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A Systems-based Approach to Longevity: Integrating Mitochondria, Hormones, and Inflammation through Case-based Precision Endocrinology

Angela D. Mazza

ABSTRACT

Aging is a multifactorial biological process driven by progressive declines in cellular energy production, hormonal signaling, and immune regulation. While advances in geroscience have identified key molecular hallmarks of aging, translation into practical, clinician-friendly frameworks remains limited. Current medical approaches often address metabolic, endocrine, and inflammatory dysfunction in isolation, which may fail to capture the interconnected biology underlying accelerated aging and chronic disease.

The Longevity Triad is presented as a systems-based clinical framework integrating three interdependent pillars-mitochondrial resilience, hormonal orchestration, and inflammation modulation-to guide precision longevity care.

Keywords: longevity; aging biology; mitochondrial dysfunction; hormonal aging; inflammaging; precision medicine; integrative endocrinology; metabolic health; geroscience; systems-based medicine.

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Aging is a multifactorial biological process driven by progressive declines in cellular energy production, hormonal signaling, and immune regulation. While advances in geroscience have identified key molecular hallmarks of aging, translation into practical, clinician-friendly frameworks remains limited. Current medical approaches often address metabolic, endocrine, and inflammatory dysfunction in isolation, which may fail to capture the interconnected biology underlying accelerated aging and chronic disease.

The Longevity Triad is presented as a systems-based clinical framework integrating three interdependent pillars-mitochondrial resilience, hormonal orchestration, and inflammation modulation-to guide precision longevity care. Mitochondria regulate cellular energy availability, redox balance, and stress adaptation; hormonal networks coordinate metabolism, reproduction, and tissue repair; and chronic low-grade inflammation acts as a central accelerator of biological aging. Dysregulation in any one pillar can destabilize the others, creating self-reinforcing feedback loops that promote metabolic decline, immune dysfunction, and reduced physiologic reserve.

This manuscript synthesizes emerging mechanistic and clinical evidence linking the Longevity Triad to established hallmarks of aging and demonstrates its application through case-based clinical examples. Diagnostic strategies including functional metabolic testing, comprehensive endocrine assessment, inflammatory and immune biomarkers, and

lifestyle-related exposure evaluation are discussed. Targeted interventions encompassing lifestyle modification, nutritional and micronutrient support, exercise prescription, and individualized hormonal optimization-are illustrated to show how coordinated, multi-pillar treatment can restore physiologic balance and improve patient-centered outcomes.

The Longevity Triad offers a practical, integrative roadmap for clinicians seeking to move beyond symptom-based management toward systems-level, personalized strategies that support healthy aging, metabolic flexibility, and long-term resilience.

Keywords: longevity; aging biology; mitochondrial dysfunction; hormonal aging; inflammaging; precision medicine; integrative endocrinology; metabolic health; geroscience; systems-based medicine.

I. INTRODUCTION

1.1 Aging as a Systems Phenomenon

Aging is increasingly recognized as a complex, systems-level biological process rather than the linear decline of individual organs or pathways. Chronological aging is accompanied by progressive loss of physiological resilience, impaired stress adaptation, and diminished capacity for cellular repair, ultimately increasing vulnerability to chronic disease, frailty, and functional decline [1]. Rather than arising from isolated defects, these changes reflect the cumulative interaction of metabolic, endocrine, immune, and mitochondrial processes that

collectively determine biological aging trajectories [2,3].

Advances in molecular biology and translational research have revealed that aging is driven by interconnected cellular mechanisms—including mitochondrial dysfunction, altered nutrient sensing, hormonal signaling changes, and chronic low-grade inflammation—that operate across tissues and organ systems [1,4]. This systems-based view of aging provides a critical foundation for developing clinical frameworks that address root causes of age-related decline rather than downstream manifestations alone.

1.2 Limitations of Siloed Endocrine and Metabolic Care

Despite growing recognition of aging as a networked biological process, clinical practice often remains fragmented. Endocrine, metabolic, and inflammatory disorders are frequently evaluated and treated in isolation—thyroid dysfunction managed independently from insulin resistance, menopausal transition addressed separately from cardiometabolic risk, and chronic inflammation considered a consequence rather than a driver of disease. This siloed approach may obscure shared upstream mechanisms and contributes to incomplete symptom resolution, polypharmacy, and suboptimal long-term outcomes.

For example, patients presenting with fatigue, weight gain, cognitive complaints, or musculoskeletal pain are often evaluated through single-pathway lenses—thyroid hormone replacement, glycemic control, or anti-inflammatory therapy—without systematic assessment of mitochondrial energy capacity, hormonal network interactions, or immune-metabolic feedback loops. Such reductionist strategies may fail to identify early biological aging processes that precede overt disease and limit opportunities for preventive or restorative interventions [5].

1.3 Geroscience and the Hallmarks of Aging

The field of geroscience has provided a unifying biological framework by identifying conserved

mechanisms that drive aging and age-related disease. The “hallmarks of aging,” originally proposed in 2013 and expanded in subsequent updates, describe interrelated processes including mitochondrial dysfunction, genomic instability, loss of proteostasis, dysregulated nutrient sensing, cellular senescence, altered intercellular communication, and chronic inflammation [3,6]. These hallmarks are not independent; rather, they form an integrated network in which perturbations in one domain amplify dysfunction in others.

Importantly, many hallmarks are modifiable through lifestyle, nutritional, pharmacologic, and hormonal interventions, suggesting that aging biology is amenable to clinical influence [2,7]. Mitochondrial health, endocrine signaling, and inflammatory tone emerge repeatedly as central nodes within this network, linking cellular metabolism to organismal aging, resilience, and disease risk. However, translating these mechanistic insights into practical clinical workflows remains a significant challenge.

