.

On the basis of the results of the present study, several strategies could be planned when performing shaving procedures for craniofacial FD. Shaving procedures are highly recommended in patients aged \(\geq 16\) years, when indicated, because both the natural tumor growth and postoperative tumor regrowth rates were significantly lower in patients aged \(\geq 16\) years than in those aged \(<16\) years. Hence, a lower clinical recurrence rate would be expected. In patients aged \(<16\) years, the shaving procedures need to be delayed as much as possible until they reach 16 years old. When shaving procedures are deemed necessary in patients aged \(<16\) years, risk-benefit assessment and patient counseling would be warranted, as a higher remnant tumor volume can be associated with a higher clinical recurrence rate. We believe that this information is especially important for patients who are expected to have a postoperative remnant volume of more than 100 cm\(^3\), because these patients showed clinical recurrence, although the tumor growth rates were less than 10% per year in our data (Figure 5).

This study had some limitations. We could only include shaving procedures because of the small number of patients who underwent radical procedures. The single-center and retrospective study design could also be a limitation. Multicenter or population-based cohort studies are needed to confirm the reference age for surgical indication suggested by the present study, considering that craniofacial FD is a relatively rare disease and the largest cohort to date is limited to \(<100\) patients.\(^\text{6}\) However, the present study is, to the best of our knowledge, the first clinical series to evaluate serial quantitative data on the volume of craniofacial FD. The natural tumor growth and postoperative tumor regrowth rates after the shaving procedure presented in this study may help determine the timing and amount of shaving required in patients with craniofacial FD.

## CONCLUSIONS

Our results suggest that the growth rate of craniofacial FD is significantly decreased in patients aged \(\geq 16\) years both before and after a shaving procedure. If possible, the shaving procedure could be recommended for patients aged \(\geq 16\) years. In patients aged \(<16\) years, surgical procedures may be delayed; moreover, risk-benefit assessment and patient counseling are needed when the shaving procedure is deemed necessary. Further larger studies are warranted to confirm the change point suggested in the present study. The definition of recurrence or regrowth of FD needs to be refined on the basis of a quantitative volumetric analysis because the clinical assessment of recurrence or regrowth may be affected by the initial tumor volume.

## CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

## ETHICS STATEMENT

The study protocol was approved by the Institutional Review Board of Samsung Medical Center (IRB no.: SMC 2019-05-119). Patients or their parents or guardians provided written consent for the use of patient images.
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