Review Article

Liposuction: an actualization of the risk factors and their clinical and surgical relevance

Lipoaspiração: atualização dos fatores de riscos metabólicos e sua importância clínico-cirúrgica

GUILHERME PINTARELLI[1]
ROGERIO SCHUTZLER GOMES[2]
JULIANA DOMINGOS ROCHA[3]

Affiliation: Work performed at the Beiramar Clinic for Plastic Surgery (Clínica Beiramar de Cirurgia Plástica), Florianópolis, SC, Brazil.

Article received: November 4, 2012.
Article accepted: May 19, 2013.

DOI: 10.5935/2177-1235.2014RBCP0082

■ **ABSTRACT**

Liposuction is one of the most frequently performed procedures by plastic surgeons. The increased safety associated with the surgical settings, technical refinements, and level of patient satisfaction have contributed to the popularity gained by this intervention since it was first introduced by Ilouz in 1979 (4). Moreover, among medical communities and the media, concerns have risen regarding not only the drastic changes in patients' appearance but also the safety of the procedure. Fat tissue is known to act as a legitimate endocrine organ (5), being the primary depository for triglycerides, which classically relate to atherosclerosis and insulin resistance (6, 7). Recent work has linked lipid metabolism in adipocytes to the maintenance of low levels of systemic inflammation through a series of mediators (8-10). Scientific evidence (11) revealed an increase in the percentage of obese people in our country, as well as a considerable proportion of overweight people. This study also investigates the relationship between the prevalence of diabetes and hypertension. The classic association between body mass index and common metabolic diseases has led to investigations focused on several factors involved in this relationship, along with research work directed at the treatments available. The discovery of leptin in the 1990s (12) highlights the regulatory properties of the adipose tissue, whereas recent studies (5, 13) have established a link with the synthesis of other factors. In this study, we aimed to perform a review of literatures that discuss the current state-of-the-art of scientific research, in which we organized published works in a didactic manner in order to facilitate better understanding, and promote the safety and efficacy of liposuction.

Keywords: Lipectomy; Cholesterol; Tumor Necrosis Factor Alpha; Triglycerides; Interleukins.

[1]Associated Member of the Brazilian Society of Plastic Surgery (SBCP), Member of the clinical staff of the Beiramar Clinic for Plastic Surgery (Clínica Beiramar de Cirurgia Plástica), Florianópolis, SC, Brazil.

[2]Full Member of the Brazilian Society of Plastic Surgery (SBCP), Director of the Beiramar Clinic for Plastic Surgery (Clínica Beiramar de Cirurgia Plástica), Florianópolis, SC, Brazil.

[3]General Surgeon, Trainee at the Beiramar Clinic for Plastic Surgery (Clínica Beiramar de Cirurgia Plástica), Florianópolis, SC, Brazil.

■ **RESUMO**

A lipoaspiração permanece como um dos procedimentos mais realizados pelos cirurgiões plásticos (1-3). O aumento da segurança no ambiente cirúrgico, o refinamento da técnica e a satisfação das pacientes contribuem para a popularidade desta intervenção idealizada por Ilouz, em 1979 (4). Tem-se observado, ainda, tanto no ambiente médico quanto na mídia, uma crescente preocupação não apenas com a nova forma dos pacientes, mas também com a segurança. O tecido adiposo atua como um verdadeiro órgão endócrino (5) e é o principal depósito de triglicerídeos, que têm uma relação clássica com doença aterosclerótica e resistência insulínica (6, 7). Estudos recentes ligaram ainda o metabolismo lipídico dos adipócitos à manutenção de um estado inflamatório sistêmico de baixo grau, através de vários mediadores (8-10). Há evidências científicas (11) que mostram o aumento do percentual de obesos em nosso país e uma importante taxa de pessoas, com sobrepeso. Este estudo também relaciona a prevalência de diabetes e de hipertensão. A clássica inter-relação entre a quantidade de gordura corporal e as chamadas doenças metabólicas tem suscitado a investigação dos elementos envolvidos neste processo e de tratamentos para o controle dos mesmos. A descoberta da leptina na década de 1990 (12) chamou a atenção para a propriedade reguladora do tecido adiposo. Estudos posteriores (5, 13) relacionaram ainda a síntese de outros fatores. Decidimos fazer uma revisão da literatura para esclarecer o estágio atual das pesquisas, tentando ordená-las de forma didática para melhor compreensão e auxílio para uma conduta mais segura e eficiente nos pacientes submetidos à lipoaspiração.

Descritores: Lipectomia; Colesterol; Leptina; Fator de Necrose Tumoral Alfa; Triglicerídeos; Interleucinas.

INTRODUCTION

Liposuction is the surgical procedure used for the removal of fat deposits in areas perceived as unaesthetic. It was initially designed to treat specific regions, but the technical advances have expanded its application to include large areas, which requires consideration of hematological and metabolic changes and procedural adaptations. Because of these changes, the application of liposuction has become versatile, ranging from minor surgical interventions performed in private practices to more elaborate surgeries performed in hospitals, accompanied by all the required support measures.

Liposuction has evolved over time and remains as one of the most frequently performed procedures by plastic surgeons[1-3]. The increased safety in surgical settings, technical refinement, and levels of patient satisfaction have contributed to its gain in popularity since it was first introduced by Ilouz in 1979[4]. Furthermore, among medical communities and the media, concerns have arisen regarding not only the drastic changes in patients' appearance but also the safety of the procedure, which includes hematological and metabolic alterations, as well as its associated potential complications.

Currently, adipose tissue is known to act as a legitimate endocrine organ[5], in addition to being the main storage of triglycerides, molecules classically related to atherosclerosis and insulin resistance[6,7]. Recent work has linked lipid metabolism in adipocytes to the maintenance of low levels of systemic inflammation, mediated by a series of factors[8-10].

Scientific evidence[11] showed that the percentage of obese people among the total population of Brazil has increased, from 11.4% in 2006 to 15.8% in 2011, and that the proportion of overweight people is high at 48.5%. This study also links the prevalence of diabetes (6% of the general population) and hypertension (22.7% of the general population) to obesity. The classic close relationship between the amount of body fat and metabolic diseases has led to research focused on the elements involved in this process and on treatment options.

The discovery of leptin in the 1990s highlighted the regulatory properties of the adipose tissue through the production and secretion of proteins. Meanwhile, more studies have been performed[5,13], establishing further connections to the synthesis of other factors such as interleukin 6, angiotensinogen, tumor necrosis factor α (TNF-α), transforming growth factor β (TGF-β), adiponectin, apolipoproteins, and resistin.

In light of the considerable amount of recently published evidence on the hematological and metabolic changes associated with liposuction, published sporadically and often not integrated in a wider context, we decided to review the literature to determine the actual state-of-the-art of the research and to organize and present published works in a more informative manner to facilitate better understanding, in the hope that it will lead to a safer and more efficient management of patients undergoing liposuction.

SERUM LIPID LEVELS

The identification of cholesterol as a constituent of atheroma plaques has raised questions regarding the contribution of lipid metabolism in the development of coronary disease[14,15]. Cholesterol is present in several tissues as part of cell membranes and as a precursor for bile acids and steroid hormones. It is transported in the bloodstream as part of lipoproteins, particles formed by lipid and protein moieties, which can be divided into three main classes, namely low-density lipoproteins (LDLs), high-density lipoproteins (HDLs), and very-low-density lipoproteins (VLDLs).