1.4 Rationale for a Tri-Pillar Clinical Model

To bridge the gap between geroscience and everyday clinical practice, there is a need for integrative frameworks that are biologically grounded, clinically actionable, and adaptable to individual patient phenotypes. The Longevity Triad is proposed as such a model, organizing aging-related biology into three interdependent pillars: mitochondrial resilience, hormonal orchestration, and inflammation modulation.

Mitochondria serve as the energetic and metabolic foundation of cellular function, regulating ATP production, redox balance, and adaptive stress responses. Hormonal networks—including thyroid, adrenal, gonadal, and metabolic hormones—coordinate energy utilization, tissue repair, reproduction, and circadian alignment. Chronic inflammation, often described as “inflammaging,” acts as a key accelerator of biological aging, disrupting mitochondrial efficiency and hormonal signaling while promoting metabolic and immune dysregulation [4,8].

By conceptualizing aging through these interconnected pillars, the Longevity Triad provides a systems-based lens through which clinicians can identify dominant drivers of biological aging, prioritize diagnostics, and implement coordinated interventions. This model moves beyond symptom-based care toward precision strategies aimed at restoring physiologic balance, enhancing resilience, and supporting healthy aging across the lifespan.

II. BIOLOGICAL RATIONALE FOR THE LONGEVITY TRIAD

The Longevity Triad is grounded in converging evidence from geroscience, endocrinology, and metabolic medicine demonstrating that aging is driven by interdependent disruptions in cellular energy production, hormonal signaling, and immune regulation. Mitochondria, hormones, and inflammation represent biologically central and clinically actionable domains that both influence and are influenced by recognized hallmarks of aging. Together, these pillars provide a translational bridge between molecular aging biology and practical clinical care.

2.1 Mitochondria as the Energetic Foundation

Mitochondria play a central role in aging biology by regulating cellular energy production, redox homeostasis, apoptotic signaling, and adaptive stress responses. Oxidative phosphorylation (OxPhos) within the mitochondrial electron transport chain is responsible for the majority of cellular adenosine triphosphate (ATP) generation, enabling energy-intensive processes such as tissue repair, immune regulation, and hormonal signaling [9]. With aging, mitochondrial efficiency declines, leading to reduced ATP output, increased electron leak, and excess reactive oxygen species (ROS) generation [10].

Redox imbalance resulting from mitochondrial dysfunction contributes to oxidative damage of lipids, proteins, and DNA, accelerating multiple hallmarks of aging including genomic instability and loss of proteostasis [1]. Mitophagy—the selective removal of damaged mitochondria—is a critical quality-control mechanism that preserves

mitochondrial integrity. Impairment of mitophagy with age allows dysfunctional mitochondria to accumulate, further amplifying oxidative stress and inflammatory signaling [11].

Clinically, early mitochondrial dysfunction often precedes overt disease and manifests as fatigue, reduced exercise tolerance, metabolic inflexibility, and impaired stress resilience. Biomarkers such as lactate and pyruvate provide insight into shifts toward anaerobic metabolism and redox imbalance, while elevated lactate-to-pyruvate ratios suggest impaired oxidative capacity [12]. Nicotinamide adenine dinucleotide (NAD⁺) is a central cofactor in mitochondrial metabolism, supporting OxPhos, sirtuin activity, DNA repair, and mitophagy. Age-related NAD⁺ decline has been linked to mitochondrial dysfunction and impaired cellular resilience [13].

Cardiorespiratory fitness, quantified by maximal oxygen consumption (VO₂ max), offers a functional, integrative measure of mitochondrial health. VO₂ max reflects the capacity of mitochondria to utilize oxygen for ATP production and is a strong predictor of cardiovascular and all-cause mortality, often outperforming traditional risk markers [14]. Declines in VO₂ max may therefore serve as an early indicator of compromised mitochondrial function and accelerated biological aging, even in the absence of diagnosed disease.

2.2 Hormones as Systems Orchestrators

Hormones function as global signaling molecules that integrate energy availability, metabolism, reproduction, circadian rhythms, and tissue repair. Thyroid hormone, in particular, exerts profound effects on mitochondrial biogenesis, oxidative metabolism, and thermogenesis, directly influencing several hallmarks of aging. Triiodothyronine (T₃) regulates transcription of genes involved in mitochondrial respiration, antioxidant defense, and lipid and glucose metabolism [15]. Subtle alterations in thyroid hormone signaling—even within reference ranges—may contribute to fatigue, weight gain, cognitive dysfunction, and reduced metabolic efficiency commonly observed with aging [16].

Midlife hormonal transitions further illustrate the role of endocrine signaling in aging trajectories. Perimenopause is characterized by fluctuating and ultimately declining estrogen and progesterone levels, which are associated with changes in body composition, insulin sensitivity, sleep architecture, and inflammatory tone [17]. Estrogen plays a protective role in mitochondrial function, glucose homeostasis, and antioxidant defense; its decline may therefore amplify metabolic and inflammatory stress during aging [18].

Insulin resistance represents another key hormonal and metabolic inflection point. Impaired insulin signaling disrupts nutrient sensing pathways, promotes mitochondrial dysfunction, and enhances inflammatory signaling, linking metabolic disease to accelerated aging [19]. In parallel, dysregulation of adrenal rhythms—particularly altered cortisol diurnal patterns—can impair mitochondrial efficiency, disrupt sleep and circadian alignment, and exacerbate immune dysfunction [20].

Collectively, age-related hormonal decline and dysregulation act as signal amplifiers of aging biology. When endocrine coordination deteriorates, mitochondrial inefficiency and inflammation are magnified, accelerating functional decline and reducing physiologic reserve.

