Evaluation of Coleman Lipostructure for Treatment of Facial Lipoatrophy in Patients With Human Immunodeficiency Virus and Parameters Associated With the Efficiency of This Technique

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Objective: To evaluate the efficiency of Coleman lipostructure in patients infected with human immunodeficiency virus (HIV).

Design: Open-label study and survey.

Setting: Ambulatory dermatosurgery department of a university hospital.


Interventions: Clinical examination, blood tests, and standardized photographs at baseline and 1 year after the lipostructure.

Mean Outcome Measures: Efficiency was assessed by the agreement of 3 independent medical specialists on facial lipodystrophy improvement after surgery and by patient satisfaction.

Results: Facial lipoatrophy was improved in 12 patients (36%; 95% confidence interval, 20%-52%) as judged by all 3 evaluators. Quantity of fat injected ($P = .01$) and a low serum triglyceride level before surgery ($P = .03$) were significantly associated with improvement of facial lipoatrophy. Of the 33 patients, 14 (43%) were very satisfied, 17 (50%) were partly satisfied, and 27 (81%) had a better quality of life. The most common comment was that the patient looked better and appeared less ill.

Conclusion: Our 1-year evaluation of Coleman lipostructure for correction of facial lipoatrophy in HIV-infected patients proved the efficiency of this treatment when measured conservatively by agreement on improvement by 3 independent specialists and demonstrated a patient satisfaction rate of 93%.

Arch Dermatol. 2005;141:1220-1224

Highly active antiretroviral therapy (HAART) with protease inhibitors and nucleoside reverse transcriptase inhibitors has greatly improved the prognosis of human immunodeficiency virus 1 (HIV-1) infection by suppressing viral load and increasing CD4 cell counts. However, a high proportion of patients develop metabolic alterations (hyperlipidemia and insulin resistance) and clinical lipodystrophy. The exact pathogenesis of lipodystrophy is not well understood. The lipodystrophy is characterized clinically by the symmetrical loss of subcutaneous fat tissue from the body surface. In contrast, there can be local fat deposition in the buttocks and abdomen, giving the impression of obesity. However, most disfigurement is caused by the disappearance of subcutaneous fat from the face. There is a cachectic appearance as a result of the loss of buccal, parotid, and preauricular fat pads with sunken eyeballs, prominent zygomatic, and sharply defined nasolabial folds. The stigma by which one can be recognized in public as being infected with HIV has switched from the Kaposi's sarcoma to lipodystrophy. There is no medical treatment to correct facial lipodystrophy, and the benefit of switching these patients to other antiretroviral drug classes is controversial. Structural autologous fat grafts for the enhancement of facial contours were proposed by Coleman.
The purpose of this study was to evaluate the efficiency of autologous fat grafts by Coleman lipostructure technique in HIV-infected patients with facial lipoatrophy 1 year after surgery.

METHODS

PATIENTS

All HIV-infected patients undergoing Coleman lipostructure at the same institution between April 2000 and November 2001 were enrolled consecutively in this study. Patients were excluded from surgery if they had a contraindication to general anesthesia or inadequate abdominal subcutaneous fat. All patients had mixed lipodystrophy with facial fat wasting and abdominal fat accumulation.

Thirty-three HIV-1–infected patients undergoing lipostructure were included in this study between April 2000 and November 2001. An evaluation was performed at baseline and 1 year after the lipostructure that comprised clinical examination, blood tests (HIV viral load, CD4 cell count, and serum triglyceride level) and standardized photographs (full facial picture, side face, and three-quarters face). Antiretroviral combination was recorded. The mean age of patients was 45 years (range, 33-70 years), and the male-female ratio was 4.5:1. Most of the patients were men having sex with men (76%). Median body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) was 22.5 (range, 18.6-28.4). Mean duration of HIV infection was 13 years (range, 7-16 years). Highly active antiretroviral therapy was given for a median of 7 years (range, 3-13 years). According to the 1993 revised criteria of the Centers for Disease Control and Prevention,18 patients were classified as AIDS stage A, 2 as AIDS stage B, and 12 as stage C.