LDL, which carries approximately 70% of the total cholesterol in the serum, is the lipoprotein that mostly contributes to atheromas, as observed in the population affected by genetic conditions leading to hypercholesterolemia and precocious atherosclerosis[16]. It is formed by only one apolipoprotein (apo B) and is currently the main target of risk reduction therapies[17]. HDL associates with 20–30% of the serum cholesterol and is formed by the apolipoproteins A-I e A-II. It is considered an independent risk factor, and several studies have associated its low levels with an increase in morbidity and mortality[18,19].

Concerning triglycerides, some reports have established an association with coronary disease[7,20]. However, other studies that conducted multivariate analyses did not recognize triglycerides as an isolated risk factor[21]. Triglycerides are believed to indirectly lower the levels of circulating HDL, thus contributing to atherosclerosis[22]. The main therapies currently used toward improving lipid levels are the use of fibrates and nutrition re-education combined with physical activity[17].

Samdal[23] was the first to test the response of serum lipids after liposuction. In a study with nine obese female patients, a significant increase in HDL and apolipoprotein A-I was observed 1 year after surgery. Baxter[24] later detected a decrease in total cholesterol levels without changes in the HDL/HDL ratio. Vanderweyer[25] determined the lipid profile during and immediately after liposuction in 10 patients, thus establishing the metabolic safety of this procedure. Robles-Cervantes[26] detected in a patient with 3 weeks of postsurgical follow-up a significant decrease in total cholesterol level. Other authors have also reported positive results[27,28]. Conversely, some reports[29-32] showed a lack of correlation between surgical fat removal and the improvement of lipid profiles, which emphasizes the importance of maintaining a negative energetic balance to maintain the benefits of the procedure. The complex metabolism of adipocytes warrants new investigations that can improve understanding of the exact role of liposuction in controlling risk variables.

GLUCOSE METABOLISM

Since the development of surgeries and other procedures that lead to significant weight loss[33-35], many patients have been able to lower their insulin resistance and even to totally control type 2 diabetes. Taking these data into account and considering the positive effect of traditional weight loss plans[36-38], several authors have suggested that the surgical removal of body fat can lead to improved glucose metabolism.

According to Perez[39], the observed results can have two possible explanations as follows: either the removal of hypertrophic adipocytes, with increased leptin levels, or the reduction of ghrelin levels, which has been shown to occur after liposuction[40]. The new hormonal configuration would lead to decreased energy intake[5] and, consequently, an increase in insulin sensitivity. Based on studies concerning women who had undergone dermolipectomy, Rizzo[41] linked lower levels of free fatty acids detected with improved glucose metabolism to the procedure. The author refers to the well-known inhibitory role of these markers in insulin activity and oxidative metabolism.

Positive results were described in several publications. Giese[32], in a pilot study including 14 patients, observed a significant reduction in serum insulin level after 4 months of postsurgical follow-up. In a study with 15 nonobese women, Robles-Cervantes[26] observed a reduction in blood sugar levels and insulin secretion (determined by the homeostasis model assessment test[42]) at 3 postoperative weeks. Giugliano[27] also described improved insulin resistance in 30 obese patients. By contrast, Klein did not detect any changes in the glycemic profiles and insulin stimulation test results in both diabetic and nondiabetic patients in two studies performed[30,31]. Critics[43] have argued that perhaps the short follow-up was the reason for the negative results. Ybarra[44] also showed no significant results at 4 postoperative months, despite a reduction in the levels of other metabolic markers.

Insulin resistance is well known to link type 2 diabetes and obesity, as well as cardiovascular pathological conditions associated with these conditions. Recent studies[45-48] have established a direct relationship between increased serum insulin levels and adverse events such as endothelial malfunctions, atherosclerotic processes, and thrombogenic processes, even in patients with similar glycemic profiles. This information suggests the importance of new research to address the possible beneficial effects of liposuction.

LEPTIN

Leptin is a helicoidal hormone secreted by the adipose tissue and mostly detected in the plasma and cerebrospinal fluid[49]. Its discovery originated from the study of recessive mutations in the genes ob and db in rats with morbid obesity phenotype[12,50]. Its name was later coined from the Greek root *leptos*, meaning "thin, fine." Leptin has a central activity over certain hypothalamus areas, which control energy ingestion[51]. Leptin stimulates the production of anorexigenic peptides and also increases energy consumption.

A direct link between leptin level and body mass index BMI has been demonstrated, and increased leptin level is also associated with alcohol ingestion. Nevertheless, leptin levels are lower in thin people and during fasting. These observations highlight the role of leptin in regulating body energy consumption, through the control of energy stored in the form of fat[5]. Leptin injections have been shown to reduce body weight in guinea pigs[52]. This hormone is also known to regulate immune response in patients with malnutrition, whereas immune system suppression could be reverted by leptin injections[53]. Despite being a well-studied mediator that has a known function, leptin was not considered a viable treatment option for obesity. This is because several possible parameters compromise its activity and food intake can be controlled by numerous variables.

Our conclusion, from the point of view of plastic surgery, is that the benefits of this molecule have not been fully exploited. Schreiber[40] observed a tendency for leptin levels to increase after liposuction in 35 rats with an obesity phenotype. On the contrary, Rizzo[41] reported a reduction in serum leptin levels on the 40th postoperative day in 20 obese patients who had undergone dermolipectomy and liposuction.

ADIPONECTIN AND RESISTIN

Adiponectin is a protein that has a gene expression exclusive to the adipose tissue and structural homology to collagen types 8 and 10, as well as to the complement C1q factor[5]. Its activity has anti-inflammatory effects and improves insulin resistance via its direct and indirect effect on glucose absorption[13,27,49]. Some studies showed that plasma adiponectin levels are reduced in patients with obesity, diabetes, and coronary disease; eventually, serum levels can normalize after significant weight loss.

The possibility of modulating this system led to the inclusion of this cytokine in studies that evaluate the surgical removal of fat tissue. In a study with 30 obese and 30 normal-weight women, Giugliano[27,58] observed reduced presurgical levels of the hormone in the obese group. Approximately 6 postoperative months, a significant increase in adiponectin level was observed in both groups, which was directly proportional to the recovered volume and inversely proportional to TNF-α levels. Rizzo[41] also showed an inverse relationship between serum adiponectin level and BMI (BMI = weight/height^2), as well as an increase in adiponectin levels after dermolipectomy. Klein[31] and Schreiber[40]—the latter study used guinea pigs—did not report any alterations in the adiponectin levels before and after liposuction.

Resistin is another hormone of the adipose tissue that was recently described, being secreted mostly by adipocytes, monocytes, and other adjacent cells[49]. Its exact role is still a matter of debate, but some studies have shown an increase in insulin resistance after its administration to guinea pigs, as well as an improvement in glycemic profiles after injection of anti-resistin antibodies[59]. This can be further evidence of a relationship between obesity and diabetes, but so far, no reports have correlated serum levels with the liposuction procedure.

INTERLEUKIN 10

Interleukin 10 (IL-10) is a main mediator of immunity, acting on various immune cell types[60]. Its central role is to inhibit and stop inflammatory response by regulating tolerance to external agents and contributing, for example, to tissue damage control during infection. Genes that are homologous to human IL-10 can be found in viruses such as the Epstein-Barr virus and cytomegalovirus, which stresses the repressive role of this interleukin. The purpose would be to facilitate viral infection by suppressing immunological response.