2.3 Inflammation as the Accelerator

Chronic low-grade inflammation, often termed *inflammaging*, is a defining feature of biological aging and a central driver of age-related disease [21]. Unlike acute inflammation, which is adaptive and self-limited, inflammaging reflects persistent immune activation driven by metabolic dysfunction, cellular senescence, mitochondrial damage, and environmental exposures. This sustained inflammatory state disrupts endocrine signaling, impairs mitochondrial function, and promotes tissue degeneration across organ systems [5].

The gut–immune–endocrine axis plays a pivotal role in modulating inflammatory tone. Age-related changes in gut microbiota composition,

reduced microbial diversity, and increased intestinal permeability facilitate translocation of endotoxins such as lipopolysaccharide (LPS), triggering systemic immune activation [22]. These processes directly influence insulin signaling, thyroid hormone metabolism, and sex hormone balance, reinforcing the interconnected nature of the Longevity Triad.

Environmental and metabolic factors further accelerate inflammatory aging. Exposure to endocrine-disrupting chemicals, heavy metals, ultra-processed foods, and excess caloric intake can activate inflammatory pathways and impair mitochondrial and hormonal function [23,24]. Metabolic inflammation associated with visceral adiposity and insulin resistance increases circulating cytokines such as interleukin-6 and tumor necrosis factor- α , which interfere with insulin and thyroid hormone signaling and promote further mitochondrial dysfunction [19].

Within the Longevity Triad, inflammation functions as a biological accelerator-intensifying dysfunction in mitochondrial and hormonal systems and driving the progression from subclinical imbalance to overt disease. Addressing inflammatory drivers is therefore essential for restoring system-wide resilience and supporting healthy aging. These interconnected biological processes are integrated within the Longevity Triad model, which frames aging as a systems-level phenomenon rather than isolated pathway dysfunction (Figure 1)

III. INTERDEPENDENCE OF THE LONGEVITY TRIAD

A defining feature of biological aging is the interdependence of core regulatory systems, rather than dysfunction within isolated pathways. Mitochondrial energetics, hormonal signaling, and inflammatory regulation operate as a tightly coupled network, with continuous bidirectional communication across cellular, tissue, and organ levels. Within the Longevity Triad, disruption of any single pillar initiates compensatory and maladaptive responses in the others, producing self-reinforcing cycles that accelerate biological aging and disease progression.

3.1 Bidirectional Signaling Across the Triad

Bidirectional signaling between mitochondria, hormones, and the immune system is fundamental to maintaining physiologic resilience. Mitochondria regulate endocrine and immune function through energy availability, redox signaling, and metabolite production. Conversely, hormonal and inflammatory signals directly influence mitochondrial biogenesis, efficiency, and turnover [10].

For example, thyroid hormone modulates mitochondrial oxidative phosphorylation, mitochondrial DNA transcription, and uncoupling protein activity, thereby influencing basal metabolic rate and thermogenesis [15]. At the same time, mitochondrial dysfunction alters thyroid hormone conversion and signaling, contributing to reduced T₃ activity at the tissue level despite normal circulating hormone concentrations [13]. Similarly, proinflammatory cytokines such as interleukin-6 and tumor necrosis factor- α impair insulin and thyroid hormone signaling while suppressing mitochondrial respiration, linking immune activation to metabolic decline [5].

These reciprocal interactions demonstrate that mitochondrial, hormonal, and inflammatory pathways do not operate in parallel but rather as mutually regulatory systems, each shaping the function of the others in real time.

3.2 Feed-Forward Loops and Accelerated Aging

When regulatory balance is lost, bidirectional signaling can evolve into feed-forward loops that amplify dysfunction. Mitochondrial inefficiency increases reactive oxygen species production, which activates inflammatory pathways and promotes cellular senescence [1]. Senescent cells, in turn, secrete proinflammatory cytokines and chemokines—collectively termed the senescence-associated secretory phenotype (SASP)—that further impair mitochondrial function and disrupt endocrine signaling [26].

Hormonal dysregulation similarly participates in feed-forward aging loops. Declining estrogen levels during perimenopause reduce

mitochondrial antioxidant capacity and insulin sensitivity, increasing oxidative stress and inflammatory burden [18]. Insulin resistance exacerbates mitochondrial dysfunction by impairing nutrient sensing and promoting lipid accumulation, which further stimulates inflammatory signaling within adipose and immune tissues [19]. Altered cortisol rhythms may compound these effects by disrupting circadian regulation of mitochondrial metabolism and immune activity [20].

These reinforcing loops help explain why age-related symptoms often cluster—fatigue, weight gain, cognitive changes, and musculoskeletal pain rarely arise in isolation—and why progression from subclinical imbalance to overt disease can occur rapidly once compensatory capacity is exceeded. When regulatory balance is lost, bidirectional signaling across the Longevity Triad can evolve into feed-forward loops that amplify dysfunction and accelerate aging biology (Figure 2).

3.3 Why Treating one Pillar Alone Fails

Traditional clinical approaches often target a single dominant abnormality—thyroid hormone replacement for fatigue, glucose-lowering therapy for insulin resistance, or anti-inflammatory agents for chronic pain. While such interventions may produce partial or short-term improvements, they frequently fail to restore durable physiologic balance because upstream and parallel drivers of dysfunction remain unaddressed.

For instance, optimizing thyroid hormone levels without addressing mitochondrial insufficiency may not resolve fatigue or exercise intolerance if ATP production and redox balance remain impaired. Similarly, improving glycemic indices without reducing inflammatory burden or restoring hormonal coordination may leave patients vulnerable to ongoing metabolic stress and disease progression [19]. Anti-inflammatory strategies that do not address underlying metabolic dysfunction, gut permeability, or mitochondrial damage may blunt symptoms while allowing aging biology to advance unchecked [5].

