REVIEW

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Metabolic aging and cutaneous markers of metabolic syndrome: a narrative review

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ABSTRACT

Metabolic syndrome (MetS) is a constellation of metabolic abnormalities—including central obesity, dyslipidemia, hypertension, and impaired glucose regulation—that considerably increases cardiometabolic risk. Recent evidence emphasizes that MetS significantly influences the skin, which serves as a visible indicator of underlying metabolic dysfunction. The emerging concept of *metabolic aging* describes the acceleration of biological aging driven by chronic metabolic stress through mechanisms such as *inflammaging*, oxidative stress, mitochondrial dysfunction, microvascular injury, and the accumulation of advanced glycation end products (AGEs). Cutaneous signs associated with insulin resistance—including acanthosis nigricans, skin tags, acne in PCOS, hidradenitis suppurativa, and early-onset androgenetic alopecia (AGA)—are increasingly recognized as reliable clinical markers of metabolic dysregulation. Early-onset AGA has a strong epidemiological association with insulin resistance, dyslipidemia, and increased cardiometabolic risk. Understanding these links is essential for dermatologists and aesthetic practitioners, as metabolic dysfunction affects wound healing, treatment response, and procedural safety. This narrative review aims to summarize current evidence on the relationship between metabolic syndrome, metabolic aging, and cutaneous manifestations, with particular emphasis on clinically observable dermatologic markers of insulin resistance and their implications for dermatology and aesthetic practice.

Keywords: Acanthosis nigricans, androgenetic alopecia, insulin resistance, metabolic aging, metabolic syndrome.
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INTRODUCTION

Metabolic syndrome (MetS) consists of central obesity, hypertension, dyslipidemia, and impaired glucose metabolism, cumulatively increasing the risk of type 2 diabetes and cardiovascular disease.[1] While MetS is traditionally viewed as a disorder affecting internal organs, growing evidence suggests that it has substantial dermatologic relevance.[2,3] The skin often manifests early signs of metabolic dysfunction, making dermatologists uniquely positioned to identify at-risk individuals.[1-3]

The concept of metabolic aging unifies metabolic disease and cutaneous aging. It refers to the acceleration of tissue aging driven by chronic metabolic stress, mediated by *inflammaging*, oxidative stress, mitochondrial decline, microvascular dysfunction, and AGEs accumulation. These pathways collectively impair epidermal turnover, dermal matrix synthesis, and follicular biology, leading to clinically recognizable aging patterns.[4–7] This review summarizes the mechanistic links between MetS and skin aging, examines cutaneous markers of metabolic dysfunction, and discusses clinical implications for dermatology and aesthetic practice.

METABOLIC AGING AND CUTANEOUS MANIFESTATIONS OF METABOLIC SYNDROME

Metabolic syndrome as a systemic "aging accelerator"

Metabolic syndrome (MetS) is increasingly recognized as a chronic state of metabolic stress rather than a discrete disease category. Visceral adipose tissue, abundant in MetS, behaves as an endocrine organ that secretes pro-inflammatory adipokines including TNF-α, IL-6, leptin, resistin, and free fatty acids.[1–3] These mediators induce systemic low-grade inflammation, oxidative stress, and endothelial dysfunction—central features of accelerated biological aging.

This framework aligns with inflammaging, an age-associated chronic inflammatory state that underlies frailty and age-related diseases.[4,6] Franceschi et al. proposed that inflammaging arises from a lifetime burden of antigenic and metabolic stressors, with MetS acting as a potent amplifier.[4] Khalaf et al. integrated this into the broader framework of metabolic aging, whereby metabolic dysfunction, mitochondrial decline, and immune dysregulation form a reinforcing cycle that accelerates biological aging across organ systems.[5] The skin, as the largest organ with substantial metabolic activity, is among the earliest tissues to exhibit visible signs of metabolic aging.[4-6]

Mechanistic pathways of metabolic aging in the Skin

The cutaneous microenvironment is highly sensitive to metabolic insults. Several pathophysiologic pathways link MetS to accelerated skin aging:

Chronic low-grade inflammation

Pilkington et al. described how aging skin accumulates senescent fibroblasts and keratinocytes that adopt a senescence-associated secretory phenotype (SASP).

