Facial Wasting Rehabilitation: A Personal Algorithm

Raffaele Rauso*

University of Foggia, Italy

Abstract: Facial lipoatrophy, also known as facial wasting (FW), defined as flattening or indentation of normally convex facial contours, is the most distressing manifestation for HIV patients. It can be stigmatizing, severely affecting quality of life and self-esteem, and it may result in reduced antiretroviral adherence. Several surgical or non surgical techniques exists, however to restore facial features in HIV-related lipoatrophy fillers and structural fat graft seems2 to be the procedures most performed. In this article the authors present his experience in FW rehabilitation, and his decisional algorithm of choice.

Keywords: Filler, facial lipoatrophy, structural fat graft, facial wasting, HIV.

1. INTRODUCTION

The use of highly active retroviral therapy (HAART) with protease inhibitors, first descrive in the United States in 1997, has demonstrated a significant clinical benefit in the treatment of HIV infection [1,2]. Within one year of its introduction, mortality rates dropped by 45%, and there was a significant decline in the number of reported AIDS-defining diseases. But, as the most part of chronic pharmacologic therapies, there are several side effects such as: diarrhea, renal calculi, nausea, and perioral paraesthesias [3,4].

One medication-associated condition that has become prevalent among HIV-infected patients is HIV-associated lipodystrophy, a syndrome characterized by abnormal fat metabolism and deposition. Broadly speaking the lipodystrophy syndrome is composed of three componente [5,6] :1) Lipoatrophy (subcutaneous fat loss in the face, limbs, and buttocks) 2) Lipohypertrophy (fat accumulation in the abdomen, and dorso-cervical fat pad) 3) Metabolic disturbance (insulin resistance, hypercholesterolemia, and hypertriglyceridemia).

Despite the initial reports of an association between protease inhibitors and lipodystrophy, it soon became apparent that other drugs were implicated. In 1999, an association between thymidine analogues, particularly d4T, and fat wasting was reported, supported by improvements in subcutaneous fat and serum triglyceride levels after switching d4T to zidovudine (AZT) or abacavir (ABC) [7]. Over the course of time it has been realized that the components of lipodystrophy syndrome are, at least partially, independent processes [8,9], different antiretrovirals are associated with different types and degree of toxicity[10,11], and lipodystrophy syndrome is the result of a complex interaction between a variety of factors [12]. In general thymidine analogues, especially d4T, are associated with lipoatrophy and protease inhibitors with lipohypertrophy and dyslipidaemia [13].

Lipoatrophy is common on HAART-treated subjects; cross-sectional studies reveal prevalence between 13% and 38% [8, 14-16]. Differences in estimates of lipoatrophy prevalence are likely secondary to differences in defining/assessing lipoatrophy, duration of antiretroviral therapy, and duration of thymidine analogue use. It is therefore impossible to compare rates of lipoatrophy across the different studies [17].

Facial lipoatrophy, also known as facial wasting (FW), is the most distressing manifestation for HIV patients. It can be stigmatizing, severely affecting quality of life and self-esteem, and it may result in reduced antiretroviral adherence [18]. Defining the prevalence for FW is hampered by differing definitions of the syndrome across studies making cross-study comparisons very difficult. Many studies report the incidence rates of lipodystrophy in general, not lipoatrophy specifically, and the overlapping nature of the components of the lipodystrophy syndrome complicates matters further [20].

At this time, a number of medical, pharmacological, and surgical therapies are used to treat HIV lipodystrophy. In addition to exercise and nutritional counseling to prevent the loss of lean body mass, anabolic steroid hormones, testosterone, and human growth hormone have increasingly being used in these patients, with varied success and significant side effects [19-23]. Therefore, ever-increasing numbers of HIV patients receiving HAART are presenting to facial plastic surgeons and requesting reconstructive surgery

*Address correspondence to this author at the Centro Polispecialistico Santa Apollonia, *Via* Martiri del Dissenso, 47, 81055 S. Maria C. V. (CE), Italy; Tel: 0039823843286; 00393397772305; E-mail: dr.raffaele.rauso@gmail.com

E-ISSN: 2414-2093/17

Table 1: James/Carruthers Facial Lipoatrophy Severity Scale

GRADE	DESCRIPTION
1	Mild and localized facial lipoatrophy
2	Deeper and longer atrophy, with the facial muscles beginning to show through
3	Atrophic area is even deeper and wider, with the muscle clearly showing through
4	Lipoatrophy covers a wide area, extending up towards the eye sockets, and the facial skin lies directly on the muscle

to ameliorate the unwanted side effects of their treatment protocol such as FW.

Up to now the most used classification for FW is the James/Carruthers Facial Lipoatrophy Severity Scale (Table **1**) [24].

Aim of this paper is to analyze the different options in FW rehabilitation and discuss about author's experience.

In FW rehabilitation surgical and non surgical techniques are available, following are summarized the most known and performed.

2. HYALURONIC ACID (HA) FILLERS

HA fillers are commonly used for wrinkle treatment, fold filling, and regional volumizing [25]. It is a naturally occurring linear polysaccharide composed of repeting disaccharide units of N-acetylglucosamine and D-glucuronic acid. These glycosaminoglycan chains coil in on themselves, resulting in an elastic and viscous matrix. Because HA is a substance that is uniform throughout nature (no species or tissue specifity), immunogenic reactions are extremely rare and no preinjection testing is required. Several HA fillers are sold, and the biggest difference among them is the amount of molecular cross-linking: theoretically more cross-linking lengthens the clinical half-life of the filler. Usually their clinical volumizing effectiveness is between 3 and 6 months [25].

HA fillers are very useful in the treatment of FW grade 1 of the James/Carruthers Facial Lipoatrophy Severity Scale, when there is a mild and localized facial lipoatrophy, a clinical situation very close to the beginning of the facial aging process [26].

3. L-POLY-LACTID ACID (PLLA) FILLER

PLLA is a synthetic material that has been in use for enhancing facial volume for over a decade in Europe and, more recently in the United States.

The mechanism of action of PLLA is based on its ability to stimulate fibroblast proliferation and neocollagenogenesis [27]. It is postulated that this is due to a foreign body reaction to the injected material, which stimulates a cellular inflammatory response. The resultant formation of a vascularised, connective tissue capsule ensues, which is eventually composed of fibroblasts and new collagen deposits. The breackdown of PLLA occurs by hydrolysis into lactate, which is eventually converted to pyruvate, and oxidized into carbon dioxide for release [27-30].

The stimulatory action of PLLA is one of the main characteristics that differentiate it from other fillers. Most other filler, such as HA, have a passive and direct effect on enhancing volume. Their augmentation is limited to the persistence of the filler material and, once degraded, further injection is required. Likewise, the augmentation effects of PLLA tipically require multiple injections and are delayed in nature. But the new collagen deposition yields results that last long after the injected material is absorbed [27-29].

PLLA filler, before its use, must be reconstituited with sterile, bacteriostatic injectable water; sufficient time to reconstitution is paramount, usually 24 hours. Inadequate mixing of PLLA with water leads to inadvertent injections of clumps of dry micro-particles, increasing the risk of nodule formation when they hydrate *in vivo* [31].

Final outcomes with PLLA are delayed and require multiple session, spaced every 4 to 6 weeks apart, to allow adequate time for augmentation and avoid overcorrection.