The Longevity Triad framework emphasizes that effective longevity care requires coordinated, multi-pillar intervention. By identifying dominant drivers while simultaneously supporting interconnected systems, clinicians can interrupt feed-forward loops, restore adaptive signaling, and shift the biological aging trajectory toward resilience rather than decline. This integrative approach aligns with geroscience principles and provides a practical roadmap for translating aging biology into clinical action.

IV. CASE-BASED APPLICATION OF THE LONGEVITY TRIAD

To translate the Longevity Triad from conceptual framework to clinical practice, case-based application provides a pragmatic illustration of how mitochondrial resilience, hormonal orchestration, and inflammation modulation interact in real patients. The following cases demonstrate how dominant pillar dysfunction can be identified, prioritized, and addressed while supporting interconnected systems to restore physiologic balance and improve outcomes.

Case 1: Mitochondrial Dysfunction as the Dominant Driver

A 48-year-old woman presented with chronic fatigue, brain fog, and poor exercise tolerance despite unremarkable standard laboratory evaluation. Her history included high occupational stress, disrupted sleep, and a sedentary lifestyle. Thyroid indices were within reference ranges, though free T₃ was low-normal, and cortisol rhythm testing demonstrated a mild diurnal flattening.

a) Diagnostics

Given the symptom profile suggestive of impaired cellular energy production, mitochondrial assessment was prioritized. Urinary organic acid testing (OAT) revealed elevations in lactate and pyruvate with reduced Krebs cycle intermediates, indicating a shift toward inefficient oxidative metabolism and redox imbalance [27]. Serum nutrient analysis demonstrated low coenzyme Q10 levels, while cardiorespiratory fitness testing revealed a reduced VO₂ max for age and sex,

consistent with impaired mitochondrial oxidative capacity [14].

Together, these findings supported early mitochondrial dysfunction preceding overt metabolic disease, a pattern increasingly recognized in aging biology [10].

b) Interventions

Interventions focused on restoring mitochondrial efficiency and adaptive capacity. Targeted supplementation included NAD⁺ precursors to support redox balance and sirtuin activity, ubiquinol to enhance electron transport chain function, and acetyl-L-carnitine to improve fatty acid transport into mitochondria [13,28]. Exercise was prescribed with an emphasis on gradual progression, incorporating low-intensity aerobic movement and limited high-intensity interval training (HIIT) to stimulate mitochondrial biogenesis [29]. Sauna therapy was added as an adjunctive hormetic stressor shown to upregulate heat shock proteins and mitochondrial adaptive pathways [30].

c) Outcomes

At three-month follow-up, the patient reported marked improvement in energy and cognitive clarity, with resolution of post-exertional fatigue. Objective gains included a meaningful increase in VO₂ max and normalization of lactate-to-pyruvate ratio, supporting improved oxidative metabolism. This case illustrates how mitochondrial dysfunction may represent an early and reversible driver of biological aging when appropriately identified and treated.

Case 2: Hormonal Dysregulation Amplifying Aging Biology

A 50-year-old woman with known Hashimoto thyroiditis presented with fatigue, weight gain, vasomotor symptoms, mood lability, and declining metabolic resilience during perimenopause. She was receiving stable levothyroxine therapy with thyroid-stimulating hormone (TSH) within reference range but continued to experience persistent symptoms.

a) Diagnostic Considerations

Expanded endocrine assessment revealed thyroid autoimmunity with elevated anti-thyroid peroxidase antibodies, low-normal free T₃, and evidence of insulin resistance based on fasting insulin and homeostatic model assessment of insulin resistance (HOMA-IR). Fluctuating estradiol and low luteal progesterone levels were consistent with perimenopausal transition. Given emerging evidence linking estrogen metabolism to gut microbiota, the consideration of estrobolome function and fiber intake was incorporated into the clinical assessment [31,32].

b) Interventions

Therapeutic strategy focused on restoring hormonal coordination while mitigating downstream metabolic and inflammatory effects. Micronutrients with evidence for thyroid and metabolic support—including selenium, myo-inositol, and vitamin D—were initiated [33,34]. Botanical interventions such as diindolyl-methane (DIM) and chasteberry were used to support estrogen metabolism and progesterone balance [34]. Insulin sensitivity was addressed through dietary modification, resistance training, and use of insulin-sensitizing nutraceuticals when appropriate.

Hormone replacement therapy (HRT) was discussed as a future option, with emphasis on individualized, low-dose transdermal estrogen combined with micronized progesterone when clinically indicated. Emerging evidence suggests that appropriate sex hormone replacement during midlife may support mitochondrial function, metabolic health, and longevity-related pathways [18].

c) Clinical Implications

This case demonstrates how hormonal dysregulation acts as a signal amplifier of aging biology, magnifying mitochondrial inefficiency and inflammatory burden. Addressing endocrine orchestration within the Longevity Triad framework allowed for symptom improvement while targeting upstream aging mechanisms.

Case 3: Chronic Inflammation Driving Systemic Decline

A 53-year-old man with metabolic syndrome presented with low energy, central adiposity, joint stiffness, and progressive cardiometabolic risk. Laboratory evaluation revealed elevated hemoglobin A1c, fasting insulin, dyslipidemia, and markedly elevated high-sensitivity C-reactive protein and proinflammatory cytokines, consistent with chronic low-grade systemic inflammation.

a) Diagnostic Findings

Further evaluation highlighted gut-immune axis disruption, including reduced microbial diversity and elevated markers of intestinal permeability. Environmental exposure screening revealed borderline elevations in heavy metals, raising concern for inflammatory and endocrine-disrupting contributors. Chronic inflammation in this context reflected both metabolic dysfunction and cumulative environmental burden [5,23].

b) Interventions

Intervention prioritized inflammation modulation while supporting metabolic and mitochondrial recovery. A Mediterranean-style, anti-inflammatory dietary pattern was implemented alongside time-restricted eating to improve insulin sensitivity. Omega-3 fatty acids, curcumin, magnesium, and zinc were prescribed to reduce inflammatory signaling and support immune balance [36,37].