Work in guinea pigs[61-67] showed that exogenous administration of IL-10 controlled bronchial reactivity, delayed beta-cell destruction in type 1 diabetes, and contributed to the management of other conditions such as Crohn disease and rheumatoid arthritis. Another experimental[68] work also stressed the role of IL-10 in endothelial protection in diabetic rats, which also seems to occur in patients with acute myocardial infarction (AMI), where reduced IL-10 production is associated with poorer prognosis and plaque instability.

This cytokine seems to also participate in glycemic control, perhaps by increasing insulin sensitivity[58,69,70], thus counterbalancing the effects of IL-6 and TNF-α. Moreover, low IL-10 levels have been linked to the development of metabolic syndrome and type 2 diabetes[69,70]. In a study with 20 obese patients who had undergone dermolipectomy, Rizzo[41] reported a significant increase in serum IL-10 level approximately 40 postoperative days. These increased levels, together with the low levels of other markers, are suggested to reflect a decrease in systemic inflammation as a consequence of adipose tissue removal.

INTERLEUKIN 6

Interleukin 6 (IL-6) is a cytokine with an important role in the physiopathological mechanisms of several diseases[71]. It has been implicated in the development of autoimmunity, hypothyroidism, atherosclerosis, osteopenia, and other metabolic disorders. IL-6 still controls the hypothalamic-pituitary-adrenal axis by stimulating the release of the adrenocorticotropic hormone and acting as a regulator of metabolic responses in trauma. Its mechanism of action is mostly unknown, but IL-6 is known to have a series of tissue receptors, which can antagonize the activities of other markers, thus being known for both its anti-inflammatory and pro-inflammatory potentials. Some studies[72] used IL-6 quantification of prognosis in patients with unstable angina and AMI.

Its involvement in controlling energy balance and lipid metabolism is another role of IL-6 that is particularly of interest to plastic surgeons. Among the several cell types that secrete Il-6, adipocytes are responsible for approximately one third[73] of the production, and its high plasma levels correlate with increased insulin resistance, the levels of circulating fatty acids, and the risk of type 2 diabetes[58]. Molecularly, the inhibitory action of IL-6 compromises the signal transduction of insulin receptors in hepatocytes[74].

In a study with 60 patients (30 obese and 30 nonobese), Giugliano[27] compared IL-6 levels before surgery between the two groups and detected IL-6 less frequently in the patients with normal weights. The obese patients then underwent large-volume liposuction, and quantitative assessments were repeated 6 months later, with IL-6 showing much lower levels compared with the other markers. Conversely, Klein[31] studied 15 patients who had undergone the same procedure and did not detect any changes in IL-6 levels at the end of 4 months.

Studies that focused on testing the effects of liposuction on IL-6 level are scarce, perhaps because of difficulties in collecting and transporting the samples outside of academic centers. However, this is a relevant topic that provides an avenue for discussing current issues such as obesity and metabolism in the field of plastic surgery.

C-REACTIVE PROTEIN

C-reactive protein (CRP) is produced in the liver, and small amounts can usually be found in the plasma. Its structure has been preserved throughout evolution, with homologs in several vertebrate and invertebrate species[75]. The mechanism of action of CRP is complex and seems to act both as an anti- and pro-inflammatory factor. In guinea pigs, this protein has a protective role in that it recognizes pathogens and triggers the complement cascade, thus regulating the host response to infection and delaying the development of autoimmune diseases in preconditioned models[76-79]. Other *in vitro* studies that used human recombinant CRP identified proatherosclerotic properties that were possibly caused by inhibition of basal nitric oxide synthesis and the release of molecules that facilitate cell adhesion[80].

With inflammation, CRP levels increase up to a thousand times, which led to the choice of CRP as the central marker of inflammatory status, being routinely assayed in laboratory tests. Recently, a series of studies showed an important association between small increases in serum levels and the development of cardiovascular diseases, metabolic syndrome, and some types of cancer[81]. These results support the hypothesis that subclinical chronic inflammation can affect the development of such conditions.

Other studies have also showed a positive correlation between higher levels of body fat and circulating CRP[82-84], also in association with higher risk of diabetes. Giugliano[27] quantified CRP before liposuction and found higher levels in obese patients than in nonobese patients. After liposuction, a considerable reduction of this marker was observed in both groups. Klein[31] did not detect any changes in CRP level 3 months after liposuction in 15 obese patients.

TUMOR NECROSIS FACTOR ALPHA

Tumor necrosis factor alpha (TNF-α) is an inflammatory cytokine secreted by activated macrophages, extensively studied throughout the literature, and already used in established therapies for autoimmune diseases[85-87] and cancer[88-90]. TNF was first hinted at in the 19th century, when spontaneous tumor regressions in cancer patients were reported, mostly in cases of concomitant bacterial infections[91]. However, it was only in the 1970s that Old[92] described TNF based on tumor necrosis that developed after infusion with plasma from rats infected with Bacillus Calmette-Guérin. The purification of this plasma led to the isolation of a protein with apoptotic capacities over various neoplastic tissues.

TNF-α is produced as a 25-kD protein, posteriorly cleaved to 17 kD, when it enters circulation. It acts on two receptors (types 1 and 2)[93], which can be found in most tissues, as well as in soluble forms, which is believed to modulate TNF-α effects[94,95]. This cytokine has, generally, a regulatory function in immune cells, inducing cachexia, fever, sepsis, apoptosis, inhibition of viral replication, among others[96,97]. Due to its potent role as inducer of inflammatory responses, TNF-α is responsible for a part of the clinical manifestations that associate with autoimmune conditions such as rheumatoid arthritis, asthma, and psoriasis. Recently, these manifestations have been counteracted with the use of monoclonal antibodies (infliximab) or fusion proteins (etanercept) that neutralize TNF-α activity.

Besides its roles in the immune system, TNF-α also regulates energy balance, acting mostly at the level of the metabolism of adipocytes[93]. The activity of TNF-α has been implicated in the development of diseases such as obesity, dyslipidemia, diabetes, and atherosclerosis[58]. Concerning lipid metabolism, TNF-α seems to stimulate lipolysis[98-101] and inhibit the recovery of free fatty acids[102], which may be a possible explanation for the hyperlipidemia observed in patients with infections and obesity. High TNF-α levels are also responsible for the development of insulin resistance in cancer, sepsis, trauma and, as recently reported, in obese patients[93]. The reasons behind these observations are believed to be, among others, the disruption of signal transduction that facilitates glucose uptake by cells. A direct relationship between TNF-α and leptin levels was also observed, which could intensify the anorexigenic and adipostatic effects of leptin[103-105].

Giugliano[27,58] observed a reduction in the levels of this marker in obese patients who underwent liposuction. Rizzo[41] established a positive correlation between BMI and TNF-α levels before surgery, as well as a reduction of this factor after dermolipectomy surgery. It should be stressed that both authors have also reported a considerable improvement in insulin resistance after surgery, which emphasizes the role of TNF-α in this context. In sharp contrast, Klein[31] observed neither any reduction in the levels of this factor nor any improvement in insulin resistance in a study that included 15 obese patients.

LEUCOCYTE COUNT

The link between leukocytosis and cardiovascular diseases was proposed in the final years of the 1920s[106]. Since the 1940s, some studies have reported that patients that had AMI and presented with leukocyte counts higher than 15,000 had a significantly worse prognosis than those with counts below 11,000[107,108]. Further studies have corroborated these results[109-111], and a meta-analysis that included more than 7,000 patients with 8 years of medical follow-up showed a relative risk of 1.5 for coronary disease in patients with leukocyte counts in the upper third of the reference range[81].