The principle should be one of serial application to achieve augmentation goals. Patients should be counselled on the length of the process and goals with each subsequent application. In addition it should be noted that areas treated with PLLA are likely to

decrease in volume within the first 24 to 48 hours as the body reabsorb the sterile, bacteriostatic injectable water within the solution [31].

This filler is very useful in the treatment of FW grade 2 or 3 of the James/Carruthers Facial Lipoatrophy Severity Scale [32, 33], however patients who do not seem likely to tolerate long treatment periods, or have unrealistic expectations, may be better suited to augmentation with agents that produce immediate results, avoiding frustration for the patient and physician.

4. CALCIUM HYDROXYAPATITE (CAHA) FILLER

CH, the main mineral component of bone and teeth, is a naturally occurring substance found in humans, making it compatible and contributing to its nonantigenic properties. Radiesse is a dermal filler composed of (35%) synthetic CaHa microspheres, suspended in aqueous gel (65%) containing water, glycerine and carboxymethylcellulose. The formulation allows 1:1 implant-to-tissue volume defect correction and minimizes the need for overcorrection [34, 35].

CaHa fillers provide immediate correction, and following injection, the gel carrier is absorbed over several months. The CaHa microspheres left behind from a scaffold for ingrowth of fibroblasts. New collagen fibers are formed, which anchor the microspheres in place and prevent the migration of the implant. The microspheres gradually dissolve and are broken down to its metabolites, calcium and phosphate ions, over a period of several months to years. Histological and immunohistochemical analysis studies have shown a local histyocitic and fibroblastic response resulting in new collagen production around the microspheres. Primarily, type I collagen and a small amount of type III collagen were found within the infiltrating fibrovascular stroma, consistent with the process of remodeling [34-37].

Usually less volume is required with Radiesse to produce the desired correction as compared with HA fillers. The longevity of CaHa fillers seems to depend on several factors, including the site of injection, the injection technique, and the patient's metabolism of the product; however the durability of the correction persist for 9 to 18 months and can last longer if deposited in areas of minimal facial mobility [35-37].

Radiesse is currently FDA-approved for correction of moderate to severe facial wrinkles and folds, such as nasolabial folds, and for facial augmentation in HIV patients with facial lipoatrophy [38]. Author already described a "one-step technique" for the rehabilitation of FW [39].

5. PERMANENT SOFT TISSUE FILLERS

The first permanent facial filler developed was paraffin oil in the early 20th century [40]. This was followed by a variety of other synthetic fillers such as beeswax, lanolin, and mineral oils. However, all these products were associated with a high rate of foreign body granuloma formation. It was not until the 1960s with the emergence of liquid silicone that injectable facial fillers started to gain popularity [40, 41]. The use of permanent fillers is still debated: proponents of nonpermanent fillers stress the importance of how aging will continually change the overlying structure of a person's face. They can fear that as a person ages, the placement of the permanent filler will become out of proportion. However the use of permanent fillers is very debated between the physicians, but very often patients affected by FW ask for a permanent solution [42-44].

The most common permanent filler used nowadays for FW rehabilitation are: Artefill (Suneva Medical, San Diego, CA), a polymethyl methacrylate (PMMA) and bovine collagen injectable filler; Bio-Alcamid (Polymekon, Milan, Italy), a polyalkylimide gel composed of 96% apyrogenic water and 4 % polyalkylimide; Aquamid (Contura International A/S, Soeborg, Denmark), an hydrogel filler composed of 97,5% apyrogenic water and 2,5% polyacrylamide [44].

Author, in the field of non absorbable fillers, experienced only with polyacrylamide hydrogel filler [45, 46].

6. STRUCTURAL FAT GRAFT

Fat grafting was used successfully for soft tissue augmentation in the 1893 for the first time, however during the last century this technique gained and lost popularity due to the inconstant results related to fat resorption [49-51].

In 1994, Coleman first described his technique, which uses a syringe, cannula, and centrifuge, for

structural fat grafting. He later refined and popularized his technique for fat graft harvesting and processing with the Coleman instruments and centrifuge and a centrifugation protocol, often referred to as the Coleman technique [52]. By using his established technique for fat graft harvesting and processing along with his refined placement technique, many surgeons are able to achieve good long-term results with structural fat grafting; however, performing structural fat graft for FW rehabilitation, the Coleman technique can't be used as described by the author because, as stated by Davison *et al,* [54], fat of infected patients can't be centrifuged due to the risk of virus aerosolization, so in these cases sedimentation, washing or other fat purifying procedures must be done.

Nowadays structural fat graft is one of the most popular technique used in facial plastic surgery, and of course is used for FW rehabilitation too. However only for the patients where FW and lipohypertrophy of the body are both present this technique can be used [46, 47]. Moreover, in literature, are described some cases where a disfiguring facial lipohypertrophy at the graft site occurred when the fat was harvested from buffalo hump deformity [55].

7. MATERIAL AND METHODS

We retrospectively analyzed patients affected by FW treated by the author (RR), between the July 2008 and the December 2013. All patients received clinical and blood examinations, the count of CD4 in all the cases was at least 250/mm3 or greater, and the viral load minor than 5000 copies/mL.

Patients were scored with the James/Carruthers Facial Lipoatrophy Severity Scale.

Sixty-two patients (38 M, 24 F) were treated; patients severity scale is in Table **2**. In twelve cases (8M, 4F), patients presented both FW and body trunk lipohypertrophy; in those cases FW was rehabilitated with structural fat graft; in the same surgical time, body contouring procedures were done (2 gynecomastya; 4 liposuction of buffalo hump; 6 liposuction of lower abdomen); in all the cases facial wasting scored 2 or more than 2.

Patients presenting only facial wasting without body lipohypertrophy were treated with facial fillers injections; in cases of grade 1 sec. James/Carruthers of facial wasting, 4 cases (all males), were treated with hyaluronic acid fillers (mean injected volume 2 mL). Fourty-six more patients, ranging from grade 2 to grade 4 sec. James/Carruthers, were rehabilitated with permanent or long lasting dermal fillers. Twenty-eight (18 M, 10 F) on 46 were rehabilitated with a polyacrylamide hydrogel based filler (Aquamid, Contura International A/S, Soeborg, Denmark), mean injected volume 13,6 mL; eighteen (8 M, 10 F) on 46 with a calcium hydroxyapatite based filler (Radiesse, Merz, Palo Alto, California), mean injected volume 12,8 mL. All the cases, whatever dermal filler used, were rehabilitated in one session, using protocols already described by the author [40,55].