Gut barrier repair strategies included probiotics, prebiotic fibers, and targeted mucosal support. Sauna therapy and selected binding agents were used cautiously to assist with toxin mobilization and elimination, alongside lifestyle strategies to reduce ongoing exposures [4].

c) Outcomes

Within three months, the patient experienced substantial improvement in energy, joint symptoms, and body composition, accompanied by reductions in inflammatory markers and improved metabolic indices. This case highlights inflammation as a central accelerator within the Longevity Triad, capable of destabilizing

mitochondrial and hormonal systems if left unaddressed.

d) Clinical Synthesis

Together, these cases illustrate how the Longevity Triad enables clinicians to identify dominant drivers of aging while addressing interconnected pathways. Rather than treating fatigue, weight gain, or metabolic dysfunction in isolation, a tri-pillar approach facilitates interruption of feed-forward loops and supports restoration of physiologic resilience.

V. INTEGRATED CASE: APPLYING THE LONGEVITY TRIAD IN CLINICAL PRACTICE

To illustrate the integrative power of the Longevity Triad, an aggregated case example demonstrates how mitochondrial dysfunction, hormonal dysregulation, and chronic inflammation commonly coexist in midlife patients and require coordinated intervention. This case highlights triad mapping, prioritization logic, synergistic treatment design, and measurable outcomes.

5.1 Triad Mapping

Maria, a 52-year-old woman, presented with persistent fatigue despite adequate sleep, progressive central weight gain, cognitive “brain fog,” and diffuse joint discomfort limiting physical activity. Her medical history was notable for perimenopausal symptoms and a family history of cardiometabolic disease. Standard laboratory testing had been previously reported as “normal,” yet symptoms persisted and progressed.

Using the Longevity Triad framework, diagnostic findings were mapped across all three pillars:

- **Mitochondria:** Reduced VO_2 max for age and sex, elevated lactate-to-pyruvate ratio, and low serum coenzyme Q10 suggested impaired oxidative phosphorylation and reduced energetic reserve.
- **Hormones:** Elevated thyroid-stimulating hormone with low-normal free T₃ and free T₄, elevated thyroid peroxidase antibodies, fluctuating estradiol, low luteal progesterone, and elevated fasting insulin indicated thyroid

autoimmunity, perimenopausal transition, and insulin resistance.

- **Inflammation:** Elevated high-sensitivity C-reactive protein and interleukin-6, along with reduced gut microbial diversity and increased intestinal permeability markers, reflected chronic low-grade systemic inflammation.

This comprehensive mapping revealed that Maria’s symptoms were not attributable to a single abnormality but rather to convergent dysfunction across all three pillars, consistent with accelerated biological aging rather than isolated disease.

5.2 Prioritization Logic

Although all three pillars were impaired, prioritization was guided by identifying dominant drivers and feed-forward interactions. In Maria’s case, mitochondrial dysfunction and inflammation were identified as proximal contributors to fatigue and metabolic inflexibility, while hormonal dysregulation functioned as a signal amplifier perpetuating both processes.

Accordingly, early intervention emphasized restoring cellular energy production and reducing inflammatory burden while simultaneously supporting hormonal coordination. This approach aligns with geroscience principles suggesting that improving energetic capacity and inflammatory tone may enhance responsiveness to endocrine interventions and improve overall physiologic resilience [1,2].

5.3 Synergistic Intervention Strategy

A coordinated, multi-pillar intervention plan was implemented:

- **Mitochondrial Support:** NAD⁺ precursors, ubiquinol, and acetyl-L-carnitine were initiated to support redox balance, electron transport chain efficiency, and fatty acid oxidation. Structured physical activity emphasized daily low-intensity movement with gradual introduction of high-intensity interval training to stimulate mitochondrial biogenesis [24]. Sauna therapy was added as a

hormetic intervention to promote mitochondrial adaptation and reduce inflammatory signaling [30].

- **Hormonal Optimization:** Thyroid therapy was titrated with attention to free T3 and free T4 rather than TSH alone, and selenium and myo-inositol were introduced to support thyroid autoimmunity and hormone conversion. Perimenopausal support focused on nutritional strategies, circadian alignment, and discussion of future individualized hormone replacement therapy as symptoms and risk profile evolved. Insulin resistance was addressed through time-restricted eating, resistance training, and dietary protein optimization [17].
- **Inflammation Modulation:** A Mediterranean-style, anti-inflammatory diet rich in polyphenols and omega-3 fatty acids was prescribed. Targeted supplementation included omega-3 fatty acids and curcumin to reduce cytokine signaling. Gut barrier repair strategies incorporated probiotics, prebiotic fiber, and mucosal support nutrients, while environmental exposure reduction and sauna-assisted detoxification were used to lower inflammatory burden [4,5].

Importantly, several interventions—exercise, sauna therapy, nutrient repletion—were intentionally selected for their cross-pillar effects, reinforcing synergy rather than redundancy.

5.4 Objective and Subjective Outcomes

At three-month follow-up, Maria reported substantial improvement in energy, mental clarity, sleep quality, and joint discomfort. Afternoon fatigue and post-exertional crashes resolved, and she resumed regular physical activity without symptom exacerbation.

