

# The Effect of Lipectomy/Liposuction on Lipid Profiles in Antiretroviral Drug-induced Lipodystrophy Syndrome

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**Background:** One of the adverse effects of antiretroviral (ARV) drugs in the treatment of human immunodeficiency virus is lipodystrophy, which is often associated with metabolic complications such as hyperlipidemia, increased cardiovascular risk factors, and altered body fat distribution. This is characterized by a dorsal hump, hypermastia, or abdominal pannus deformity. The reasons for corrective surgery are aesthetic, psychosocial, and medical benefits.

**Methods:** This is a prospective study investigating 52 consecutive patients with ARV-induced lipodystrophy syndrome referred for surgical correction (liposuction for dorsal hump, abdominoplasty for increased abdominal pannus, and bilateral breast reduction for hypermastia). Fasting serum lipograms, including cholesterol, triglycerides, high-density cholesterol (HDL), and low-density cholesterol (LDL), were taken preoperatively and repeated 9–12 months post lipectomy/liposuction.

**Results:** A subgroup of 35 patients with deranged preoperative triglycerides ( $P = 0.004$ ), cholesterol ( $P = 0.001$ ), and or LDL cholesterol ( $P = 0.017$ ) showed a statistically significant ( $P < 0.05$ ) decrease in postoperative levels. If preoperative lipogram values were normal, there is no statistically significant reduction postoperatively.

**Conclusions:** In ARV-associated lipodystrophy, when the preoperative fasting lipograms are deranged, then after surgical correction there is a statistically significant reduction in triglyceride, total cholesterol, and LDL levels. This influences their cardiovascular risk profile, mortality, morbidity, and quality of life. (*Plast Reconstr Surg Glob Open* 2020;8:e3171; doi: [10.1097/GOX.0000000000003171](https://doi.org/10.1097/GOX.0000000000003171); Published online 29 October 2020.)

## INTRODUCTION

The World Health Organization recommendation is that all 36.7 million people living with human immunodeficiency virus (HIV) (67% in Sub-Saharan Africa) are eligible for antiretrovirals (ARV) drugs.<sup>1</sup> There is still a controversy over how frequently lipodystrophy occurs, especially with the presumption that the prevalence of

lipodystrophy will be lower with the increased use of newer ARV drugs.<sup>2</sup> There is also an association with the duration of treatment, and certain drugs have irreversible side effects.<sup>3</sup> Therefore, lipodystrophy syndrome, in the form of lipohypertrophy and lipoatrophy, is still prevalent. Lipodystrophy is associated with disorders in lipid metabolism such as elevated serum concentrations of total cholesterol, triglycerides, low-density lipoproteins (LDL), and very low levels of high-density lipoproteins (HDL).<sup>4–6</sup>

The consequences of lipodystrophy syndrome are both psychosocial and medical.<sup>7</sup> The associated dyslipidemia has a 20%–80% increased risk for cardiovascular disease.<sup>8</sup> Lipohypertrophy presents with fat redistribution and disfigurement in the form of a buffalo hump increased abdominal pannus or macromastia.<sup>8,9</sup>

The aim of this study was to determine the role of surgical intervention in the medical (change in serum lipogram levels), physical, and psychosocial management of ARV-associated lipodystrophy.

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## STATISTICAL ANALYSIS

Statistical analysis using a probability of 95% is 2-tailed, with  $P < 0.05$  and a confidence interval of 95% being considered statistically significant. Parametric testing using the t-test and ANOVA, and nonparametric testing with Wilcoxon signed ranks test and Kruskal–Wallis were done. A descriptive statistical analysis for central tendency, homogeneity of variances, equality of means, and effect size was implemented.

## PATIENTS AND METHODS

This prospective clinical trial was conducted at Chris Hani Baragwaneth Academic Hospital in Soweto, South Africa. Sixty-one consecutive patients with ARV-associated lipodystrophy had a surgical intervention in the form of lipectomy or liposuction. Nine patients were lost to follow-up; therefore, 52 patients were included in the study. One patient underwent both a bilateral breast reduction (BBR) and liposuction for buffalo hump, and therefore the total data are for 53 surgical procedures.