INJECTION OF AUTOLOGOUS FATTY TISSUE

Treatment consisted of lipostructure by plastic surgeons, as described by Coleman,5,7 with the patient under general anesthesia or inadequate abdominal subcutaneous fat. All patients had mixed lipodystrophy with facial fat wasting and abdominal fat accumulation.

The quantity of fat injected (range, 4-40 mL) was carefully analyzed before reinjecting the purified fat. Abdominal subcutaneous adipose tissue was harvested without negative pressure with a blunt cannula. The quantity of fat harvested, about 40 mL when possible, was bound to the quantity of abdominal subcutaneous fat available and to facial lipoatrophy severity. The aspirated subcutaneous material was centrifuged for 4 minutes at 3500 rounds per minute to separate blood and oil from ruptured parcels of fat at the top. The middle layer consisting of parcels of fatty tissue was transferred to a 1-mL Luer-lock syringe. Fat grafting was implanted without any storage into subcutaneous tissue submuscularly, intramuscularly, and directly to the periosteum and without positive pressure with an 18-gauge lipoinfiltrator cannula. The purification of the fat tissue is more efficient compared with standard autologous transfer. The median quantity of adipose tissue injected was 21.6 mL (range, 4-40 mL). Patients left the hospital after 6 hours of observation without a facial bandage, with analgesic medication but no antibiotic prophylaxis. They were ordered not to work for 1 week because of the postoperative edema and pain.

EVALUATION OF THE TREATMENT

The efficiency of the lipostructure technique was assessed by (1) the agreement of 3 independent medical specialists blinded to clinical and biological data (improvement vs no improvement or deterioration) on global facial lipodystrophy improvement after surgery by comparing preoperative and postoperative photographs and (2) a self-administered questionnaire that was completed by patients 1 year after surgery. The questionnaire assessed the patient’s satisfaction (very satisfied vs partly satisfied or unsatisfied) and the impact on his or her quality of life.

STATISTICAL ANALYSIS

Agreement among specialists on improvement was measured by Cohen κ coefficients, and 95% confidence intervals (CIs) were calculated. Testing for a difference between groups was performed using the paired, 2-tailed t test for quantitative data and the χ2 test or exact Fisher test for binary data. All statistical analyses were performed using SAS 8.2 software (SAS Institute, Cary, NC).

RESULTS

THE EVALUATION

Pairwise agreement among specialists on improvement was good (κ coefficients between 0.46 and 0.5; all coefficients were notably above 0). Facial lipoatrophy was improved in 12 patients (36%; 95% CI, 20%-52%) as judged by all 3 evaluators, in 17 patients (52%; 95% CI, 35%-69%) by at least 2 evaluators, and in 25 patients (76%; 95% CI, 61%-91%) by at least 1 evaluator (Figure 1 and Figure 2).

The quantity of fat injected (P = .01) and the serum triglyceride level before surgery (P = .03) were the 2 parameters associated with the success of Coleman technique as judged by all 3 evaluators (Table). Otherwise, younger patients (P = .11) and women (odds ratio, 2 [95% CI, 0.3-12]) tended to have a better result, which did not reach statistical significance. There was no association with HIV viral load level, CD4 cell count, HAART duration, or...
change of HAART after lipostructure (with the suppression of nucleoside reverse transcriptase inhibitors, in particular, stavudine and lamivudine, or protease inhibitors). The quantity of fat injected \((P = .02)\) and AIDS stages \(B\) and \(C\) \((P = .03)\) were significantly associated with amelioration as judged by at least 2 evaluators (data not shown).

**PATIENT SATISFACTION**

Twenty-eight patients (85%) had completed the self-administered satisfaction questionnaire. Fourteen patients (50%) were partly satisfied, and 12 (43%) were very satisfied with the results of the lipostructure. Only 2 (7%) of 28 patients were dissatisfied. Agreement between the specialists’ evaluation of improvement and the patient’s satisfaction was low and not significant \((\kappa\) coefficients ranged from 0.08-0.27). There were no dissatisfied patients when all 3 evaluators scored improvement. Twelve patients (43%) were satisfied (partly or very satisfied) when at least 2 evaluators scored no improvement.