Leukocytosis is not only a sign of systemic inflammation, as well as its associated metabolic consequences, but also in itself a cause of damage. An increase in the number of leukocytes would lead to a prothrombotic state through platelet recruitment and adhesion, the production of oxygen free radicals, interleukins, metaloperoxidase, and growth factors[112-114]. Concerning white cells, neutrophils and monocytes are closely related to new ischemic events[115-117], which lead to the production of inflammatory mediators known for their roles in arteriogenesis. Another study tested approximately 6,000 patients in order verify that higher leukocyte levels lead to the development of cancer and an increase in mortality associated with AMI or other factors. The same report also showed a 14% decrease in mortality for each thousand points of reduction in leukocyte count.

Obesity has been associated with the maintenance of subclinical inflammatory status, and some reports have shown a positive relationship between BMI and leukocyte counts[119-121]. The mechanisms behind these findings are complex and unknown; however, the release of proinflammatory cytokines by the adipose tissue, such as IL-6 and TNF-α, should be taken into consideration. A reduction in body weight, either due to diet or exercise, led to reduced counts of neutrophil, among other markers[122]. Swanson[29] reported reduced levels of leukocytes in the third postoperative month in patients who underwent liposuction, suggesting that surgical removal of body fat can have metabolic benefits.

DISCUSSION

The importance of assaying hematological alterations relates with the fact that blood loss usually accompany any surgical procedure, including liposuction. When blood loss volume is large (>5000 mL in total), support measures may be required, as well as prolonged hospitalization, readmission, and even blood transfusion.

Metabolic alterations have recently gained attention with the discovery of the endocrine function of adipose tissue. The clinical implications are particularly important for obese patients who undergo removal of large fat tissue volumes via liposuction. Moreover, new risk markers of atherosclerosis and degenerative conditions are being developed. Hence, body fat can be considered as an agent that promotes chronic inflammatory status. Some of the studies discussed here have shown a significant reduction in inflammation after liposuction. Conversely, a randomized study by Benatti[123] showed an increase in visceral fat deposition after liposuction, without any changes in adipocyte size or gene expression of the factors associated with lipid metabolism.

Safety protocols are difficult to establish owing to the many variables that should be considered. The Federal Council of Medicine, in its resolution number 1711, from December 2003, established the following maximum values for fat removal: 7% of body weight for any infiltrative procedure and 5% for dry procedures. However, it is not specified if the values refer to the total volume aspired or just the removed fat. In addition, the area to be treated was restricted to 40% of the total body area.

For each patient, the choice of treatment depends on the clinical status of the patient, including BMI, number of regions to be subjected to surgery, previous diseases, and volume to be removed, as well as on the preferences of the plastic surgeon concerning the technical aspects of the surgery, the infiltration procedure, whether anesthetics should be used, the type of anesthesia, and the volume to be removed. With this many variables to be taken into consideration, a meta-analysis type of review, which was our intention from the beginning, became impossible owing to the lack of standardized procedures reported in the literature.

Future studies that guide evaluations of specific liposuction procedures, always accounting for blood and/or metabolic changes, will be required for the establishment of increasingly reliable security criteria, which will minimize the adverse effects of liposuction.

CONCLUSION

From its beginning, liposuction procedures were accompanied by concerns regarding blood loss. Currently, parameters for consideration have been established and legislation has been specifically enforced. However, as the frequency of use of liposuction procedures has increased worldwide, metabolic alterations and their effect on patient recovery and final outcome have become a current concern. This has led to a new era in liposuction research. Taking into consideration variables such as the techniques used, infiltration type, and anesthesia, the need to investigate specific metabolic changes for each different procedure has become more imperative to ensure safety and quality. Current reports have been published but are discrepant and have not been extensively corroborated. Therefore, new research that specifically focuses on each technique is warranted to guide the standardization of the discussed parameters.

REFERENCES

1. American Society for Aesthetic Plastic Surgery–ASAPS. ASAPS 1998 statistics on cosmetic surgery. New York: ASAPS; 1998.
2. American Society for Aesthetic Plastic Surgery–ASAPS. ASAPS 1999 statistics on cosmetic surgery. New York: ASAPS; 1999.
3. Sociedade Brasileira de Cirurgia Plástica–SBCP. Matéria Folha de São Paulo: Brasil: cirurgias realizadas em 2011 [Internet]. 2013. Disponível em: http://www2.cirurgiaplastica.org.br/materia-folha-de-sao-paulo/.
4. Illouz YG. Illouz's technique of body contouring by lipolysis. Clin Plast Surg. 1984;11(3):409-17. PMid:6467804.
5. Ahima RS. Adipose tissue as an endocrine organ. Obesity (Silver Spring). 2006;14(Suppl 5):242S-9S. http://dx.doi.org/10.1038/oby.2006.317.PMid:17021375
6. Wilson PW, and the CDC and AHA. CDC/AHA Workshop on markers of inflammation and cardiovascular disease: application to clinical and public health practice: ability of inflammatory markers to predict disease in asymptomatic patients: a background paper. Circulation. 2004;110(25):e568-71. http://dx.doi.org/10.1161/01.CIR.0000149077.87074.DE. PMid:15611383
7. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol. 1998;81(4):7B-12B. http://dx.doi.org/10.1016/S0002-9149(98)00031-9.PMid:9526807
8. Misiak B, Leszek J, Kiejna A. Metabolic syndrome, mild cognitive impairment and Alzheimer's disease—the emerging role of systemic low-grade inflammation and adiposity. Brain Res Bull. 2012;89(3-4):144-9. http://dx.doi.org/10.1016/j.brainresbull.2012.08.003. PMid:22921944
9. Johnson AR, Milner JJ, Makowski L. The inflammation highway: metabolism accelerates inflammatory traffic in obesity. Immunol Rev. 2012;249(1):218-38. http://dx.doi.org/10.1111/j.1600-065X.2012.01151.x. PMid:22889225
10. Scarpellini E, Tack J. Obesity and metabolic syndrome: an inflammatory condition. Dig Dis. 2012;30(2):148-53. http://dx.doi.org/10.1159/000336664. PMid:22722429
11. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Vigitel Brasil: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Brasília: Ministério da Saúde; 2011.
12. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. Nature. 1994;372(6505):425-32. http://dx.doi.org/10.1038/372425a0.PMid:7984236
13. Trayhurn P, Beattie JH. Physiological role of adipose tissue: white adipose tissue as an endocrine and secretory organ. Proc Nutr Soc. 2001;60(3):329-39. http://dx.doi.org/10.1079/PNS200194. PMid:11681807
14. Albrink MJ, Man EB. Serum triglycerides in coronary artery disease. AMA Arch Intern Med. 1959;103(1):4-8. http://dx.doi.org/10.1001/archinte.1959.00270010010002.PMid:13605296
15. Keys A, Menotti A, Aravanis C, Blackburn H, Djordevic BS, Buzina R, et al. The seven countries study: 2,289 deaths in 15 years. Prev Med. 1984;13(2):141-54. PMid:6739443.
16. Brown MS, Goldstein JL. A receptor-mediated pathway for cholesterol homeostasis. Science. 1986;232(4746):34-47. http://dx.doi.org/10.1126/science.3513311. PMid:3513311
17. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106(25):3143-421. PMid:12485966.
18. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97(18):1837-47. http://dx.doi.org/10.1161/01.CIR.97.18.1837.PMid:9603539
19. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, et al. High-density lipoprotein cholesterol and cardiovascular disease: four prospective American studies. Circulation. 1989;79(1):8-15. http://dx.doi.org/10.1161/01.CIR.79.1.8.PMid:2642759
20. Assmann G, Schulte H, Funke H, von Eckardstein A. The emergence of triglycerides as a significant independent risk factor in coronary artery disease. Eur Heart J. 1998;19(Suppl M):M8-14. PMid:9821011.
21. Hulley SB, Rosenman RH, Bawol RD, Brand RJ. Epidemiology as a guide to clinical decisions: the association between triglyceride and coronary heart disease. N Engl J Med. 1980;302(25):1383-9. http://dx.doi.org/10.1056/NEJM198006193022503.PMid:7374696
22. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. Am J Cardiol. 1998;81(4):18B-25B. http://dx.doi.org/10.1016/S0002-9149(98)00033-2. PMid:9526809
23. Samdal F, Birkeland KI, Ose L, Amland PF. Effect of large-volume liposuction on sex hormones and glucose and lipid metabolism in females. Aesthetic Plast Surg. 1995;19(2):131-5. http://dx.doi.org/10.1007/BF00450248.PMid:7598023