Patients were referred from HIV specialist centers. The diagnosis of lipohypertrophy is based on clinical assessment. The inclusion criteria are: HIV positive on ARVs, referred with ARV-induced lipodystrophy syndrome, had at least one change by an HIV specialist in their ARV regime, the lipodystrophy was stable for at least 1 year, over the age of 18 years, surgically fit, and gave informed consent as laid out by ethics committee at the University of Witwatersrand, under their approval.

The primary end point of surgical correction was medical risk reduction measured by serum fasting lipograms (total cholesterol, triglyceride, and LDL and HDL cholesterol) taken 24–48 hours preoperatively and a repeat fasting lipogram 9–12 months postoperatively. The normal ranges are defined as total cholesterol  $<5$  mmol/L, triglycerides  $<1.7$  mmol/L, LDL cholesterol  $<3$  mmol/L, and HDL cholesterol  $>1.2$  mmol/L. No specific dietary or lifestyle advice was given, and patients returned to their preoperative lifestyle and activity level 1 month after surgical correction. A subcohort of 35 patients who had deranged preoperative lipograms was analyzed in the same way.

The secondary end points of this study include: the impact of surgical intervention on the patients, postoperative complications, and recurrence rates. This was done via patient feedback, clinical examination, and measurements. These were done preoperatively, 1, 3, and 9–12 months postoperatively.

## RESULTS

The mean age is 26 years (range 22–54), and 51 of the 52 patients (98.1%) are women.

Fifty-two patients had 53 surgical procedures. In total, 23 patients with macromastia had BBR, 11 patients with increased abdominal pannus had abdominoplasty, and 19 patients had liposuction for their dorsal humps. Overall, there is no statistically significant difference in any of the preoperative and postoperative lipogram values, as summarized in Table 1.

**Table 1. Data for All Patients**

	Preoperative Median Value (mmol/L)	Postoperative Median Value (mmol/L)	<i>P</i>	Normal Range (mmol/L)
Total cholesterol	4.938	4.938	0.379	$<5$
Triglycerides	1.594	1.506	0.965	$<1.7$
HDL cholesterol	1.310	1.312	0.168	$>1.2$
LDL cholesterol	2.839	2.698	0.137	$<3$

Of the 52 patients, 35 had some form of derangement on their preoperative fasting lipograms. Twenty-four patients had raised total cholesterol, 18 raised triglycerides, 21 raised LDL cholesterol, and 4 lowered HDL cholesterol values. The patient who had both a BBR and liposuction had a normal preoperative fasting lipogram.

The subgroup of patients with one or more deranged value on their preoperative fasting lipogram show a statistically significant ( $P < 0.05$ ) decrease in their postoperative cholesterol ( $P = 0.001$ ), triglycerides ( $P = 0.004$ ), and LDL cholesterol ( $P = 0.017$ ). There was no statistically significant change in the HDL cholesterol ( $P = 0.066$ ). Most clinically significant in terms of risk factors are the triglyceride levels. Figure 1 shows, in the subgroup with elevated/abnormal preoperative triglycerides, the statistically significant ( $P < 0.004$ ) effect of surgical intervention on triglyceride levels postoperatively. The median preoperative and postoperative cholesterol, triglyceride, and LDL and HDL cholesterol in this subgroup are indicated in Table 2.

Three patients presented with recurrence, 1 patient with post BBR at 12 months (this patient has a reoperative procedure that did not form part of this trial), and 2 patients with dorsal humps had recurrences at 9 and 11 months, respectively.

The median resection mass of all surgical corrective procedures was 1,150 g. There was no statistically significant difference between resection mass and changes in lipogram values ( $P = 0.965$ ). The median resection volume postliposuction for dorsal hump was 650 ml. In this group, there was also no statistically significant difference ( $P = 0.84$ ) between resection volume and alteration in lipogram values.

No major complications were reported. The minor complications in each group are seen in Table 3. All complications were treated conservatively and did not require hospital admission or subsequent surgical management or intervention.

