Single-Slice Computed Tomography and Anthropometric Skinfold Analysis for Evaluation of Facial Lipoatrophy in HIV-Infected Patients

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We assessed the value of computed tomography (CT) and anthropometric skinfold analysis for evaluating subcutaneous facial fat in human immunodeficiency virus–infected patients. Patients with facial lipoatrophy had smaller areas of facial adipose tissue, lower ratios of adipose tissue area to total tissue area of the face, and lower malar skinfold values, compared with patients without facial wasting. CT may be a useful technique to diagnose and monitor facial lipoatrophy.

Lipodystrophy has been increasingly described in HIV-infected persons treated with antiretroviral drugs [1]. Examples of abnormal fat distribution in such individuals include fat accumulation in the abdomen and fat wasting in the limbs, buttocks, and face. Facial lipoatrophy is of particular concern because, for some patients, it is the most disfiguring and potentially stigmatizing feature of HIV-associated lipodystrophy syndrome.

Although some imaging techniques are available to quantify abdominal and peripheral fat [2, 3], the diagnosis of fat loss in the face currently relies exclusively on clinical examination. There is an urgent need for objective measurements to quantify facial wasting in HIV-infected patients undergoing therapeutic interventions, both for research and clinical purposes. The aim of the present study was to evaluate the value of quantitative CT and anthropometric skinfold analysis for evaluating subcutaneous facial fat in this population.

**Materials and methods.** We performed an exploratory cross-sectional study involving 61 consecutive HIV-infected patients receiving antiretroviral therapy. Lipodystrophy was defined on the basis of self report by the patients and was confirmed by results of clinical evaluation by their treating physicians. Given the results of these clinical evaluations, body changes were standardized as subcutaneous facial and/or peripheral lipoatrophy (i.e., isolated lipoatrophy) and/or as central obesity (i.e., mixed lipodystrophy). An independent clinician used a questionnaire to clinically rate facial fat loss according to 1 of 4 categories, ranging from absent to severe.

Facial fat composition was estimated by means of quantitative CT of the right region of the face. One measurement per patient was made. CT was performed with a Xpress/Gx helical CT scanner (Toshiba Medical Systems Europe). Exposure parameters were 120 kVp and 200 mAs. The area of adipose tissue was quantified in square centimeters by manufacturer-supplied software that sums the area of pixels in the CT scan that have values of −150 to −50 Hounsfield units, which corresponds to the density of adipose tissue. The total tissue area (TTA) and the adipose tissue area (ATA) of the right side of the face were assessed with a single 7-mm image slice at the level of the upper lip. The ratio of ATA to TTA in the face was automatically calculated by the software described above. The area of the right side of the face was determined by drawing a line along the skin surface that continued along external surface of maxilla, the ascending ramus of the mandible, and the posterior surface of the parotid gland (figure 1). All CT images were analyzed in a matrix of 512 × 512 pixels by 1 radiologist who was blinded to the clinical details of each patient.

A coefficient of variation of 1.2%–1.7% for successive CT-based analyses of abdominal fat area has been reported elsewhere [4]. In our study, the coefficient of variation for 10 successive CT-based analyses of 2 patients was determined to be 0.98%–2.19% for facial TTA, 1.48%–4.9% for facial ATA, and 1.28%–5.56% for the ratio of ATA to TTA in the face. Intra- and interobserver reproducibilities were determined by measurements, made by 3 observers, of ATA and TTA for 3 volunteers who had different grades of facial lipoatrophy severity. Each observer measured the facial fat area 6 times.

Caliper measurements (Tanner/Whitehouse Skinfold Caliper; Holtain Ltd.) of facial skinfold thickness at right malar region were performed once by an independent observer who was unaware of the objective of the study. While the patient was in a sitting position, an imaginary line was traced between the right mandible angle and the right lips angle, and the skinfold thickness between these 2 points was measured by holding the
caliper in a horizontal position. To determine the intraobserver reproducibility of this technique, the skinfold thickness on the face of 1 volunteer patient was measured by 3 observers 20 times each. Interobserver variation was tested on the basis of measurements, made by 5 observers, of skinfold thickness on the faces of 5 volunteers who had different grades of facial lipodystrophy severity.