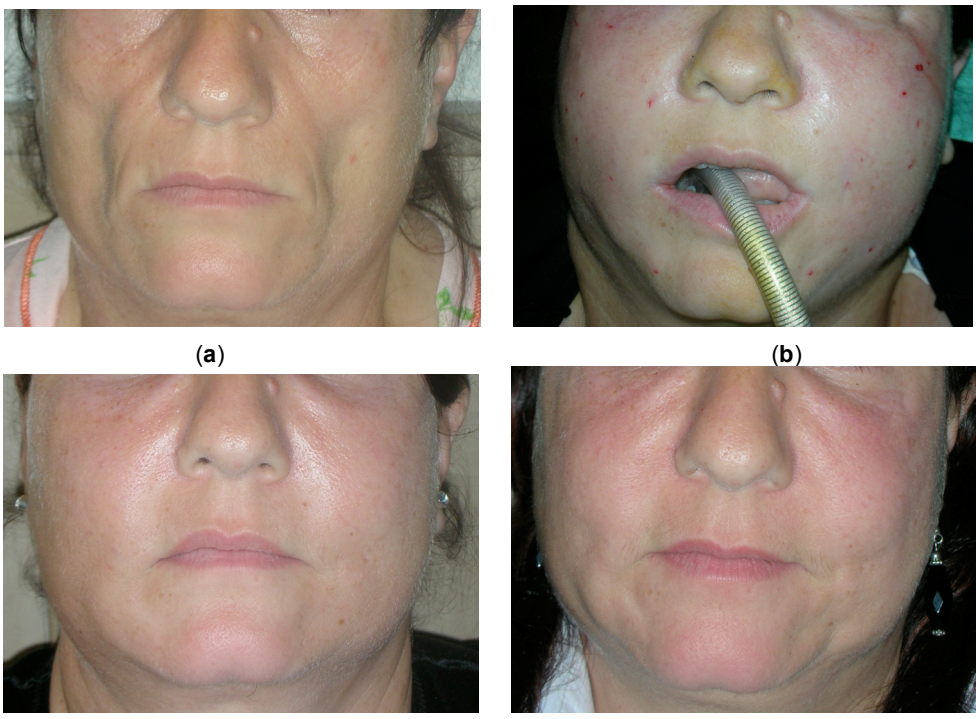
Patient's features are listed in Table **2**.

8. RESULTS

Minimum follow up for each patient was 24 months; patients treated with permanent fillers were followed up at least for 36 months, the longest was 52 months. In all patients treated with structural fat graft, except one where a progressive facial lipohypertrophy was noted (Figure **1a-d**), a variable degree of fat resorption was

Table 2: Patient's Features

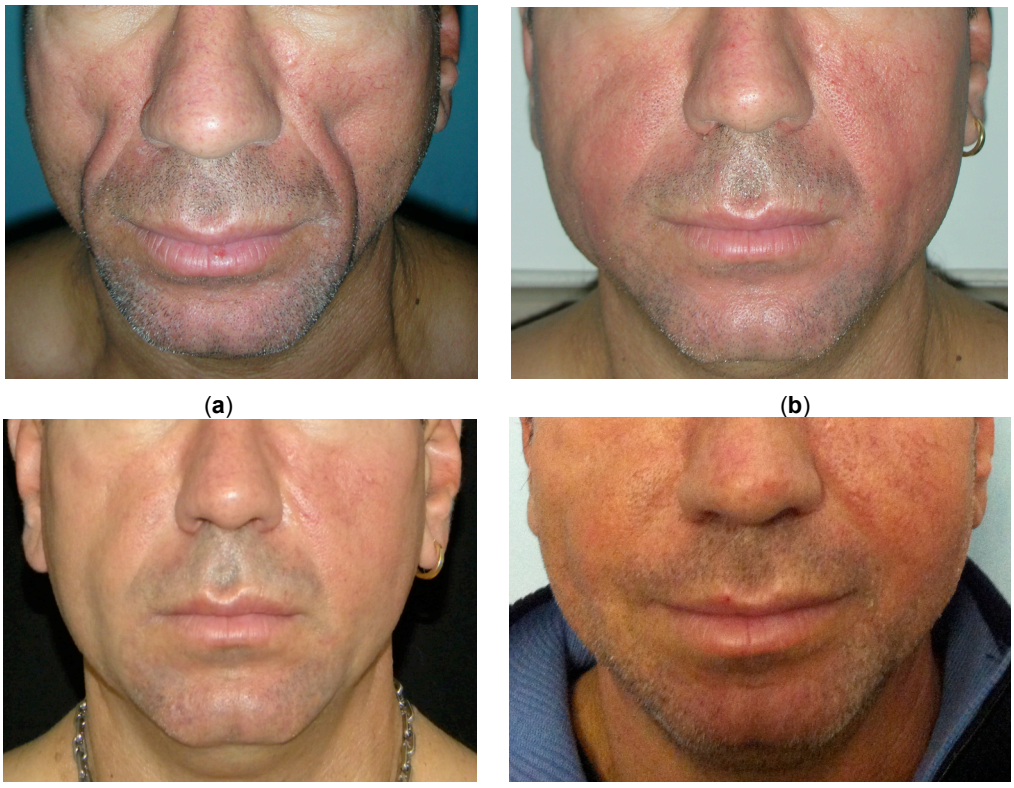
	Fat graft	HA filler	CaHa filler	Non resorbable filler
n. Patients	12	4	18	28
Gender				
Male	8	4	8	18
Female	4	0	10	10
Initial Facial Lipoatrophy Severity Sec James/Carruthers				
Grade 1	0	4	0	0
Grade 2	7	0	10	15
Grade 3	5	0	6	12
Grade 4	0	0	2	1



(**a**) (**b**)

(**c**) (**d**)

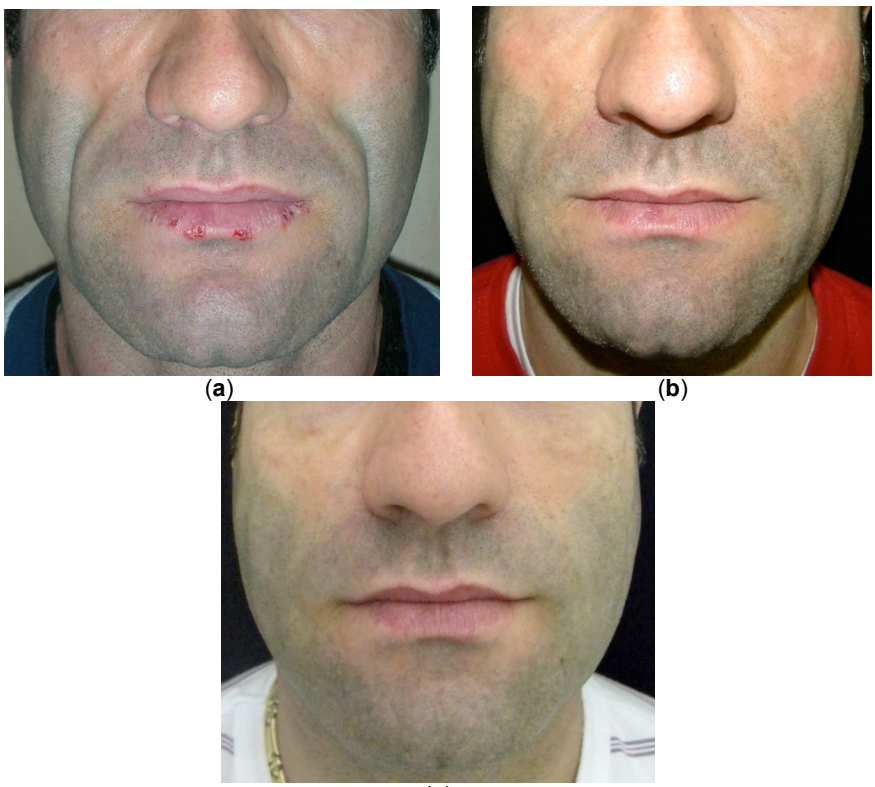
Figure 1: (**a**) pre operative picture of a 44 y.o woman affected by facial lipoatrophy planned for structural fat graft harvested from buffalo hump; (**b**) immediate post operative, overfilling is always performed during structural fat graft; (**c**) result 3 months after treatment; (**d**) at 1 year post operative a light lipohypertrophy bilaterally at the cheeks was observed, patient resumed any others treatments.