24. Baxter RA. Serum lipid changes following large-volume suction lipectomy. Aesthet Surg J. 1997;17(4):213-5. http://dx.doi.org/10.1016/S1090-820X(97)80001-5. PMid:19327717

25. Vandeweyer E. Does liposuction influence lipidogram in females: in vivo study. Aesthetic Plast Surg. 2002;26(1):17-9. http://dx.doi.org/10.1007/s0026601-0034-6. PMid:11891591

26. Robles-Cervantes JA, Yánez-Díaz S, Cárdenas-Camarena L. Modification of insulin, glucose and cholesterol levels in nonobese women undergoing liposuction: is liposuction metabolically safe? Ann Plast Surg. 2004;52(1):64-7. http://dx.doi.org/10.1097/01.sap.0000096448.59407.43. PMid:14676702

27. Giugliano G, Nicoletti G, Grella E, Giugliano F, Esposito K, Scuderi N, et al. Effect of liposuction on insulin resistance and vascular inflammatory markers in obese women. Br J Plast Surg. 2004;57(3):190-4. http://dx.doi.org/10.1016/j.bjps.2003.12.010.PMid:15006519

28. Hong YG, Kim HT, Seo SW, Chang CH, Rhee EJ, Lee WY. Impact of large-volume liposuction on serum lipids in Orientals: a pilot study. Aesthetic Plast Surg. 2006;30(3):327-32. http://dx.doi.org/10.1007/s00266-005-0010-7.PMid:16733777

29. Swanson E. Prospective clinical study reveals significant reduction in triglyceride level and white blood cell count after liposuction and abdominoplasty and no change in cholesterol levels. Plast Reconstr Surg. 2011;128(3):182e-97e. http://dx.doi.org/10.1097/PRS.0b013e31822213c6.PMid:21865992

30. Mohammed BS, Cohen S, Reeds D, Young VL, Klein S. Long-term effects of large-volume liposuction on metabolic risk factors for coronary heart disease. Obesity (Silver Spring). 2008;16(12):2648-51. http://dx.doi.org/10.1038/oby.2008.418. PMid:18820648

31. Klein S, Fontana L, Young VL, Coggan AR, Kilo C, Patterson BW, et al. Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. N Engl J Med. 2004;350(25):2549-57. http://dx.doi.org/10.1056/NEJMoa033179. PMid:15201411

32. Giese SY, Bulan EJ, Commons GW, Spear SL, Yanovski JA. Improvements in cardiovascular risk profile with large-volume liposuction: a pilot study. Plast Reconstr Surg. 2001;108(2):510-9, discussion 520-1. http://dx.doi.org/10.1097/00006534-200108000-00035. PMid:11496197

33. Kelley DE, Thaete FL, Troost F, Huwe T, Goodpaster BH. Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance. Am J Physiol Endocrinol Metab. 2000;278(5):E941-8. PMid:10780952.

34. Lebovitz HE. Science, clinical outcomes and the popularization of diabetes surgery. Curr Opin Endocrinol Diabetes Obes. 2012;19(5):359-66. http://dx.doi.org/10.1097/MED.0b013e328358301f. PMid:22914565

35. Ritter S, Vetter ML, Sarwer DB. Lifestyle modifications and surgical options in the treatment of patients with obesity and type 2 diabetes mellitus. Postgrad Med. 2012;124(4):168-80. http://dx.doi.org/10.3810/pgm.2012.07.2578. PMid:22913905

36. Rexrode KM, Manson JE, Hennekens CH. Obesity and cardiovascular disease. Curr Opin Cardiol. 1996;11(5):490-5. http://dx.doi.org/10.1097/00001573-199609000-00007. PMid:8889375

37. Andersen RE, Wadden TA, Bartlett SJ, Zemel B, Verde TJ, Franckowiak SC. Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. JAMA. 1999;281(4):335-40. http://dx.doi.org/10.1001/jama.281.4.335. PMid:9929086

38. Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, et al. Abdominal adiposity and coronary heart disease in women. JAMA. 1998;280(21):1843-8. http://dx.doi.org/10.1001/jama.280.21.1843. PMid:9846779

39. Perez RA. Liposuction and diabetes type 2 development risk reduction in the obese patient. Med Hypotheses. 2007;68(2):393-6. http://dx.doi.org/10.1016/j.mehy.2006.06.048. PMid:17011727

40. Schreiber JE, Singh NK, Shermak MA. The effect of liposuction and diet on ghrelin, adiponectin, and leptin levels in obese Zucker rats. Plast Reconstr Surg. 2006;117(6):1829-35. http://dx.doi.org/10.1097/01.prs.0000209966.11255.4f.PMid:16651955

41. Rizzo MR, Paolisso G, Grella R, Barbieri M, Grella E, Ragno E, et al. Is dermolipectomy effective in improving insulin action and lowering inflammatory markers in obese women? Clin Endocrinol (Oxf). 2005;63(3):253-8. http://dx.doi.org/10.1111/j.1365-2265.2005.02337.x. PMid:16117810

42. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9. http://dx.doi.org/10.1007/BF00280883. PMid:3899825

43. Esposito K, Giugliano G, Giugliano D. Metabolic effects of liposuction—yes or no? N Engl J Med. 2004;351(13):1354-7. http://dx.doi.org/10.1056/NEJM200409233511320. PMid:15385667

44. Ybarra J, Blanco-Vaca F, Fernández S, Castellví A, Bonet R, Palomer X, et al. The effects of liposuction removal of subcutaneous abdominal fat on lipid metabolism are independent of insulin sensitivity in normal-overweight individuals. Obes Surg. 2008;18(4):408-14. http://dx.doi.org/10.1007/s11695-007-9261-5. PMid:18264836

45. Meigs JB, Nathan DM, Wilson PW, Cupples LA, Singer DE. Metabolic risk factors worsen continuously across the spectrum of nondiabetic glucose tolerance. The Framingham Offspring Study. Ann Intern Med. 1998;128(7):524-33. http://dx.doi.org/10.7326/0003-4819-128-7-199804010-00002. PMid:9518396

46. Baron AD. Vascular reactivity. Am J Cardiol. 1999;84(1):25-7. http://dx.doi.org/10.1016/S0002-9149(99)00354-9. PMid:10418855

47. McGill JB, Schneider DJ, Arfken CL, Lucore CL, Sobel BE. Factors responsible for impaired fibrinolysis in obese subjects and NIDDM patients. Diabetes. 1994;43(1):104-9. http://dx.doi.org/10.2337/diab.43.1.104.PMid:8262307