SASP cytokines—IL-6, IL-1β, TNF-α—promote extracellular matrix degradation and impair barrier repair. Metabolic stress exacerbates this through sustained hyperinsulinemia and adipokine exposure.[6]

Oxidative stress and mitochondrial dysfunction

Agrawal et al. reported that inflammaging increases ROS generation while reducing mitochondrial efficiency. Mitochondrial dysfunction impairs ATP-dependent processes including collagen synthesis, elastin remodeling, and keratinocyte turnover.[7]

Advanced glycation end products (AGEs)

Hyperglycemia drives non-enzymatic glycation of proteins, forming AGEs. AGEs crosslink dermal collagen, increasing stiffness and reducing elasticity, while RAGE activation further enhances ROS and inflammation.[4,5]

Microvascular impairment

Insulin resistance induces endothelial dysfunction, reducing nitric oxide and impairing microcirculatory perfusion. This limits oxygen, glucose, and nutrient availability, slowing wound healing and weakening dermal repair processes.[3]

Extracellular matrix remodeling failure

Matrix metalloproteinases (MMPs) are chronically upregulated in inflammaging, degrading collagen and elastin. Combined with AGEs accumulation and fibroblast dysfunction, the dermis undergoes structural collapse then clinically seen as sagging, dullness, and early wrinkling. Collectively, these mechanisms form the biological signature of *metabolaged skin*.[6]

Acanthosis nigricans and skin tags as clinical "red flags" of insulin resistance

Acanthosis nigricans (AN) is a hallmark cutaneous sign of hyperinsulinemia. Excess insulin activates IGF-1 receptors on keratinocytes, promoting epidermal proliferation and papillomatosis.[8–10] Barbato et al. demonstrated strong correlations between AN, fasting insulin, body mass index (BMI), and homeostatic model assessment of insulin resistance (HOMA-IR).[8,11] Bustan et al. further showed that AN severity parallels metabolic severity in obese adults.[10] Skin tags (acrochordons) represent another highly predictive sign. Their presence correlates with insulin resistance, atherogenic lipid profiles, and increased waist circumference.[8,12] Misitzis et al. highlighted that multiple skin tags in women are strongly linked to underlying metabolic risk.[12] Clinically, AN and skin tags should prompt metabolic evaluation, even in patients seeking cosmetic consultation.

Androgenetic alopecia (AGA) as a metabolic marker across age groups

A robust body of evidence supports the association between AGA, particularly early-onset AGA and metabolic dysfunction.

Epidemiologic evidence

A substantial body of epidemiologic data demonstrates that AGA, particularly when it occurs at a young age, is strongly linked to metabolic dysfunction. A comprehensive meta-analysis by Qiu et al. confirmed that individuals with AGA have significantly higher odds of developing metabolic syndrome (MetS), as well as adverse lipid profiles, compared with controls.[13] This association is further emphasized in the scoping review by Liu et al., which found that early-onset AGA consistently co-occurs with insulin resistance, hypertension, and dyslipidemia—even in individuals without obesity—indicating that hair loss may signal underlying metabolic risk before conventional symptoms arise.[14]

Complementing these findings, Sarkar et al. reported that men with early-onset AGA exhibit significantly higher fasting insulin, triglycerides, and waist circumference, supporting the role of hyperinsulinemia and androgen–metabolic interactions in the pathogenesis of both AGA and MetS.[15] Similarly, Saif et al. identified early-onset AGA as a marker of increased MetS prevalence and subclinical cardiovascular risk in young men, highlighting its utility as an early cardiometabolic warning sign.[16] Importantly, this association extends to younger populations. Özcan et al. demonstrated that adolescents with AGA already show increased rates of insulin resistance, obesity, and dyslipidemia, suggesting that AGA may represent one of the earliest visible phenotypes of metabolic imbalance.[17] Taken together, these epidemiologic studies firmly establish early-onset AGA as a clinically meaningful and easily observable indicator of metabolic and cardiovascular risk across age groups.