(**a**) (**b**)

(**c**) (**d**)

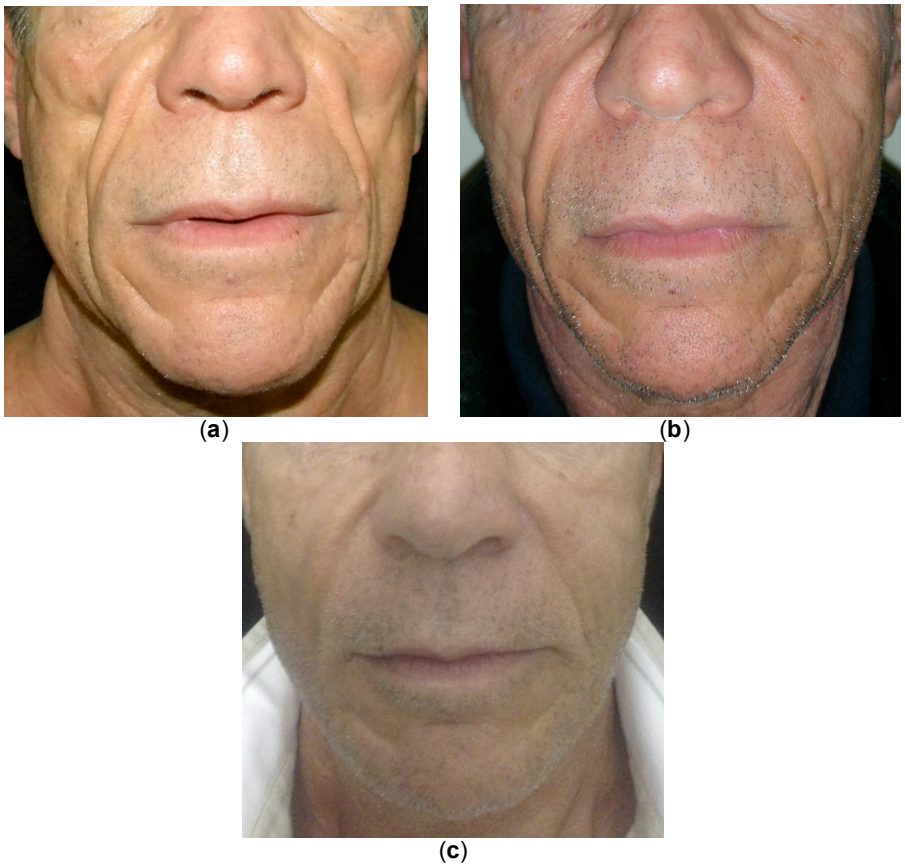
Figure 2: (**a**) pre operative picture of a 46 y.o. man affected by facial lipoatrophy planned for structural fat graft harvested from pectoral area; (**b**) 3 months post operative result; (**c**) 12 months post operative result: an high degree of fat resorption can be observed so the patient was planned for a second session of facial structural fat graft; (**d**) 12 months result after the second treatment.



(**a**) (**b**)

(**c**)

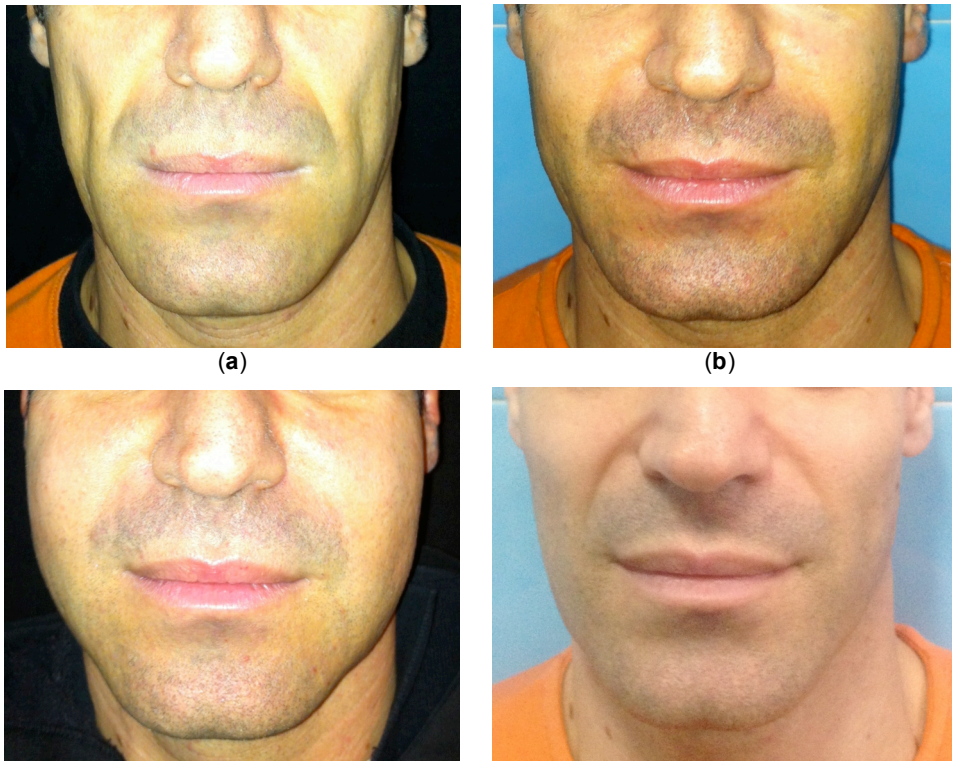
Figure 3: (**a**) pre operative picture of a 42 y.o. man affected by facial lipoatrophy planned for non absorbable filler injections; (**b**) 12 months post operative result; (**c**) 24 months post operative result.



(**a**) (**b**)

(**c**)

Figure 4: (**a**) pre operative picture of a 52 y.o. man affected by facial lipoatrophy planned for non absorbable filler injections; (**b**) 12 months post operative result; (**c**) 30 months post operative result.



(**a**) (**b**) (**c**) (**d**)

Figure 5: (**a**) pre operative picture of a 40 y.o. man affected by facial lipoatrophy planned for CaHa filler injections; (**b**) 2 weeks post operative result; (**c**) swelling appeared after 1 months from the injections without an apparent cause, self resolved in 2 more weeks; (**d**) 3 months post operative result.