Objective measures demonstrated parallel improvement, including increased VO₂ max, normalization of lactate-to-pyruvate ratio, reduced inflammatory markers, improved fasting insulin, and stabilization of thyroid parameters. Waist circumference decreased, and metabolic flexibility improved as reflected by more stable energy levels throughout the day.

5.5 Clinical Insight

This integrated case demonstrates how the Longevity Triad framework facilitates identification of interconnected drivers of aging, guides prioritization without oversimplification, and supports synergistic intervention strategies. By addressing mitochondrial resilience, hormonal orchestration, and inflammation modulation concurrently, clinicians can interrupt feed-forward aging loops and shift patients toward improved physiologic reserve and healthier aging trajectories.

VI. CLINICAL WORKFLOW FOR PROVIDERS: OPERATIONALIZING THE LONGEVITY TRIAD

For longevity-focused care to be clinically effective and scalable, conceptual models must translate into structured, reproducible workflows. The Longevity Triad provides a practical framework that integrates intake, diagnostic prioritization, and tiered intervention while preserving individualization. This section outlines a stepwise clinical workflow designed for use in endocrine, metabolic, and integrative medicine practices. A stepwise clinical workflow integrating intake, triad mapping, diagnostic layering, and tiered intervention is illustrated in Figure 3.

6.1 Intake and Risk Stratification

The initial patient encounter emphasizes identification of early aging signals rather than established disease alone. A comprehensive intake focuses on symptoms commonly associated with declining physiologic resilience, including fatigue, sleep disturbance, cognitive changes, weight gain, exercise intolerance, mood shifts, and chronic pain. Detailed personal and family histories assess cardiometabolic, autoimmune, neurodegenerative, and oncologic risk, while lifestyle and environmental exposure histories capture contributors often overlooked in conventional care.

Validated symptom inventories, fatigue scales, and metabolic questionnaires can assist in risk stratification and longitudinal tracking. Early identification of multisystem symptoms may

signal accelerated biological aging even when routine laboratory values fall within reference ranges [6].

6.2 Triad Mapping

Following intake, clinical data are mapped across the three pillars of the Longevity Triad to identify dominant and contributory drivers of dysfunction:

- **Mitochondria:** Fatigue, reduced exercise tolerance, metabolic inflexibility, recurrent illness.
- **Hormones:** Thyroid dysfunction, insulin resistance, perimenopausal or andropausal symptoms, adrenal rhythm disruption.
- **Inflammation:** Chronic pain, autoimmunity, cardiometabolic disease, gut dysbiosis, toxin burden.

If dysfunction is identified in two or more pillars, a synergistic, multi-pillar intervention is prioritized. When one pillar predominates, it becomes the initial therapeutic anchor while the remaining systems are concurrently supported to prevent compensatory imbalance. This mapping process provides clarity without oversimplification and allows clinicians to move beyond symptom-based treatment.

6.3 Diagnostic Layering

Rather than indiscriminate testing, diagnostic evaluation is layered based on triad mapping and clinical suspicion. This strategy improves diagnostic yield and reduces patient burden.

- **Mitochondrial Assessment:** targeted metabolic markers such as lactate and pyruvate, nutrient cofactors (eg, coenzyme Q10, carnitine), and functional testing including VO₂ max or submaximal exercise testing [14].
- **Hormonal Evaluation:** comprehensive thyroid panels (TSH, free T4, free T3, thyroid antibodies), metabolic markers (fasting insulin, HbA1c), sex hormone assessment during midlife transition, and cortisol rhythm testing when indicated [15].
- **Inflammatory and Immune Markers:** high-sensitivity C-reactive protein, cytokines when appropriate, advanced lipid panels, gut

permeability and microbiome testing, and selective toxin or exposure screening [5].

This layered approach aligns with geroscience principles by focusing on modifiable aging drivers rather than isolated disease endpoints [2].

6.4 Tiered Intervention Framework

Interventions are structured into phased tiers to allow progressive restoration of physiologic resilience while maintaining flexibility for individual response.

6.5 3-Month Intensive Phase

The initial phase focuses on stabilization and repletion. Core goals include reducing inflammatory burden, correcting nutrient deficiencies, improving sleep and circadian alignment, and initiating foundational lifestyle interventions. Early mitochondrial support and gentle movement are emphasized to generate rapid functional gains and improve patient engagement.

6.6 6-Month Integration Phase

During this phase, interventions are refined and expanded. Exercise prescriptions progress to include resistance training and targeted high-intensity intervals as tolerated. Hormonal optimization is adjusted based on clinical response and laboratory trends. Gut health, metabolic flexibility, and stress resilience strategies are reinforced to consolidate gains.

6.7 12-Month Maintenance Phase

Long-term maintenance emphasizes durability and prevention. Focus shifts toward sustaining metabolic health, preserving muscle and bone, minimizing inflammatory exposures, and reassessing biological aging markers. Patients are encouraged to transition from intensive support toward self-efficacy and lifestyle mastery.

Tiered care pathways support adherence while acknowledging that longevity optimization is an ongoing, adaptive process rather than a finite treatment course.

6.8 Monitoring and Reassessment Strategies

Monitoring combines objective biomarkers with patient-reported outcomes to assess progress and guide iteration. Reassessment at approximately three months includes repeat symptom inventories, targeted laboratory testing, and functional measures such as exercise tolerance or VO₂ max when feasible. Six-month evaluations emphasize trend analysis and intervention refinement, while annual assessments support long-term risk reduction and preventive strategy adjustment.

Wearable technologies and self-tracking tools—including heart rate variability, sleep metrics, and glucose monitoring—may provide additional insight into physiologic adaptation and patient engagement [38]. Continuous feedback reinforces adherence and allows timely intervention before decline becomes clinically apparent.