Mechanistic pathways

Hyperinsulinemia plays a pivotal role in linking metabolic dysfunction to androgenetic alopecia. Excess circulating insulin suppresses sex hormone–binding globulin (SHBG), leading to a rise in free androgen levels that directly accelerates follicular miniaturization in genetically susceptible scalp areas.[15] At the same time, the chronic metabolic inflammation characteristic of MetS disrupts perifollicular microcirculation, reducing oxygen and nutrient delivery to the follicle and impairing its regenerative capacity.[13–16] Compounding these effects, the accumulation of advanced glycation end products (AGEs) stiffens the perifollicular extracellular matrix, diminishing its elasticity and long-term support for follicular cycling.[4,5] Together, these metabolic insults create an environment in which hair follicles age prematurely and progressively miniaturize. For this reason, early-onset AGA should be regarded not merely as a cosmetic concern, but as a clinically meaningful dermatologic biomarker signaling underlying cardiometabolic risk.

Inflammatory dermatoses and the metabolic–inflammatory loop

Hidradenitis suppurativa (HS)

HS strongly associates with obesity, insulin resistance, dyslipidemia, and systemic inflammation.[3,18] Cartron and Driscoll emphasized shared inflammatory pathways between HS and MetS—including elevated TNF-α, IL-17, and CRP.[18]

Acne in PCOS

In PCOS, insulin resistance increases ovarian androgen synthesis, driving

persistent acne, often resistant to treatment.[12,19] Cureus study reinforces the clinical relevance of IR screening in moderate-to-severe acne, especially in women.[11] These dermatoses reflect a bidirectional relationship where metabolic dysfunction worsens skin inflammation, and chronic skin inflammation worsens metabolic stress.

Implications for dermatology and aesthetic medicine

Metabolic dysfunction has important implications for dermatology and aesthetic medicine. The presence of insulin resistance, microvascular impairment, and chronic low-grade inflammation affects wound healing capacity, increases susceptibility to post-procedural complications, and reduces the biological responsiveness of the skin to regenerative interventions.[8-12,13-18] Patients with metabolic syndrome may exhibit delayed recovery following laser procedures, chemical peels, or surgical interventions due to impaired dermal perfusion and fibroblast dysfunction.[3,6] Furthermore, the accumulation of advanced glycation end products and mitochondrial energy deficits may blunt the clinical response to regenerative therapies such as platelet-rich plasma, polynucleotides, exosomes, and collagen biostimulators.[5–7,13] Recognizing cutaneous markers such as acanthosis nigricans, multiple skin tags, early-onset androgenetic alopecia, persistent acne, and hidradenitis suppurativa allows dermatologists to identify metabolic risk early and to integrate metabolic optimization into aesthetic treatment planning. Collaboration with internists or endocrinologists, lifestyle modification, and improvement of glycemic control are therefore essential components of safe and effective aesthetic practice.

CONCLUSION

Metabolic syndrome accelerates cutaneous aging through inflammaging, oxidative stress, mitochondrial dysfunction, microvascular injury, and AGEs accumulation. Cutaneous signs—including AN, skin tags, HS, persistent acne in PCOS, and particularly early-onset AGA—are powerful external markers of systemic metabolic dysfunction. Recognizing these indicators enables earlier metabolic screening, safer aesthetic procedures, and more effective anti-aging strategies. Dermatologists and aesthetic physicians are uniquely positioned to detect metabolic aging early and guide comprehensive patient care.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: TH, data curation: TH, writing – original draft: TH, writing – review & editing: IMJ, supervision: IMJ.

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Generative artificial intelligence tools were used solely for language refinement, grammar correction, and clarity improvement. All scientific content, data interpretation, and conclusions were generated by the authors, who take full responsibility for the integrity of the manuscript.

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