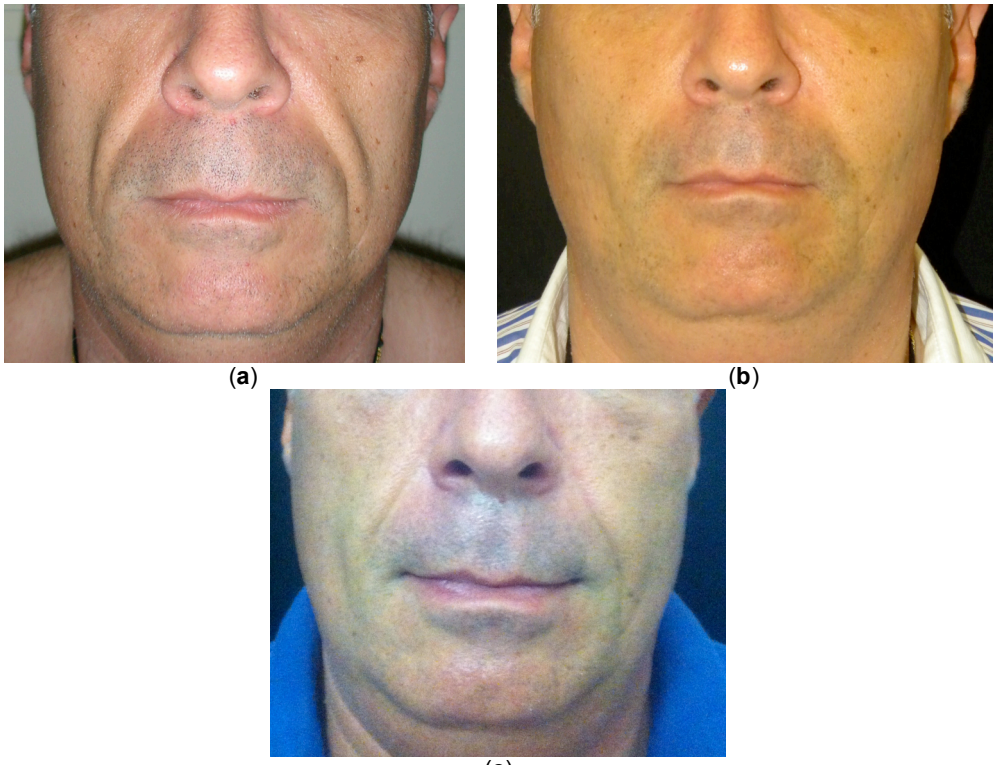
observed in the first 12 months; 1 of this patients started with the injections of calcium hydroxyapatite filler and 3 with polyacrylamide hydrogel based filler; in all the cases the re-touch with dermal fillers were performed at least 12 months after the structural fat graft; in 2 more cases structural fat graft was performed once again after 14 months (Figure **2a-d**). About the "filler study group" all the patients treated with hyaluronic acid fillers required another treatment after about 6 months, side effects or other complications were not recorder. Patients treated with polyacrylamide hydrogel based filler reported swelling and ecchymosis after the treatment, self resolving in 7 days, major complications such as infection or migration of the filler were never recorded; in 6 cases non visible but palpable nodules, well tolerated by the patients, were recorded; patients were happy with the result and no re-treatments were required during all the follow up (Figure **3a-c**, **4a-c**). Patients treated with calcium hydroxyapatite based filler reported swelling and ecchymosis after the treatment, self resolving in 7 days, major complications such as infection was never recorded; in 1 cases after 1 months from the injections swelling occurred without an apparent cause, and self resolved in 15 days (Figure **5a-d**); in all the cases a touch up of 3 mL of filler on average was performed 8 to 14 months after the first treatment (Figure **6a-c**).

9. DISCUSSION

Facial lipoatrophy, defined as flattening or indentation of normally convex facial contours, is the major stigma for HIV-infected people. It can have dramatic effects on their self-esteem and socialization, and it may result in reduced antiretroviral adherence [18].

Yang *et al*. performed a study comparing patients with lipoatrophy and controls without lipodystrophy or wasting [57]. MRI examinations to evaluate superficial fat volume, defined as the sum of the temporal, cheek and periorbital fat compartments, was performed in both groups. The mean difference in superficial facial fat between lipoatrophy and controls was greater than 20 mL on each side.

Davison *et al*. described the defects of facial wasting as a series of triangles [53]. The first triangle is observed above the zygomaticus major, the second below it, and the last is based at the zygomatic arch, extending superiorly. Rauso *et al*. described a characteristic triangular area, between the naso labial



(**a**) (**b**)

(**c**)

Figure 6: (**a**) pre operative picture of a 51 y.o. man affected by facial lipoatrophy planned for CaHa filler injections; (**b**) 2 months post operative result; (**c**) 10 months post operative picture shows the need to have a touch up to restore the desired result.

grove, the anterior margin of the masseter and the zygoma, as a facial marker for FW rehabilitation [58].

Facial volumization in this patient populations is quite different from patients requiring fillers or structural fat graft for cosmetic purpose, because, as already investigated, the amount of facial fat pads is high reduced; this issue can clearly justify the big amount of filler's volume used for FW rehabilitation, especially for the patients scoring between 2 and 4 in James/Carruthers scale.

Some authors described alternative surgical options as the use of malar implants, parotid flap, and so on, [59-61] however structural fat graft in medical literature looks to be much more performed than others procedures [62,63].

The use of the peripheral hypertrophied fat, harvested with suction assisted lipectomy, to restore the FW, theoretically seems the best option achievable, however different results have been reported in literature regarding the percentage of fat resorption, in fact also in author experience there is a quite high percentage (almost 50%) of patients that need a re-treatment with structural fat graft or filler injections; however when lipoatrophy of the face and lipohypertrophy of the body also are present, harvesting fat graft from the peripheral hypertrophied areas to restore facial areas seems to be reasonable, however the procedure must be explained carefully to the patients having them understanding the limitation of this procedure about facial filling and the benefits about body improvements; moreover attention must be paid if buffalo hump fat is used to restore facial features, because it can induce the developing of facial fat hypertrophy, as happened in a patients treated by the author and in a few already described cases present in literature [55].

Facial fillers looks as really reasonable option when facial lipoatrophy is the only stigmata of lipodystrophy, In a recent article, Sturm *et al,*. [64] performed a systematic review to determine the safety and efficacy of permanent and semipermanent dermal fillers to treat the visible effects of HIV-associated facial lipoatrophy [64].

They affirmed that the small number of well-designed studies limited the ability to draw firm conclusions; however, polylactic acid and polyacrylamide gel were the dermal fillers most used, and the studies cited by the authors showed that these fillers do not tend to cause serious short-term adverse events. Minor adverse events such as edema, ecchymosis, and erythema were associated with the

injection process, but they usually resolved within a matter of days. No granulomas were reported, but the incidence of lumps was higher with polylactic acid than with polyacrylamide gel. Lana *et al*. concluded that the higher incidence of lumps with the use of polylactic acid may be attributable to the large volume of product required (up to 20 ml per cheek) [64].

Ho¨nig, [65] reported high patient levels of satisfaction with the use of polyalkylimide gel (Bio-Alcamid, Polymekon, Italy) for the rehabilitation of facial lipoatrophy in HIV+ patients. In that study 7–16 ml of substance was injected into each cheek per treatment, up to a maximum of 25 ml (mean = 12 ml). Karim *et al,* [66] also reported a significant improvement in the quality of life of the patients after single-stage injection of Bio-Alcamid. A mean volume of 14 cc was injected subcutaneously at one or more sites of the face in a single stage. Favorable results with the use of polyacrylamide hydrogel (Aquamid) for reconstruction of facial lipoatrophy of the face in significantly immunocompromised individuals have been reported in the literature [63,67,68].

De Santis *et al*. reported a positive experience at 2 and 5 years in the management of HIV-related facial lipoatrophy in a very high-risk group in terms of susceptibility to infections; [67,69] in the longest follow up, 5 years long, with a very large number of patients (251), a total of 104 adverse events in 73 patients (29 percent) were reported throughout the 60-month follow-up period. These included edema, gel accumulation, hematoma, infection, and pain, with 53 (51 percent) being classified as treatment related and occurring in 40 patients (15.9 percent). All treatment-related adverse events had been resolved at study completion. Of the 53 treatment-related adverse events, 22 occurred in 18 patients (7.2 percent) within 30 days and 27 adverse events occurred in 21 patients (8.4 percent) beyond 30 days from the last injection. Nine serious adverse events occurring within 30 days of the injection were reported during the entire study. Only two of these were classified as treatment related. Both were infections and both were resolved within 11 and 14 days, respectively, of the 27 adverse events occurring in 21 patients beyond 30 days from the last injection, four were classified as treatment related, with two being serious [69].