48. Festa A, D'Agostino R JR, Mykkänen L, Tracy R, Howard BV, Haffner SM. Low-density lipoprotein particle size is inversely related to plasminogen activator inhibitor-1 levels: The Insulin Resistance Atherosclerosis Study. Arterioscler Thromb Vasc Biol. 1999;19(3):605-10. http://dx.doi.org/10.1161/01.ATV.19.3.605. PMid:10073963

49. Rajala MW, Scherer PE. Minireview: the adipocyte—at the crossroads of energy homeostasis, inflammation, and atherosclerosis. Endocrinology. 2003;144(9):3765-73. http://dx.doi.org/10.1210/en.2003-0580. PMid:12933646

50. Chen H, Charlat O, Tartaglia LA, Woolf EA, Weng X, Ellis SJ, et al. Evidence that the diabetes gene encodes the leptin receptor: identification of a mutation in the leptin receptor gene in db/db mice. Cell. 1996;84(3):491-5. http://dx.doi.org/10.1016/S0092-8674(00)81294-5. PMid:8608603

51. Zigman JM, Elmquist JK. Minireview: From anorexia to obesity—the yin and yang of body weight control. Endocrinology. 2003;144(9):3749-56. http://dx.doi.org/10.1210/en.2003-0241. PMid:12933644

52. Pelleymounter MA, Cullen MJ, Baker MB, Hecht R, Winters D, Boone T, et al. Effects of the obese gene product on body weight regulation in ob/ob mice. Science. 1995;269(5223):540-3. http://dx.doi.org/10.1126/science.7624776. PMid:7624776

53. Farooqi IS, Matarese G, Lord GM, Keogh JM, Lawrence E, Agwu C, et al. Beneficial effects of leptin on obesity, T cell hyporesponsiveness, and neuroendocrine/metabolic dysfunction of human congenital leptin deficiency. J Clin Invest. 2002;110(8):1093-103. http://dx.doi.org/10.1172/JCI0215693. PMid:12393845

54. Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa J, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun. 1999;257(1):79-83. http://dx.doi.org/10.1006/bbrc.1999.0255. PMid:10092513

55. Hotta K, Funahashi T, Arita Y, Takahashi M, Matsuda M, Okamoto Y, et al. Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. Arterioscler Thromb Vasc Biol. 2000;20(6):1595-9. http://dx.doi.org/10.1161/01.ATV.20.6.1595.PMid:10845877

56. Hotamisligil GS, Spiegelman BM. Tumor necrosis factor alpha: a key component of the obesity-diabetes link. Diabetes. 1994;43(11):1271-8. http://dx.doi.org/10.2337/diab.43.11.1271. PMid:7926300

57. Kappes A, Löffler G. Influences of ionomycin, dibutyryl-cycloAMP and tumour necrosis factor-alpha on intracellular amount and secretion of apM1 in differentiating primary human preadipocytes. Horm Metab Res. 2000;32(11-12):548-54. http://dx.doi.org/10.1055/s-2007-978684. PMid:11246823

58. Esposito K, Giugliano G, Scuderi N, Giugliano D. Role of adipokines in the obesity-inflammation relationship: the effect of fat removal. Plast Reconstr Surg. 2006;118(4):1048-59. http://dx.doi.org/10.1097/01.prs.0000232281.49432.ce. PMid:16980868

59. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. Nature. 2001;409(6818):307-12. http://dx.doi.org/10.1038/35053000. PMid:11201732

60. Moore KW, de Waal Malefyt R, Coffman RL, O'Garra A. Interleukin-10 and the interleukin-10 receptor. Annu Rev Immunol. 2001;19(1):683-765. http://dx.doi.org/10.1146/annurev.immunol.19.1.683. PMid:11244051

61. Kasama T, Strieter RM, Lukacs NW, Lincoln PM, Burdick MD, Kunkel SL. Interleukin-10 expression and chemokine regulation during the evolution of murine type II collagen-induced arthritis. J Clin Invest. 1995;95(6):2868-76. http://dx.doi.org/10.1172/JCI117993. PMid:7769128

62. Persson S, Mikulowska A, Narula S, O'Garra A, Holmdahl R. Interleukin-10 suppresses the development of collagen type II-induced arthritis and ameliorates sustained arthritis in rats. Scand J Immunol. 1996;44(6):607-14. http://dx.doi.org/10.1046/j.1365-3083.1996.d01-355.x. PMid:8972743

63. Llorente L, Richaud-Patin Y, Wijdenes J, Alcocer-Varela J, Maillot MC, Durand-Gasselin I, et al. Spontaneous production of interleukin-10 by B lymphocytes and monocytes in systemic lupus erythematosus. Eur Cytokine Netw. 1993;4(6):421-7. PMid:8186374.

64. Zuany-Amorim C, Hailé S, Leduc D, Dumarey C, Huerre M, Vargaftig BB, et al. Interleukin-10 inhibits antigen-induced cellular recruitment into the airways of sensitized mice. J Clin Invest. 1995;95(6):2644-51. http://dx.doi.org/10.1172/JCI117966. PMid:7769104

65. Borish L. IL-10: evolving concepts. J Allergy Clin Immunol. 1998;101(3):293-7. http://dx.doi.org/10.1016/S0091-6749(98)70238-6. PMid:9525442

66. Powrie F, Leach MW, Mauze S, Menon S, Caddle LB, Coffman RL. Inhibition of Th1 responses prevents inflammatory bowel disease in SCID mice reconstituted with CD45RBhi CD4+ T cells. Immunity. 1994;1(7):553-62. http://dx.doi.org/10.1016/1074-7613(94)90045-0. PMid:7600284

67. Morrissey PJ, Charrier K, Braddy S, Liggitt D, Watson JD. CD4+ T cells that express high levels of CD45RB induce wasting disease when transferred into congenic severe combined immunodeficient mice. Disease development is prevented by cotransfer of purified CD4+ T cells. J Exp Med. 1993;178(1):237-44. http://dx.doi.org/10.1084/jem.178.1.237. PMid:8100269

68. Gunnett CA, Heistad DD, Faraci FM. Interleukin-10 protects nitric oxide-dependent relaxation during diabetes: role of superoxide. Diabetes. 2002;51(6):1931-7. http://dx.doi.org/10.2337/diabetes.51.6.1931. PMid:12031983

69. van Exel E, Gussekloo J, de Craen AJ, Frölich M, Bootsma-Van Der Wiel A, Westendorp RG, and the Leiden 85 Plus Study. Low production capacity of interleukin-10 associates with the metabolic syndrome and type 2 diabetes: the Leiden 85-Plus Study. Diabetes. 2002;51(4):1088-92. http://dx.doi.org/10.2337/diabetes.51.4.1088. PMid:11916930

70. Esposito K, Giugliano D, Nappo F, Marfella R, and the Campanian Postprandial Hyperglycemia Study Group. Regression of carotid atherosclerosis by control of postprandial hyperglycemia in type 2 diabetes mellitus. Circulation. 2004;110(2):214-9. http://dx.doi.org/10.1161/01.CIR.0000134501.57864.66.PMid:15197140

71. Papanicolaou DA, Wilder RL, Manolagas SC, Chrousos GP. The pathophysiologic roles of interleukin-6 in human disease. Ann Intern Med. 1998;128(2):127-37. http://dx.doi.org/10.7326/0003-4819-128-2-199801150-00009. PMid:9441573

72. Harris TB, Ferrucci L, Tracy RP, Corti MC, Wacholder S, Ettinger WH JR, et al. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. Am J Med. 1999;106(5):506-12. PMid:10335721.

73. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, et al. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab. 1997;82(12):4196-200. PMid:9398739.

74. Senn JJ, Klover PJ, Nowak IA, Zimmers TA, Koniaris LG, Furlanetto RW, et al. Suppressor of cytokine signaling-3 (SOCS-3), a potential mediator of interleukin-6-dependent insulin resistance in hepatocytes. J Biol Chem. 2003;278(16):13740-6. http://dx.doi.org/10.1074/jbc.M210689200.PMid:12560330

75. Black S, Kushner I, Samols D. C-reactive protein. J Biol Chem. 2004;279(47):48487-90. http://dx.doi.org/10.1074/jbc.R400025200. PMid:15337754

76. Mold C, Nakayama S, Holzer TJ, Gewurz H, Du Clos TW. C-reactive protein is protective against *Streptococcus pneumoniae* infection in mice. J Exp Med. 1981;154(5):1703-8. http://dx.doi.org/10.1084/jem.154.5.1703.PMid:7299351

77. Szalai AJ, Briles DE, Volanakis JE. Human C-reactive protein is protective against fatal *Streptococcus pneumoniae* infection in transgenic mice. J Immunol. 1995;155(5):2557-63. PMid:7650385.

78. Heuertz RM, Xia D, Samols D, Webster RO. Inhibition of C5a des Arg-induced neutrophil alveolitis in transgenic mice

expressing C-reactive protein. Am J Physiol. 1994;266(6 Pt 1):L649-54. PMid:8023953.

79. Russell AI, Cunninghame Graham DS, Shepherd C, Roberton CA, Whittaker J, Meeks J, et al. Polymorphism at the C-reactive protein locus influences gene expression and predisposes to systemic lupus erythematosus. Hum Mol Genet. 2004;13(1):137-47. http://dx.doi.org/10.1093/hmg/ddh021. PMid:14645206

80. Venugopal SK, Devaraj S, Yuhanna I, Shaul P, Jialal I. Demonstration that C-reactive protein decreases eNOS expression and bioactivity in human aortic endothelial cells. Circulation. 2002;106(12):1439-41. http://dx.doi.org/10.1161/01.CIR.0000033116.22237.F9. PMid:12234944

81. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA. 1998;279(18):1477-82. http://dx.doi.org/10.1001/jama.279.18.1477. PMid:9600484

82. Ziccardi P, Nappo F, Giugliano G, Esposito K, Marfella R, Cioffi M, et al. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. Circulation. 2002;105(7):804-9. http://dx.doi.org/10.1161/hc0702.104279. PMid:11854119

83. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol. 1999;19(4):972-8. http://dx.doi.org/10.1161/01.ATV.19.4.972. PMid:10195925

84. Ford ES, Galuska DA, Gillespie C, Will JC, Giles WH, Dietz WH. C-reactive protein and body mass index in children: findings from the Third National Health and Nutrition Examination Survey, 1988-1994. J Pediatr. 2001;138(4):486-92. http://dx.doi.org/10.1067/mpd.2001.112898. PMid:11295710

85. Doubrawa E, Ricca RA, Malucelli TO, Pizzol VI, Barros DH, Paiva ES. Use of infliximab in a patient with rheumatoid arthritis and chronic hepatitis B. Rev Bras Reumatol. 2012;52(4):653-5. http://dx.doi.org/10.1590/S0482-50042012000400015. PMid:22885430

86. Aletaha D, Alasti F, Smolen JS. Rituximab dissociates the tight link between disease activity and joint damage in rheumatoid arthritis patients. Ann Rheum Dis. 2013;72(1):7-12. http://dx.doi.org/10.1136/annrheumdis-2012-201970.PMid:22915619

87. Gonzalez-Juanatey C, Vazquez-Rodriguez TR, Miranda-Filloy JA, Gomez-AceboI, Testa A, Garcia-Porrua C, et al. Anti-TNF-alpha-adalimumab therapy is associated with persistent improvement of endothelial function without progression of carotid intima-media wall thickness in patients with rheumatoid arthritis refractory to conventional therapy. Mediators Inflamm. 2012;2012(2012):674265. PMid:22899879.

88. Papadia F, Basso V, Patuzzo R, Maurichi A, Di Florio A, Zardi L, et al. Isolated limb perfusion with the tumor-targeting human monoclonal antibody-cytokine fusion protein L19-TNF plus melphalan and mild hyperthermia in patients with locally advanced extremity melanoma. J Surg Oncol. 2013; 107(2):173-9. http://dx.doi.org/10.1002/jso.23168. PMid:22674435

89. Sethi G, Sung B, Kunnumakkara AB, Aggarwal BB. Targeting TNF for treatment of cancer and autoimmunity. Adv Exp Med Biol. 2009;647:37-51. http://dx.doi.org/10.1007/978-0-387-89520-8_3. PMid:19760065

90. Tansey MG, Szymkowski DE. The TNF superfamily in 2009: new pathways, new indications, and new drugs. Drug Discov Today. 2009;14(23-24):1082-8. http://dx.doi.org/10.1016/j.drudis.2009.10.002. PMid:19837186

91. Old LJ. Tumor necrosis factor (TNF). Science. 1985;230(4726):630-2. http://dx.doi.org/10.1126/science.2413547. PMid:2413547

92. Carswell EA, Old LJ, Kassel RL, Green S, Fiore N, Williamson B. An endotoxin-induced serum factor that causes necrosis of tumors. Proc Natl Acad Sci U S A. 1975;72(9):3666-70. http://dx.doi.org/10.1073/pnas.72.9.3666. PMid:1103152

93. Sethi JK, Hotamisligil GS. The role of TNF alpha in adipocyte metabolism. Semin Cell Dev Biol. 1999;10(1):19-29. http://dx.doi.org/10.1006/scdb.1998.0273. PMid:10355025

94. Van Zee KJ, Kohno T, Fischer E, Rock CS, Moldawer LL, Lowry SF. Tumor necrosis factor soluble receptors circulate during experimental and clinical inflammation and can protect against excessive tumor necrosis factor alpha in vitro and in vivo. Proc Natl Acad Sci U S A. 1992;89(11):4845-9. http://dx.doi.org/10.1073/pnas.89.11.4845. PMid:1317575

95. Liabakk NB, Sundan A, Waage A, Brockhaus M, Loetcher H, Lesslauer W, et al. Development of immunoassays for the detection of soluble tumour necrosis factor receptors. J Immunol Methods. 1991;141(2):237-43. http://dx.doi.org/10.1016/0022-1759(91)90150-E. PMid:1652609

96. Grunfeld C, Feingold KR. Regulation of lipid metabolism by cytokines during host defense. Nutrition. 1996;12(1 Suppl):S24-6. http://dx.doi.org/10.1016/0899-9007(95)00073-9. PMid:8850215

97. Stouthard JM, Romijn JA, Van der Poll T, Endert E, Klein S, Bakker PJ, et al. Endocrinologic and metabolic effects of interleukin-6 in humans. Am J Physiol. 1995;268(5 Pt 1):E813-9. PMid:7762632.

98. Hotamisligil GS, Budavari A, Murray D, Spiegelman BM. Reduced tyrosine kinase activity of the insulin receptor in obesity-diabetes. Central role of tumor necrosis factor-alpha. J Clin Invest. 1994;94(4):1543-9. http://dx.doi.org/10.1172/JCI117495. PMid:7523453

99. López-Soriano J, López-Soriano FJ, Bagby GJ, Williamson DH, Argilés JM. Anti-TNF treatment does not reverse the abnormalities in lipid metabolism of the obese Zucker rat. Am J Physiol. 1997;272(4 Pt 1):E656-60. PMid:9142888.