Of the 33 patients, 27 (81%) had a better quality of life after lipostructure. The most common comment was that they looked better and appeared less ill. Patients with a lower CD4 cell count before surgery tended to be more satisfied \((P = .07)\).

**ADVERSE EFFECTS**

No serious adverse effects occurred during and after lipostructure. The main adverse effects were moderate and transient pain at the facial injection sites and abdominal donor sites. However, we reported 1 case of overcorrection for a 48-year-old man receiving didanosine (400 mg once a day), lamivudine (150 mg twice a day), and stavudine (40 mg twice a day) for 6 years. To correct facial lipoatrophy associated with HAART, 8 mL of fat graft were placed into each cheek. The result was initially good, but 3 months after lipostructure he developed a bilateral increase in the nasogenian area, while his weight, antiretroviral combination therapy, immunovirological parameters, and lipid parameters were unchanged. Lipoaspiration was unsuccessful, and hyperplastic adipocytes were resected surgically under local anesthesia. Histologic examination showed an aspect of lipodystrophy with fibroadipose tissue and dystrophic adipocytes of various size. A nonadaptive response could be partly related to a dysfunction of adipocyte receptor expression and a mutated DNA toxicity–related mechanism; harvested lipohypertrophic adipocytes remain sensitive to the same lipohypertrophy determinants even after grafting is performed in the lipoatrophy site.

**COMMENT**

Lipodystrophy is a serious and socially disabling complication affecting many HIV-infected patients receiving HAART. Consequently, patients with a higher level of adherence may be more likely to develop lipodystrophy, and patients having lipodystrophy for more than 36 months show decreased adherence.\(^{10,11}\) Facial changes due to lipodystrophy may stigmatize patients, producing erosion of self-image and self-esteem, problems in social and sexual relations, and anxiety and depression.\(^{12}\) It has been shown previously that the impact of HIV–1–related lipodystrophy on quality of life was greater for young homosexual patients, unemployed patients, and patients undergoing current psychiatric treatment even though lipodystrophy was most important in another type of patient (old patients who had been receiving antiretroviral treatment over a longer period).\(^{13,14}\) The morphologic alterations can reduce adherence to antiretroviral therapy.\(^{10,11}\) Until then, a growing number of patients will turn to their surgeon asking for treatment, especially when the lipodystrophy affects the face and is conspicuously present. Autologous fatty tissue harvested, refined, and placed in the specific fashion as described by Coleman seems to be an exemplary agent for augmentation in soft-tissue facial recontouring.

In our study, the 1-year evaluation of lipostructure for the correction of facial lipoatrophy in 33 HIV-infected patients showed a high rate of success in the permanence of the results. Indeed, improvement was found in 12 patients (36%) by all 3 independent evaluators and 17 patients (52%) by at least 2 evaluators with 1-year follow-up. Moreover, 93% of patients were pleased with the results, and their quality of life was often improved.

In our series, we found that some subgroups of patients seem to be more improved by the Coleman technique, including patients with a low serum triglyceride level before surgery, younger patients, women, and patients with AIDS stages \(B\) and \(C\). The statistical evaluation when all 3 evaluators judged improvement is interesting because it is the most restrictive. The efficiency of lipostructure is significantly associated with the quantity of fat injected; therefore, surgeons should inject more than 25 mL of adipocytes.

Patients who are improved by lipostructure have a significant lower serum triglyceride level compared with...
other patients, suggesting that the triglyceride level may reflect the tissue viability. Because apoptosis and increased expression of tumor necrosis factor have been demonstrated in lipoatrophic tissues,16,17 the fact that patients who have a high level of triglycerides have a worse result may indicate that the triglyceride level correlates with the apoptotic phenomenon observed in adipose tissue that could be linked to a better fat graft survival rate. Concerning the patient’s age and efficiency of the technique, it is possible that older patients have less correction compared with younger patients because of subcutaneous fat atrophy being partly due to senescence.

This technique is also safe and reliable, without adverse effects such as granulomatous reactions or allergic reaction that can be observed with most injected filling substances.18,19 While treatment such as injection of hyaluronic acid or poly-L-lactic acid necessitate repeated painful injections for a mean of 4 sessions,19 in our experience liposurgery can be performed in an ambulatory session, with a satisfactory result at 1 year in our experience. Nevertheless, the Coleman technique is restricted by fat availability and cannot be used for all cases of lipoatrophy.