6.9 Clinical Implications

By embedding the Longevity Triad within a structured workflow, clinicians can systematically identify aging-related dysfunction, prioritize interventions, and monitor outcomes across interconnected biological systems. This approach facilitates early intervention, improves durability of results, and aligns clinical practice with the evolving science of healthy aging.

VII. DISCUSSION

7.1 Alignment of the Longevity Triad with Geroscience

The Longevity Triad aligns closely with the foundational principles of geroscience, which posit that aging is driven by a limited number of interconnected biological mechanisms that underlie multiple chronic diseases [2]. The hallmarks of aging framework emphasizes that processes such as mitochondrial dysfunction, dysregulated nutrient sensing, altered intercellular communication, and chronic inflammation do not act independently but form an integrated network that determines biological aging trajectories [1].

By centering mitochondrial resilience, hormonal orchestration, and inflammation modulation, the Longevity Triad operationalizes these mechanistic insights into a clinically actionable structure. Mitochondrial dysfunction maps directly to impaired energy metabolism and redox imbalance; hormonal dysregulation influences nutrient sensing, circadian alignment, and tissue repair; and chronic low-grade inflammation reflects altered intercellular communication and immune aging. This tri-pillar organization translates complex aging biology into domains that are both measurable and modifiable in clinical practice, thereby bridging the gap between bench science and patient care [1].

Importantly, the Longevity Triad emphasizes physiologic resilience rather than disease endpoints, consistent with geroscience's focus on extending healthspan rather than lifespan alone [2].

7.2 Advantages Over Single-Pathway Care

Traditional medical models frequently approach age-related symptoms through isolated pathways—targeting glycemia, thyroid function, lipid levels, or inflammatory markers independently. While such approaches may address discrete abnormalities, they often fail to account for upstream drivers and compensatory mechanisms, resulting in incomplete symptom resolution and progressive polypharmacy.

The Longevity Triad offers several advantages over single-pathway care. First, it recognizes bidirectional and feed-forward interactions among biological systems, explaining why interventions targeting only one domain frequently yield limited or transient benefits. Second, it enables prioritization without reductionism, allowing clinicians to identify dominant drivers while simultaneously supporting interconnected pathways. Third, it supports earlier intervention by identifying subclinical dysfunction—such as declining VO₂ max, mitochondrial inefficiency, or inflammatory burden—before irreversible disease manifests.

This systems-based approach aligns with emerging evidence that interventions targeting

fundamental aging mechanisms may yield broader benefits across multiple organ systems than disease-specific therapies alone [7].

7.3 Limitations

Several limitations of the Longevity Triad framework warrant consideration. First, much of the supporting evidence is derived from mechanistic studies, observational data, and case-based clinical application rather than large-scale randomized controlled trials specifically designed to test multi-pillar interventions. While this reflects the current state of geroscience translation, it limits definitive causal inference.

Second, comprehensive triad-based evaluation may require diagnostic tools and expertise not universally available, potentially limiting immediate scalability in all practice settings. Additionally, individualized, multi-domain interventions may increase short-term complexity for both clinicians and patients, emphasizing the need for clear workflows and patient education.

Finally, although the Longevity Triad is designed to be adaptable, it does not replace disease-specific guidelines or standard-of-care therapies but rather complements them. Careful integration with existing clinical standards remains essential.

7.4 Need for Prospective and Interventional Studies

Prospective research is needed to formally evaluate the Longevity Triad as a clinical strategy. Longitudinal studies assessing triad-based diagnostics and interventions could clarify their impact on functional outcomes, metabolic health, inflammatory burden, and markers of biological aging. Pragmatic trials comparing triad-guided care with standard single-pathway management would be particularly valuable in determining effectiveness, cost-efficiency, and patient-centered outcomes.

Additionally, validation of composite outcome measures-integrating functional capacity, symptom burden, and molecular aging markers-would strengthen the evidence base for systems-oriented longevity care [6].

7.5 Future Research Directions

Future research should focus on refining and validating the Longevity Triad across diverse populations and clinical contexts. Key priorities include:

1. *Biomarker development*, including integrated panels that reflect mitochondrial function, hormonal coordination, and inflammatory load.
2. *Mechanistic studies* examining how targeted interventions within one pillar influence the others over time.
3. *Implementation science*, evaluating how triad-based workflows can be efficiently incorporated into primary care, endocrine, and preventive medicine settings.
4. *Interventional trials* assessing combined lifestyle, nutritional, and hormonal strategies on healthspan-related outcomes.

As geroscience continues to mature, frameworks such as the Longevity Triad may serve as essential tools for translating aging biology into practical, patient-centered care strategies that prioritize resilience, prevention, and long-term vitality.

VIII. CONCLUSION

Longevity should be understood as a process of biological orchestration rather than isolated optimization. Efforts to correct single laboratory abnormalities or target individual pathways-while often necessary-are insufficient to meaningfully alter aging trajectories when underlying system-level dysfunction persists. The Longevity Triad reframes aging as a dynamic interaction among mitochondrial resilience, hormonal orchestration, and inflammation modulation, emphasizing balance, adaptability, and physiologic reserve as central determinants of healthy aging.

As the science of aging continues to evolve, systems endocrinology is poised to play a critical role in translating geroscience into clinical care. Endocrine networks integrate energy metabolism, immune signaling, circadian rhythms, and tissue repair, positioning hormones as both sensors and regulators of biological aging. When evaluated in

isolation, endocrine signals may appear “normal”; when interpreted within a systems framework, they reveal patterns of declining resilience and emerging dysfunction that precede overt disease.