The Ethical and Clinical Research Committee of Hospital General Universitario de Elche (Alicante, Spain) approved the study. All subjects were informed about the study and gave their consent before participation.

Results. Forty-four male patients and 17 female patients were included in the study. The median duration of HIV infection was 5.14 years (range, 16.27 years). All patients were receiving HAART, with a median exposure to antiretroviral therapy of 48 months (range, 132 months). Twenty-five patients (41.0%) were receiving nonnucleoside reverse-transcriptase inhibitors (NNRTIs), 23 (37.7%) were receiving protease inhibitors (PIs), and 13 (21.3%) were receiving NNRTI-PI–based regimens.

Lipodystrophy was present in 31 subjects (50.8%). Clinical examination revealed that 26 patients (42.6%) had subcutaneous lipodystrophy (19 had isolated lipoatrophy, and 7 had mixed lipodystrophy). The level of facial fat was clinically assessed as being abnormal in 22 patients (36.0%). Facial fat loss was rated as mild, moderate, or severe in 12 patients (54.5%), 6 patients (27.3%), and 4 patients (18.2%), respectively.

The level of reproducibility of the techniques used to measure facial fat levels was acceptable. Median intraobserver and interobserver variation coefficients for skinfold caliper measurements were 5.1% (interquartile range [IQR, defined as the difference between the third quartile and the first quartile], 0.5%) and 6.8% (IQR, 9.5%), respectively. No differences in these coefficients were found with regard to the severity of facial lipodystrophy. However, coefficients of variation for CT-based measurements tended to be higher for patients with more severe facial lipodystrophy. Thus, median intraobserver coefficients of variation for patients with mild, moderate, and severe facial lipodystrophy were 11.7% (IQR, 7.0%), 18.7% (IQR, 11.8%), and 30.4% (IQR, 17.0%), respectively, for facial ATA and were 4.6% (IQR, 11.4%), 18.2% (IQR, 14.1%), and 25.3% (IQR, 16.2%), respectively, for the ratio of ATA to TTA in the face. Likewise, median interobserver coefficients of variation for patients with mild, moderate, and severe facial lipodystrophy were 11.4% (IQR, 11.2%), 21.2% (IQR, 35.9%), and 32.9% (IQR, 23.3%), respectively, for facial ATA and were 9.1% (IQR, 5.0%), 23.8% (IQR, 37.2%), and 26.0% (IQR, 10.0%), respectively, for the ratio of ATA to TTA in the face. The lowest intra- and interobserver coefficients of variation for CT-based measurements were found in TTA values, and they were unrelated to the
severity of facial lipoatrophy. Median intraobserver coefficients of variation for TTA for patients with mild, moderate, and severe facial lipoatrophy were 7.3% (IQR, 6.3%), 1.8% (IQR, 1.7%), and 3.4% (IQR, 6.2%), respectively. Median interobserver coefficients of variation for TTA for patients with mild, moderate, and severe facial lipoatrophy were 9.8% (IQR, 6.0%), 11.2% (IQR, 1.1%), and 8.8% (IQR, 6.5%), respectively.

Patients with facial lipoatrophy had lower malar skinfold values, smaller total right-side facial TTAs, smaller facial ATAs, and lower ratios of ATA to TTA in the face, compared with patients without facial wasting (table 1). Moreover, an association between CT-based measurements and the severity of lipoatrophy was found. A similar association was observed between sex and the severity of lipoatrophy. The median facial ATA (<2.34 cm²) and the median ratio of ATA to TTA in the face (<0.10) had sensitivities of 71% and 74%, respectively, and specificities of 71% and 67%, respectively, for a diagnosis of facial fat loss. Skinfold measurements were positively correlated with facial ATA (r = 0.58; P < .01) and the ratio of ATA to TTA in the face (r = 0.34; P = .031). A facial skinfold thickness of ≤10 mm had a 58% sensitivity and a 77% specificity for a diagnosis of facial lipoatrophy.