Two previous studies attempted to demonstrate the efficiency of liposurgery in HIV-infected patients. First, Levan et al20 reported 93% of global satisfaction ("acceptable," "good," or "very good" global results) among 15 patients treated with Coleman liposurgery and followed prospectively during 6 months. Also, 13 of the 14 patients evaluated by a 5-member jury were considered to have "acceptable," "good," or "very good" global results at month 6. Second, Caye et al21 evaluated 29 HIV-infected patients. The patients were evaluated clinically and with serial photography by the surgeons themselves. The results were judged good in 72.4%, acceptable in 13.8%, and poor in 13.8%.

Whereas autologous fat transplantation injections seem to be the most physiological therapy to correct facial lipoatrophy in HIV-infected patients, other therapeutic approaches have been reported in different studies. The use of hyaluronic acid injections has been associated with a rapid decline in the degree of correction and loss of aesthetic improvement following administration.22 In 2003, Valantin et al19 reported a series of 50 patients with severe lipoatrophy treated with facial injections of polylactide acid. At the end of 96 weeks of follow-up, the median total cutaneous thickness increased significantly from baseline (+6.8 mm [range, 3.9-10.1 mm]; P <.001) with a good improvement in the quality of life. Nevertheless, in this study, the authors considered these results to be clinically relevant, but there was no clinical comparison between preoperative and postoperative photographs.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Improvement Judged by All 3 Evaluators</th>
<th>No Improvement</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>42.3 [33-55]</td>
<td>47.2 (36-70)</td>
<td>.11</td>
</tr>
<tr>
<td>Sex ratio</td>
<td>3 (9/3)</td>
<td>6 (18/3)</td>
<td>.64</td>
</tr>
<tr>
<td>Homosexual contamination</td>
<td>66.7 (6/9)</td>
<td>81.3 (13/16)</td>
<td>.63</td>
</tr>
<tr>
<td>Duration of HIV, y</td>
<td>12 [7-16]</td>
<td>12.8 [9-16]</td>
<td>.42</td>
</tr>
<tr>
<td>Duration of antiretroviral treatment, y</td>
<td>6.8 [3-13]</td>
<td>7.3 (4-12)</td>
<td>.56</td>
</tr>
<tr>
<td>BMI before lipostructure</td>
<td>22.3 [18.8-25.9]</td>
<td>22.7 (18.6-23.4)</td>
<td>.58</td>
</tr>
<tr>
<td>BMI after lipostructure</td>
<td>22.1 [19.3-25.3]</td>
<td>22.1 (18.7-23.8)</td>
<td>.96</td>
</tr>
<tr>
<td>AIDS stage A</td>
<td>22.2 (4/18)</td>
<td>77.8 (14/18)</td>
<td>.21</td>
</tr>
<tr>
<td>AIDS stage B/C</td>
<td>50 (7/14)</td>
<td>50 (7/14)</td>
<td></td>
</tr>
<tr>
<td>Triglycerides before lipostructure, mg/dL</td>
<td>238.9 [132.7-345.1]</td>
<td>672.6 (44.2-3699.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Triglycerides after lipostructure, mg/dL</td>
<td>238.9 [132.7-345.1]</td>
<td>672.6 (44.2-3699.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Cholesterol before lipostructure, mg/dL</td>
<td>238.9 [132.7-345.1]</td>
<td>672.6 (44.2-3699.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Cholesterol after lipostructure, mg/dL</td>
<td>238.9 [132.7-345.1]</td>
<td>672.6 (44.2-3699.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Serum glucose before lipostructure, mg/dL</td>
<td>7.2 [4-23.8]</td>
<td>6.2 (4.5-13.2)</td>
<td>.49</td>
</tr>
<tr>
<td>Serum glucose after lipostructure, mg/dL</td>
<td>7.2 [4-23.8]</td>
<td>6.2 (4.5-13.2)</td>
<td>.49</td>
</tr>
<tr>
<td>CD4 cell count before lipostructure, cells/µL</td>
<td>482 [0-949]</td>
<td>490 (228-1287)</td>
<td>.93</td>
</tr>
<tr>
<td>CD4 cell count after lipostructure, cells/µL</td>
<td>483 [115-972]</td>
<td>442 (167-982)</td>
<td>.70</td>
</tr>
<tr>
<td>HIV viral load before lipostructure (% undetectable)</td>
<td>50 (6/12)</td>
<td>47.6 (10/21)</td>
<td>.90</td>
</tr>
<tr>
<td>HIV viral load after lipostructure (% undetectable)</td>
<td>50 (6/12)</td>
<td>47.6 (10/21)</td>
<td>.90</td>
</tr>
<tr>
<td>Serum insulin before lipostructure, mIU/mL</td>
<td>26.4 [7.3-108.5]</td>
<td>27.5 (7.3-92)</td>
<td>.91</td>
</tr>
<tr>
<td>Serum insulin after lipostructure, mIU/mL</td>
<td>26.4 [7.3-108.5]</td>
<td>27.5 (7.3-92)</td>
<td>.91</td>
</tr>
<tr>
<td>C-peptide before lipostructure, ng/mL</td>
<td>24.6 [5.8-49]</td>
<td>22.3 (3.5-41.3)</td>
<td>.58</td>
</tr>
<tr>
<td>C-peptide after lipostructure, ng/mL</td>
<td>24.6 [5.8-49]</td>
<td>22.3 (3.5-41.3)</td>
<td>.58</td>
</tr>
<tr>
<td>Quantity of fat injected, mL</td>
<td>24.6 [5.8-49]</td>
<td>22.3 (3.5-41.3)</td>
<td>.58</td>
</tr>
<tr>
<td>Stop antiretroviral molecule inducing lipodystrophy</td>
<td>83.6 [7/11]</td>
<td>47.9 (9/19)</td>
<td>.39</td>
</tr>
<tr>
<td>Stop stavudine therapy</td>
<td>45.5 (5/11)</td>
<td>21.1 (4/19)</td>
<td>.32</td>
</tr>
<tr>
<td>Stop lamivudine therapy</td>
<td>27.3 (3/11)</td>
<td>10.5 (2/19)</td>
<td>.33</td>
</tr>
<tr>
<td>Stop protease inhibitor therapy</td>
<td>18.2 (2/11)</td>
<td>31.6 (6/19)</td>
<td>.67</td>
</tr>
</tbody>
</table>