Author's experience with non absorbable fillers is limited to the use of polyacrylamide hydrogel, this filler has been injected with a personal "one-step protocol", [56, 57] achieving pleasant results just in one treatment session; in medical literature there are different opinions about the safety of this permanent filler, however in author's experience, injecting this filler strictly following aseptic rules, looks safe and effective; choice about a permanent filler *vs* a long lasting one was up to the patient, after an extensively and clear explanations of alla the treatments available, comparing safety and durability [56, 57].

CaHa fillers are FDA-approved for facial augmentation in HIV patients with facial lipoatrophy, his safety and efficacy has been widely discussed in medical literature [39,40], author also published a personal protocol about a "one-step technique" for FW rehabilitation with CaHa based filler [40]. Results achieved by the author in this study, and also the safety and durability of this treatment, are on rate as ones already reported [39, 40].

Facial wasting rehabilitation is challenging, several techniques exists, however there is no the perfect one, from author's perspective the surgeon involved in restoring facial volume in HIV related lipoatrophy needs to be in confidence with the use of several fillers, from HA fillers to non absorbable ones, just to offer to the patient the best option available case by case; in cases scoring 1 in James and Carruthers severity scale, author prefer to use HA fillers because this patient population presents clinical features very close to the beginning of the facial aging process, represented by a moderate reduction of facial fat pads volume; when the score is higher, from 2 to 4, is preferred to use long lasting fillers or non absorbable ones, due to the big amount filler's volume needed to restore facial features. The choice between long lasting and non absorbable fillers was left to the patient after an extensive explanation about advantages and disadvantages of each product. Author did not use PLLA filler due to the need of a progressive facial features restoring; in already published studies author showed how patient's satisfaction is higher when a "one-step rehabilitation" is performed [46,56].

Surgical procedures, from author's point of view, should be left to patients presenting both facial lipoatrophy and body lipohypertrophy, in these cases the main purpose of surgery is to improve body shape and it is reasonable to perform, in the same surgical time, structural fat graft for the face, however it is really important to make the patient understand that with a quite high percentage (about 50%), others procedures such as filler or others session of structural fat graft will be needed to achieve a good aesthetic result for the

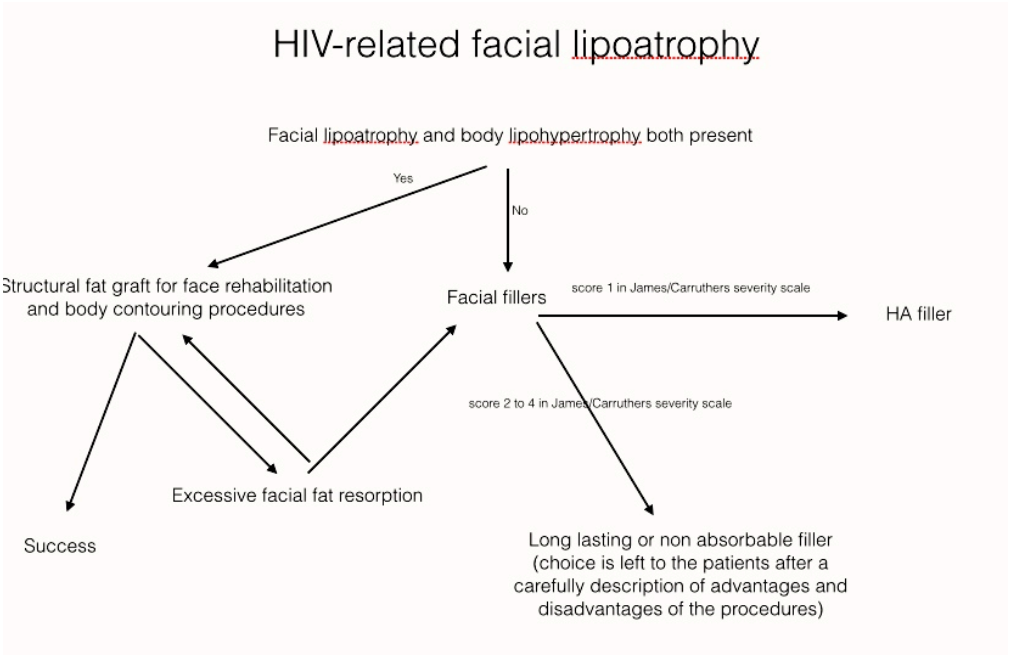


Figure 7:

face. In figure **7** is represented the algorithm followed by the author.

CONCLUSION

The perfect technique in FW rehabilitation does not exist, each clinical situation needs to be addressed in a different way, however from author's perspective if body lipohypertrophy is present surgical procedures characterized by body fat removal and structural fat graft of the face, even if we can get an high percentage of fat resorption, must be preferred instead of the use of facial fillers, and in case of failure of FW rehabilitation we can switch the treatment to the use of facial fillers; however body lipohypertrophy has been addressed. About facial fillers choices, author believe that excepting patients presenting 1 as score in lipoatrophy severity scale (in this case HA fillers are preferred due to the low amount of volume needed), the choice between long lasting and permanent fillers must be faced with the patients after a fully explanation about product advantages and disadvantages; anyway, the use of PLLA is excluded due to the need of several sessions to achieve a satisfactory result.

CONFLICT OF INTEREST

Author has nothing to disclose

REFERENCES

[1] Danner SA, Carr A, Leonard J, et al. Safety, pharmakinetics and preliminary efficacy of ritonavir, and inhibitor of HIV-1 protease. N Engl J Med 1995; 333: 1528-1533. https://doi.org/10.1056/NEJM199512073332303

[2] Hammer SM, Squires KE, Hughs MD, et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimetre or less. N Engl J Med 1997; 337: 725-733. https://doi.org/10.1056/NEJM199709113371101

[3] Carr A. HIV protease inhibitor-related lipodystrophy syndrome. Clin Infect Dis 2000; 30(Suppl 2): S135-S142. https://doi.org/10.1086/313854

[4] Waters L and Nelson M. Long-term complications of antiretroviral therapy: lipoatrophy. Int J Clin Pract 2007; 61: 999-1014. https://doi.org/10.1111/j.1742-1241.2007.01385.x

[5] Lichtenstein KA. Redefining lipodystrophy syndrome: risks and impact on clinical decision making. J Acquir Immune Defic Syndr 2005; 39: 395-400. https://doi.org/10.1097/01.qai.0000167478.28051.3a

[6] Carr A, Samaras K, Burton S, et al. Treatment response and durability of a double protease inhibitor therapy with saquinavir and ritonavir in an observational cohort of HIV-1 infected individuals. AIDS 1998; 12: F51-8. https://doi.org/10.1097/00002030-199807000-00003

[7] Domingo P, Sambeat MA, Perez A, Ordonez J, Rodriguez J and Vazquez G. Fat distribution and metabolic abnormalities in HIVinfected patients on first combination antiretroviral therapy including stavudine or zidovudine: role of physical activity as a protective factor. Antivir Ther 2003; 8: 223-31.

[8] Saint-Marc T, Partisani M, Poizot-Martin I, et al. A syndrome of peripheral fat wasting (lipodystrophy) in patients receiving longterm nucleoside analogue therapy. AIDS 1999; 13: 1659-67. https://doi.org/10.1097/00002030-199909100-00009

[9] Bacchetti P, Gripshover B, Grunfeld C, et al. Fat distribution in men with HIV infection. J Acquir Immune Defic Syndr 2005; 40: 121-31. https://doi.org/10.1097/01.qai.0000182230.47819.aa

[10] John M, Nolan D and Mallal S. Antiretroviral therapy and the lipodystrophy syndrome. Antivir Ther 2001; 6: 9-20.