Discussion. Our findings suggest that both quantitative CT of the face and anthropometric skinfold analysis may be suitable for evaluation of facial lipoatrophy in HIV-infected patients. Measurement of facial fat may allow more accurate monitoring of facial wasting during antiretroviral therapy, especially during clinical research. Although our study did not address the clinical impact of monitoring facial wasting, we believe that it might be beneficial for the management of HIV infection. Clinicians and patients may be more confident about the outcome of antiretroviral therapy if therapeutic modifications might be performed before an irreversible loss of facial fat has occurred.

Potential advantages of CT-based measurements of facial fat include objectivity, accuracy, and reproducibility. Evaluations of the sensitivity and specificity of new techniques for the diagnosis of facial lipoatrophy face a major challenge—the lack of a satisfactory “gold standard.” Clinical diagnosis may be far from the ideal standard of comparison. In our study, although the 71% sensitivity and 71% specificity of this technique, which were based on a cut-off facial ATA of <2.34 cm², were not very high, their accuracy could actually be greater because they were based on the assumption that clinical diagnosis was 100% accurate.

A potential limitation associated with the use of single-slice CT imaging to measure facial ATA may be the variation in the level at which the slice is obtained during subsequent examinations by different observers, which thereby reduces reproducibility. In our study, the degrees of inter- and intraobserver variability for single-slice CT-based measurements were acceptable, with TTA measurements showing less variation than measurements of the ratio of ATA to TTA in the face and the facial ATA. Potential disadvantages of CT of the face include radiation exposure, expense, and limited availability. Other methods, including ultrasonography [5] and laser scanning [6], have been used in research studies to assess facial lipoatrophy, but they have either failed or have not been clinically validated. In a recent study [6], results of 3-dimensional laser scans of the face have been found to be reproducible. However, this technique does not directly measure facial fat and could be biased by changes in facial contour due to hydration and nutritional status.

Although the results of this exploratory study are very encouraging, they should be regarded with caution because of the small number of patients studied. In addition, the sensitivity of these analyses might not be sufficiently high enough to detect subclinical facial fat loss. To more accurately determine the performance of these techniques in the diagnosis of facial wasting, as well as their usefulness in the detection of changes in facial fat during antiretroviral therapy, longitudinal studies that include sufficient numbers of male subjects and female subjects with a broad spectrum of facial fat composition must be performed.

Table 1. Results of measurement of facial skinfold thickness (by caliper) and evaluation of facial fat area (by quantitative CT) in the right region of the face for HIV-infected patients.

<table>
<thead>
<tr>
<th>Presence of facial lipoatrophy, severity</th>
<th>No. of patients</th>
<th>Facial skinfold thickness, mm</th>
<th>Facial TTA, cm²</th>
<th>Facial ATA, cm²</th>
<th>Ratio of ATA to TTA in the face</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>39</td>
<td>12.52 ± 3.63</td>
<td>23.39 ± 5.35</td>
<td>4.12 ± 3.10</td>
<td>0.17 ± 0.11</td>
</tr>
<tr>
<td>Yes</td>
<td>22</td>
<td>9.85 ± 2.03a</td>
<td>19.63 ± 7.97b</td>
<td>1.88 ± 1.87a</td>
<td>0.12 ± 0.17a</td>
</tr>
<tr>
<td>Mild</td>
<td>12</td>
<td>10.56 ± 1.94a</td>
<td>21.50 ± 4.29b</td>
<td>2.74 ± 2.06a</td>
<td>0.13 ± 0.11a</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>10</td>
<td>8.25 ± 1.25a</td>
<td>17.12 ± 11.01b</td>
<td>0.74 ± 0.56a</td>
<td>0.11 ± 0.23a</td>
</tr>
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</table>

NOTE. Data are mean value ± SD, unless otherwise indicated. Statistical significance was measured by means of Mann-Whitney U or Kruskal-Wallis tests. ATA, adipose tissue area; TTA, total tissue area.

* P < .01, compared with patients without facial lipoatrophy.

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References