## DISCUSSION

The prevalence of lipodystrophy in South Africa is reported as 11.7% in a random clinical cohort study of 497 patients. Significantly, 5.9% of these patients reported that they would stop taking ARVs based on this side effect alone,<sup>10</sup> which influences their morbidity and mortality and poses a potential public health risk with regard to resistance. Lipodystrophy is common in a resource-limited setting, and has implications for risk of metabolic disease; quality of life, adherence, and comprehensive evidence-based interventions are required.<sup>11</sup>

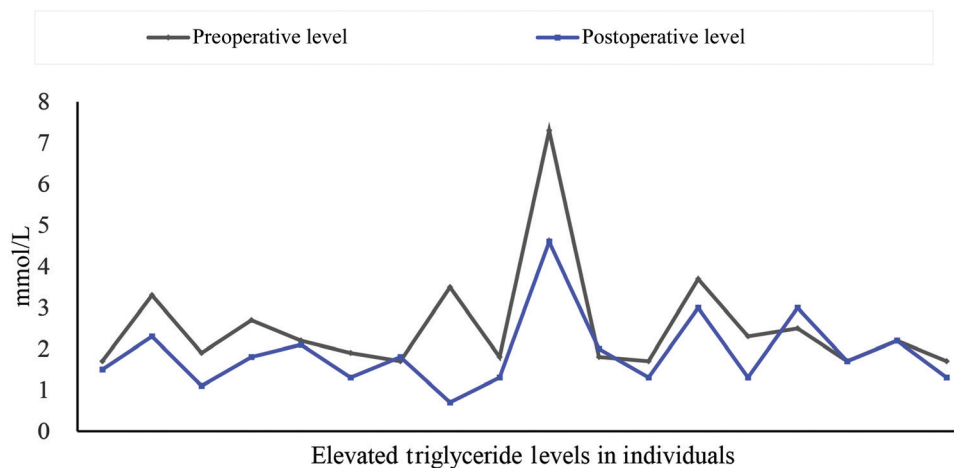


Fig. 1. Graph showing elevated presurgical and postoperative triglyceride levels in a subgroup.

**Table 2. Preoperative and Postoperative Median Cholesterol, Triglyceride, HDL and LDL Levels in a Subgroup Analysis of Patients with Abnormal Preoperative Levels**

	Cholesterol (mmol/L)		Triglycerides (mmol/L)		HDL (mmol/L)		LDL (mmol/L)	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
Median	5.750	5.400	2.050	1.750	3.600	3.305	0.825	1.175
Interquartile range	5.2–8.3	4.6–6.9	1.7–7.3	0.7–4.6	3.3–5.4	1.6–4.5	0.7–0.9	0.8–1.8

**Table 3. Postoperative Complications**

	Seroma	Sensation Loss	Wound Breakdown	Wound Infection	Hypertrophic scarring
Abdominoplasty	0	0	1	1	1
BBR	2	1	2	0	1
Dorsal hump	0	0	0	0	1

Triglyceride levels of 150 mg/dl or 1.7 mmol/L or more constitute a risk factor for metabolic syndrome,<sup>12, 13</sup> coronary artery disease, stroke, and type 2 Diabetes Mellitus and peripheral vascular disease.<sup>14</sup> Triglyceride levels are dose-dependently associated with a greater risk of cardiovascular disease, and they all affect mortality.<sup>15</sup> The incidence of coronary artery disease increases by 20% with an increase of triglycerides of 0.2 mmol/L.<sup>16</sup> In our study, in the subgroup of patients with deranged preoperative triglyceride levels, their triglyceride level decreased by an average of 1.44 mmol/L in the postoperative follow-up ( $P=0.004$ ), which can be equated to 120% risk reduction.

Evidence of a graded and strong correlation between total blood cholesterol and LDL cholesterol and risk for cardiovascular disease has been shown, and these are considered independent risk factors.<sup>17</sup> Meta-analyses of multiple statin trials demonstrate that for every 1.0 mmol/L reduction in LDL cholesterol, there is an associated 20%–25% decrease in cardiovascular mortality and nonfatal myocardial infarctions.<sup>18</sup> In our study, there was a statistically significant decrease in the total cholesterol ( $P=0.001$ ) and the LDL cholesterol ( $P=0.017$ ) in the subset of high-risk patients that has deranged preoperative lipogram values. The median LDL cholesterol levels pre and postoperatively were 3.6 and 3.2 mmol/L,

respectively, which equates to an 8%–10% decrease in cardiovascular mortality and nonfatal myocardial infarctions.