100. Uysal KT, Wiesbrock SM, Marino MW, Hotamisligil GS. Protection from obesity-induced insulin resistance in mice lacking TNF-alpha function. Nature. 1997;389(6651):610-4. http://dx.doi.org/10.1038/39335. PMid:9335502

101. Ventre J, Doebber T, Wu M, MacNaul K, Stevens K, Pasparakis M, et al. Targeted disruption of the tumor necrosis factor-alpha gene: metabolic consequences in obese and nonobese mice. Diabetes. 1997;46(9):1526-31. http://dx.doi.org/10.2337/diab.46.9.1526. PMid:9287059

102. Memon RA, Feingold KR, Moser AH, Fuller J, Grunfeld C. Regulation of fatty acid transport protein and fatty acid translocase mRNA levels by endotoxin and cytokines. Am J Physiol. 1998;274(2 Pt 1):E210-7. PMid:9486149.

103. Grunfeld C, Zhao C, Fuller J, Pollack A, Moser A, Friedman J, et al. Endotoxin and cytokines induce expression of leptin, the ob gene product, in hamsters. J Clin Invest. 1996;97(9):2152-7. http://dx.doi.org/10.1172/JCI118653.PMid:8621806

104. Sarraf P, Frederich RC, Turner EM, Ma G, Jaskowiak NT, Rivet DJ 3RD, et al. Multiple cytokines and acute inflammation raise mouse leptin levels: potential role in inflammatory anorexia. J Exp Med. 1997;185(1):171-6. http://dx.doi.org/10.1084/jem.185.1.171. PMid:8996253

105. Kirchgessner TG, Uysal KT, Wiesbrock SM, Marino MW, Hotamisligil GS. Tumor necrosis factor-alpha contributes to obesity-related hyperleptinemia by regulating leptin release from adipocytes. J Clin Invest. 1997;100(11):2777-82. http://dx.doi.org/10.1172/JCI119824.PMid:9389742

106. Keefer CS. Angina pectoris: a syndrome caused by anoxemia of the myocardium. Arch Intern Med. 1928;41(6):769-807. http://dx.doi.org/10.1001/archinte.1928.00130180002001.

107. White P. Heart Disease. New York: The MacMillan Company; 1949.

108. Cole DR, Singian EB, Katz LN. The long-term prognosis following myocardial infarction, and some factors which affect it. Circulation. 1954;9(3):321-34. http://dx.doi.org/10.1161/01.CIR.9.3.321. PMid:13141360

109. Friedman GD, Klatsky AL, Siegelaub AB. The leukocyte count as a predictor of myocardial infarction. N Engl J Med. 1974;290(23):1275-8. http://dx.doi.org/10.1056/NEJM197406062902302. PMid:4827627

110. Zalokar JB, Richard JL, Claude JR. Leukocyte count, smoking, and myocardial infarction. N Engl J Med. 1981;304(8):465-8. http://dx.doi.org/10.1056/NEJM198102193040806. PMid:7453772

111. Prentice RL, Szatrowski TP, Fujikura T, Kato H, Mason MW, Hamilton HH. Leukocyte counts and coronary heart disease in a Japanese cohort. Am J Epidemiol. 1982;116(3):496-509. PMid:7124717.

112. Charo IF, Taubman MB. Chemokines in the pathogenesis of vascular disease. Circ Res. 2004;95(9):858-66. http://dx.doi.org/10.1161/01.RES.0000146672.10582.17. PMid:15514167

113. Becker LB. New concepts in reactive oxygen species and cardiovascular reperfusion physiology. Cardiovasc Res. 2004;61(3):461-70. http://dx.doi.org/10.1016/j.cardiores.2003.10.025. PMid:14962477

114. Brennan ML, Hazen SL. Emerging role of myeloperoxidase and oxidant stress markers in cardiovascular risk assessment. Curr Opin Lipidol. 2003;14(4):353-9. http://dx.doi.org/10.1097/00041433-200308000-00003. PMid:12865732

115. Grau AJ, Boddy AW, Dukovic DA, Buggle F, Lichy C, Brandt T, et al, and the CAPRIE Investigators. Leukocyte count as an independent predictor of recurrent ischemic events. Stroke. 2004;35(5):1147-52. http://dx.doi.org/10.1161/01.STR.0000124122.71702.64. PMid:15017013

116. Gurm HS, Bhatt DL, Lincoff AM, Tcheng JE, Kereiakes DJ, Kleiman NS, et al. Impact of preprocedural white blood cell count on long term mortality after percutaneous coronary intervention: insights from the EPIC, EPILOG, and EPISTENT trials. Heart. 2003;89(10):1200-4. http://dx.doi.org/10.1136/heart.89.10.1200. PMid:12975419

117. Cooper HA, Exner DV, Waclawiw MA, Domanski MJ. White blood cell count and mortality in patients with ischemic and nonischemic left ventricular systolic dysfunction (an analysis of the Studies of Left Ventricular Dysfunction [SOLVD]). Am J Cardiol. 1999;84(3):252-7. http://dx.doi.org/10.1016/S0002-9149(99)00272-6. PMid:10496431

118. Grimm RH JR, Neaton JD, Ludwig W. Prognostic importance of the white blood cell count for coronary, cancer, and all-cause mortality. JAMA. 1985;254(14):1932-7. http://dx.doi.org/10.1001/jama.1985.03360140090031. PMid:4046122

119. Nakanishi N, Sato M, Shirai K, Nakajima K, Murakami S, Takatorige T, et al. Associations between white blood cell count and features of the metabolic syndrome in Japanese male office workers. Ind Health. 2002;40(3):273-7. http://dx.doi.org/10.2486/indhealth.40.273. PMid:12141376

120. Kullo IJ, Hensrud DD, Allison TG. Comparison of numbers of circulating blood monocytes in men grouped by body mass index (<25, 25 to <30, > or =30). Am J Cardiol. 2002;89(12):1441-3. http://dx.doi.org/10.1016/S0002-9149(02)02366-4. PMid:12062747

121. Schwartz J, Weiss ST. Host and environmental factors influencing the peripheral blood leukocyte count. Am J Epidemiol. 1991;134(12):1402-9. PMid:1776614.

122. Imayama I, Ulrich CM, Alfano CM, Wang C, Xiao L, Wener MH, et al. Effects of a caloric restriction weight loss diet and exercise on inflammatory biomarkers in overweight/obese postmenopausal women: a randomized controlled trial. Cancer Res. 2012;72(9):2314-26. http://dx.doi.org/10.1158/0008-5472.CAN-11-3092. PMid:22549948

123. Benatti F, Solis M, Artioli G, Montag E, Painelli V, Saito F, et al. Liposuction induces a compensatory increase of visceral fat which is effectively counteracted by physical activity: a randomized trial. J Clin Endocrinol Metab. 2012;97(7):2388-95. http://dx.doi.org/10.1210/jc.2012-1012. PMid:22539589

***Corresponding author:** **Rogerio Schützler Gomes**
Clínica Beiramar de Cirurgia Plástica – Av. Osvaldo Rodrigues Cabral, 1570,
sala 302 – Centro – Florianópolis, SC, Brazil
CEP 88015-710
E-mail: plasticarogerio@gmail.com