[11] Noor MA, Parker RA, O'Mara E, et al. The effects of HIV protease inhibitors atazanavir and lopinavir/ritonavir on insulin sensitivity in HIV-seronegative healthy adults. AIDS 2004; 18: 2137-44. https://doi.org/10.1097/00002030-200411050-00005

[12] Gallant JE, Staszewski S, Pozniak AL, et al. Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral- naive patients: a 3-year randomized trial. JAMA 2004; 292: 191-201. https://doi.org/10.1001/jama.292.2.191

[13] Martinez E, Mocroft A, Garcia-Viejo MA, et al. Risk of lipodystrophy in HIV-1-infected patients treated with protease inhibitors: a prospective cohort study. Lancet 2001; 357: 592-8. https://doi.org/10.1016/S0140-6736(00)04056-3

[14] Calza L, Manfredi R and Chiodo F. Dyslipidaemia associated with antiretroviral therapy in HIV-infected patients. J Antimicrob Chemother 2004; 53: 10-4. https://doi.org/10.1093/jac/dkh013

[15] Jacobson DL, Jacobson DL, Knox T, et al. Prevalence of evolution of and risk factors for fat atrophy and fat deposition in a cohort of HIV-infected men and women. Clin Infect Dis 2005; 40: 1837-45. https://doi.org/10.1086/430379

[16] Miller J, Carr A, Emery S, et al. HIV lipodystrophy: prevalence, severity and correlates of risk in Australia. HIV Med 2003; 4: 293-301. https://doi.org/10.1046/j.1468-1293.2003.00159.x

[17] Lichtenstein KA, Ward DJ, Moorman AC, et al. Clinical assessment of HIV-associated lipodystrophy in an ambulatory population. AIDS 2001; 15: 1389-98. https://doi.org/10.1097/00002030-200107270-00008

[18] Duran S, Saves M, Spire B, et al. Failure to maintain long-term adherence to highly active antiretroviral therapy: the role of lipodystrophy. AIDS 2001; 15: 2441-2444. https://doi.org/10.1097/00002030-200112070-00012

[19] Waters L and Nelson M. Long-term complications of antiretroviral therapy: Lipoatrophy. Int J Clin Pract 2007; 61(6): 999-1014. https://doi.org/10.1111/j.1742-1241.2007.01385.x

[20] Fisher K. Wasting and lipodystrophy in patients infected with HIV: A practical approach in clinical practice. AIDS Read 2001; 11: 132.

[21] Corcoran C and Grinspoon S. The use of testosterone in the AIDS wasting syndrome. AIDS Clin Care 1999; 11: 25.

[22] Gold J and Battheram M. Nandrolone decanoate: Use in HIV-associated lipodystrophy syndrome: A pilot study (Letter). Int J STD AIDS 1999; 10: 558. https://doi.org/10.1177/095646249901000814

[23] Hengge UR, Stocks K, Unger S, Faulkner S, Goos M and Dudley R. Randomized phase III trial of oxymetholone for the treatment of HIV wasting and lipodystrophy. Presented at the Ninth Conference on Retroviruses and Opportunistic Infections, Seattle, Wash 2002; 24-28.

[24] James J, Carruthers A and Carruthers J. HIV-associated facial lipoatrophy. Dermatol Surg 2002; 28: 979-986.

[25] Narins RS and Bowman PH. Injectable skin fillers. Clin Plast Surg 2005; 32: 151 https://doi.org/10.1016/j.cps.2004.12.002

[26] Bechara FG, Gambichler T, Brockmeyer NH, et al. Hyaluronic acid new formulation: experience in HIV-associated facial lipoatrophy. Dermatology 2008; 217: 244-9. https://doi.org/10.1159/000148252

[27] Woerle B, Hanke CW, Satteler G. Poly-L-lactic acid: a temporary filler for soft tissue augmentation. J Drugs Dermatol 2004; 3(4): 385Ð389.

[28] Sherman RN. Sculptra: the new three-dimensional filler. Clin Plast Surg 2006; 33(4): 539-550.

[29] Lowe NJ. Dispelling the myth: appropriate use of poly-L-lactic acid and clinical consideration. J Eur Acad Dermatol Venereol s1:2Ð6, 2006.

[30] Rendon MI. Long-term aesthetic outcomes with injectable poly-l-lactic acid: observations and practical reccomendations based on clinical experience over 5 years. J Cosmet Dermatol 2012;11(2): 93-100. https://doi.org/10.1111/j.1473-2165.2012.00609.x

[31] Ezzat WH and Keller GS. The use of poly-L-lactic acid filler in facial aesthetics. Facial Plast Surg 2011; 27(6): 503-9. https://doi.org/10.1055/s-0031-1298782

[32] Douglas RM and Humble GM. Retreatment with injectable Poly-L-Lactic Acid for HIV-associated facial lipoatrophy: 24 months extension of the blue pacific study. Dermatol Surg 2009; 35: 350-359. https://doi.org/10.1111/j.1524-4725.2008.01047.x

[33] Douglas RM and Humble GM. Safety and efficacy of Poly-L-Lactic Acid injections in the persons with HIV-associated lipoatrphy: The US experience. Dermatol Surg 2006; 32: 1336-1345.

[34] Tzikas TL. Evaluation of Radiance FN soft tissue filler for facial soft tissue augmentation. Arch Facial Plast Surg 2004; 6:34Ð239.

[35] Graivier MH, Bass LS, Busso M, Jasin ME, Narins RS and Tzikas TL. Calcium Hydroxylapatite (Radiesse) for correction of the mid- and lower face: Consensus reccomendations. Plast Reconstr Surg 2007; 120(Suppl): 55S. https://doi.org/10.1097/01.prs.0000285109.34527.b9

[36] Marmur ES, Phelps R and Goldberg DJ. Clinical, histologic, and electron microscopic findings after injection of a calcium hydroxylapatite filler. J Cosmet Laser Ther 2004; 6: 223-226. https://doi.org/10.1080/14764170410003048

[37] Alam M and Yoo SS. Technique for calcium hydroxylapatite injection for correction of nasolabial fold depressions. J Am Acad Dermatol 2007; 56: 285-289. https://doi.org/10.1016/j.jaad.2006.09.014

[38] Carruthers A, Liebeskind B, Carruthers J and Forster BB. Radiographic and computed tomographic studies of calcium hydroxylapatite for treatment of HIV- associated facial lipoatrophy and correction of naso- labial folds. Dermatol Surg 2008; 34: S78-S84. https://doi.org/10.1097/00042728-200806001-00017

[39] Rauso R, Curinga G, Rusciani A, Colella G, Amore R and Tartaro G. Safety and efficacy of one-step rehabilitation of human immunodeficiency virus-related facial lipoatrophy using an injectable calcium hydroxylapatite dermal filler. Dermatol Surg 2013; 39(12): 1887-94. Epub 2013 Nov 7. https://doi.org/10.1111/dsu.12358

[40] Kolle F. Plastic and Cosmetic Surgery. New York: Appleton 1911; 209-230.