Data are given as median [range] or percentage (absolute numbers) unless otherwise specified.

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); HIV, human immunodeficiency virus.

SI conversion factors: To convert triglycerides to millimoles per liter, multiply by 0.0113; to convert cholesterol to millimoles per liter, multiply by 0.0259; to convert insulin to picomoles per liter, multiply by 6.945; to convert C-peptide to nanomoles per liter, multiply by 0.333.

*Data as given as median [range] or percentage (absolute numbers) unless otherwise specified.
As lipodystrophy is associated with lower HAART adherence, the correction of facial lipoatrophy by this technique might improve patient’s adherence to treatment. Thus, it might be interesting to determine by a controlled study if patients with corrected facial lipoatrophy by liposculpture are more adherent compared with patients without correction.

CONCLUSIONS

Given the overall benefit of decreased morbidity and prolonged survival associated with HAART in HIV-infected patients, it is very important to propose a technique for correction of facial lipodystrophy induced by drugs. Patients with facial corrections may then adhere to their HAART and also see improvement in their quality of life.

The 1-year evaluation of Coleman liposculpture for correction of facial lipodystrophy in HIV-infected patients had a good efficiency as measured conservatively by agreement on improvement by 3 independent specialists and demonstrated a patient satisfaction rate of 93%.

Accepted for Publication: December 27, 2004.

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Financial Disclosure: None.

Disclaimer: Dr Burnouf had full access to all data in the study and takes responsibility for the integrity of the data analysis.

Acknowledgment: We thank the 3 evaluators: Philippe Gerhardt, MD, J. P. Granier, MD, and Maryse Zeig, MD.

REFERENCES