Although most evidence is based on the general population, there is some evidence and confounding factors specific to HIV- and ARV-induced lipodystrophy. Cardiovascular disease risk factors are elevated in HIV-positive patients with fat redistribution.<sup>19</sup> There is a strong association between lipohypertrophy and coronary artery calcium scores and the progression of subclinical atherosclerosis.<sup>20</sup> A meta-analysis by Viganò et al<sup>21</sup> found that the incidence of associated new-onset hypercholesterolemia and hypertriglyceridemia is 24% and 19%, respectively in lipodystrophy syndrome.

In the general population, Swanson<sup>22</sup> reported preoperative high triglycerides in 36.8% of patients who underwent liposuction. Similarly, in our study among the population of ARVs, 34% of the patients had high preoperative triglyceride levels. Earlier studies, prior to the prospective clinical study by Swanson<sup>22</sup> that look at changes in lipid levels associated with lumpectomy and liposuction, have shown incongruent results and are mostly small groups (9–15 patients), which limit its statistical significance, and are predominantly in obese female patients.<sup>23–27</sup> All studies were conducted on the general population and none exclusively on HIV-positive patients with ARV-associated lipodystrophy syndrome.

In a study by Ybarra et al,<sup>28</sup> a reduction in triglyceride levels and an increase in cholesterol levels were seen 4 months after abdominal liposuction. However, Robles-Cervantes et al<sup>29</sup> found that 1 month after abdominal liposuction there was no significant changes in lipid values. A large prospective study on 322 patients conducted by Swanson<sup>22</sup> showed a significant ( $P < 0.001$ )

reduction in triglyceride levels although the cholesterol levels remained unchanged in patients with elevated preoperative levels of triglycerides postliposuction and liposuction/abdominoplasty. The results from our study show that in the subgroup of patients with elevated preoperative triglyceride levels, there is a statically significant decrease in triglyceride levels postoperatively ( $P = 0.004$ ) as well as cholesterol ( $P = 0.001$ ) and LDL cholesterol ( $P = 0.017$ ).

Danilla et al<sup>30</sup> report, in a meta-analysis, that there is a statistically significant difference when comparing patients by treatment areas, and hence suggested that the overall volume of subcutaneous fat removed is relevant as opposed to anatomical location. Swanson<sup>22</sup> found that liposuction patients who had aspirate volumes of at least 3,000 ml had a greater reduction in triglyceride levels than those with lower aspirate volumes. Our study however had a median resection volume of 1,150 ml less than half that reported by Swanson.<sup>22</sup> No statistically significant difference between resection volumes and changes in lipogram values ( $P = 0.965$ ) was found. Nor did the subgroup of patients with elevated triglyceride levels preoperatively show a statistically significant difference in the resection volumes and response to treatment ( $P = 0.685$ ). Perhaps this is due to altered pathophysiology associated with lipodystrophy syndrome as opposed to the general population represented by studies conducted to date.

Potential limitations of this study are that it was conducted a few years ago when a large number of older ARV agents were routinely used, and that follow-up serology and blood tests were done 9–12 months later, which is a longer follow-up time than that reported for most of the other studies, as resource constraints on laboratory services exist.

## CONCLUSIONS

No previous studies, to the researcher's knowledge, have reviewed the effect of lipectomy/liposuction in HIV-positive patients with ARV-induced lipodystrophy syndrome on lipid profiles pre-and postoperatively. There was a statistically significant decrease in triglyceride, total cholesterol, and LDL cholesterol levels postoperatively in patients with elevated preoperative levels. The potential impact of this is multifactorial and could not only change the cardiovascular risk profiles of patients, affect morbidity and mortality, as well as quality of life and the burden of disease, but also provide an effective standard of treatment in the future.

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