[41] Rapaport MJ, Vinnik C and Zarem H. Injectable silicone: Cause of facial nodules, cellulitis, ulceration, and migration. Aesthetic Plast Surg 1996; 20: 267. https://doi.org/10.1007/s002669900032

[42] Ersek RA and Beisang AA. III. Bioplastique: A new textured copolymer microparticle promises permanence in soft-tissue augmentation. Plast Reconstr Surg 1991; 87: 693. https://doi.org/10.1097/00006534-199104000-00014

[43] Lemperle G, Romano JJ and Busso M. Soft tissue augmentation with Artecoll: 10-year history, indications, techniques, and complications. Dermatol Surg 2003; 29: 573. https://doi.org/10.1097/00042728-200306000-00004

[44] Broder KW and Cohen SR. An overview of permanent and semipermanents fillers. Plast Reconstr Surg 2006; 118(Suppl): 7S. https://doi.org/10.1097/01.prs.0000234900.26676.0b

[45] Rauso R, Freda N, Parlato V, Gherardini G, Amore R and Tartaro G. Polyacrylamide gel injection for treatment of human immunodeficiency virus-associated facial lipoatrophy:

18 months follow-up. Dermatol Surg 2011. https://doi.org/10.1111/j.1524-4725.2011.02131.x

[46] Rauso R, Gherardini G, Greco M and Tartaro G. Is buffalo hump fat the perfect filler for facial wasting rehabilitation? Reflection on three cases. Eur J Plast Surg 2011.

[47] Rauso R, Curinga G, Santillo V, Corvo G and Tartaro G. Comparison between lipofilling and a non resorbable filler for facial wasting rehabilitation in HIV+ patients. J Craniofac Surg. 2011; 22(5): 1684-8. https://doi.org/10.1097/SCS.0b013e31822e5cf8

[48] Neuber F. Fettransplantation Chir Kongr Verhandl Dtsch. Gesellsch Chir 1893; 22: 66.

[49] Fischer A and Fischer GM. Revised technique for cellulitis fat: Reduction in riding breeches deformity. Bull Int Acad Cosmet Surg 1977; 2: 40.

[50] Illouz YG. The fat cell "graft": A new technique to fill depressions. Plast Reconstr Surg 1986; 78: 122. https://doi.org/10.1097/00006534-198607000-00028

[51] Asken S. Liposuction Surgery and Autologous Fat Transplantation. Norwalk, Conn.: Appleton & Lange 1988.

[52] Coleman SR. Structural fat grafting. In F. Nahai (Ed.), The Art of Aesthetic Surgery: Principles and Techniques. St. Louis: Quality Medical 2005; 289-363.

[53] Davison SP, Timpone J and Hannan CM. Surgical algorithm for management of HIV lipodystrophy. Plast Reconstr Surg 2007; 120: 1843. https://doi.org/10.1097/01.prs.0000267341.14550.a7

[54] Guaraldi G, De Fazio D, Orlando G, Murri R, Wu A, Guaraldi P, et al. Facial lipohypertrophy in HIV-infected subjects who underwent autologous fat tissue transplantation. Clin Infect Dis 2004; 40(2): e13-5. https://doi.org/10.1086/426686

[55] Rauso R, Gherardini G, Parlato V, Amore R and Tartaro G. Polyacrylamide Gel for Facial Wasting Rehabilitation: How many milliliters per session? Aesthetic Plast Surg 2011. [Epub ahead of print].

[56] Yang Y, Sitoh YY, Tha NO and Paton NI. Facial fat volume in HIV-infected patients with lipoatrophy. Antiviral Ther 2005; 10: 575-581.

[57] Rauso R. 5-Year Study of a Polyacrylamide Hydrogel-Based Filler for Rehabilitation of HIV-Related Facial Lipoatrophy. Aesthete Surg J 2015; 7: pii: sjv036. [Epub ahead of print].

[58] Rauso R, Tartaro G, Freda N, Rusciani A and Curinga G. A facial marker in facial wasting rehabilitation. J Drugs Dermatol 2012; 11(2): 202-8.

[59] Talmor M, Hoffman LA and LaTrenta GS. Facial atrophy in HIV-related fat redistribution syndrome: Anatomic evaluation and surgical reconstruction. Ann Plast Surg 2002; 49: 11-18. https://doi.org/10.1097/00000637-200207000-00002

[60] Mori A, Lo Russo G, Agostini T, Pattarino J, Vichi F and Dini M. Treatment of human immunodeficiency virus-associated facial lipoatrophy with lipofilling and submalar silicone implants. J Plast Reconstr Aesthet Surg 2006; 59: 1209-1216. https://doi.org/10.1016/j.bjps.2005.12.047

[61] Claude O, Domergue Than Trong E, Blanc R, Ascher B, Bagot M, et al. Traitment des lipoatrophies facials utilisant des implants de Medpor en polyethylene poreux. Ann Chir Plast Esthet 2009; 54: 21-28. https://doi.org/10.1016/j.anplas.2008.05.009

[62] Serra-Renom JM and Fontdevila J. Treatment of facial atrophy related to treatment with protease inhibitors by autologous fat injection in patients with Human Immunodeficiency Virus infection. Plast Reconstr Surg 2004; 114: 551-5. https://doi.org/10.1097/01.PRS.0000128427.54445.63

[63] Negredo E, Higueras C, Adell X, Martinez JC, Martinez E, Puig J, et al. Reconstructive treatment for antiretroviral-associated facial lipoatrophy: a prospective study comparing autologous fat and synthetic substances. AIDS Patient Care STDS 2006; 20(12): 829-837. https://doi.org/10.1089/apc.2006.20.829

[64] Sturm LP, Cooter RD, Mutimer KL, Graham JC and Maddern GJ. A systematic review of permanent and semipermanent dermal fillers for HIV-associated facial lipoatrophy. AIDS Patient Care STDS 2009; 23: 699-714. https://doi.org/10.1089/apc.2008.0230

[65] Ho¨nig J. Cheek augmentation with Bio-Alcamid in facial lipoatrophy in HIV seropositive patients. J Craniofac Surg 2008; 19(4): 1085-1088. https://doi.org/10.1097/SCS.0b013e31811eda9c

[66] Karim RB, de Lint CA, van Galen SR, van Rozelaar L, Nieuwkerk PT, et al. Long-term effect of polyalkylimide gel injections on severity of facial lipoatrophy and quality of life of HIV-positive patients. Aesthetic Plast Surg 2008; 32(6): 873-878. https://doi.org/10.1007/s00266-008-9189-8

[67] De Santis G, Jacob V, Baccarani A, Pedone A, Pinelli M, et al. Polyacrylamide hydrogel injection in the management of human immunodeficiency virus-related facial lipoatrophy: a 2 year clinical experience. Plast Reconstr Surg 2008; 121: 644-653. https://doi.org/10.1097/01.prs.0000298108.46379.15

[68] Negredo E, Puig J, Aldea D, Medina M, Estany C, et al. Four-year safety with polyacrylamide hydrogel to correct antiretroviral-related facial lipoatrophy. AIDS Res Hum Retrovir 2009; 25: 451-455. https://doi.org/10.1089/aid.2008.0230

[69] De Santis G, Pignatti M, Baccarani A, Pedone A, Spaggiari A, et al. Long-term efficacy and safety of polyacrylamide hydrogel injection in the treatment of human immunodeficiency virus-related facial lipoatrophy: a 5-year follow-up. Plast Reconstr Surg 2012; 129(1): 101-9. https://doi.org/10.1097/PRS.0b013e3182362142

Received on 21-11-2017 Accepted on 28-12-2017 Published on 31-12-2017