The integration of precision diagnostics with aging biology represents a necessary next step in longevity medicine. Functional metabolic testing, comprehensive hormonal assessment, inflammatory and immune biomarkers, and exposure-aware evaluation allow clinicians to identify early drivers of aging and intervene before irreversible pathology develops. When combined with coordinated, multi-pillar interventions, these tools enable a shift from reactive disease management toward proactive healthspan preservation.

The Longevity Triad offers a practical, clinically adaptable framework for this transition. By aligning mechanistic insights from geroscience with real-world diagnostic and therapeutic strategies, it supports a new model of care-one that prioritizes resilience, coordination, and long-term vitality. As longevity medicine advances, embracing systems-based approaches will be essential to delivering personalized, effective, and sustainable strategies for healthy aging.

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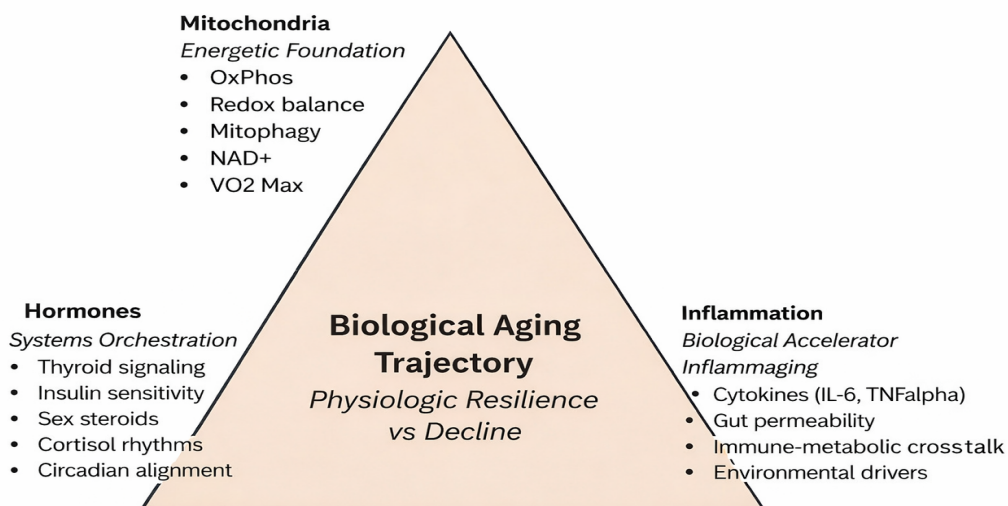


Figure 1: The Longevity Triad: A Systems-based Model of Aging Biology

The Longevity Triad conceptualizes biological aging as the dynamic interaction of three interdependent pillars: mitochondrial resilience, hormonal orchestration, and inflammation modulation. Mitochondria provide the energetic foundation for cellular function through regulation of oxidative phosphorylation, redox balance, and adaptive stress responses. Hormonal networks coordinate metabolism, circadian rhythms, reproduction, and tissue repair, while chronic low-grade inflammation (“inflammaging”) acts as a biological accelerator that disrupts mitochondrial efficiency and endocrine signaling. Bidirectional interactions among all three pillars influence physiologic resilience, metabolic flexibility, and aging trajectories, underscoring the need for integrated, systems-based clinical approaches to longevity care.

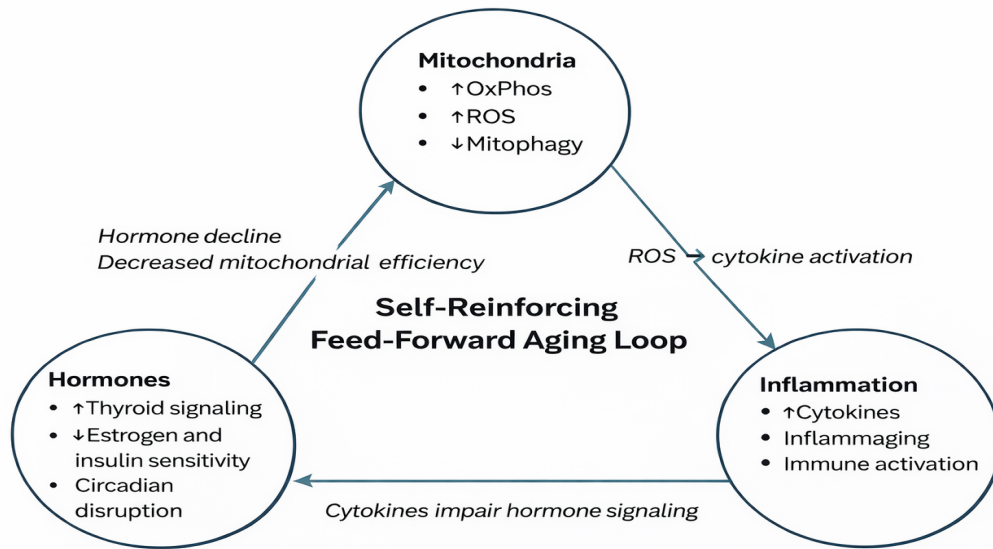


Figure 2: Feed-Forward Aging Loops within the Longevity Triad

This figure illustrates how dysfunction within any single pillar of the Longevity Triad—mitochondrial resilience, hormonal orchestration, or inflammation modulation—can initiate self-reinforcing feed-forward loops that accelerate biological aging. Mitochondrial inefficiency increases oxidative stress and inflammatory signaling; chronic inflammation disrupts

endocrine pathways; and hormonal dysregulation further impairs mitochondrial function. These bidirectional interactions amplify metabolic inflexibility, reduce physiologic reserve, and promote progression from subclinical imbalance to overt disease, explaining why single-pathway interventions often fail to produce durable clinical improvement.

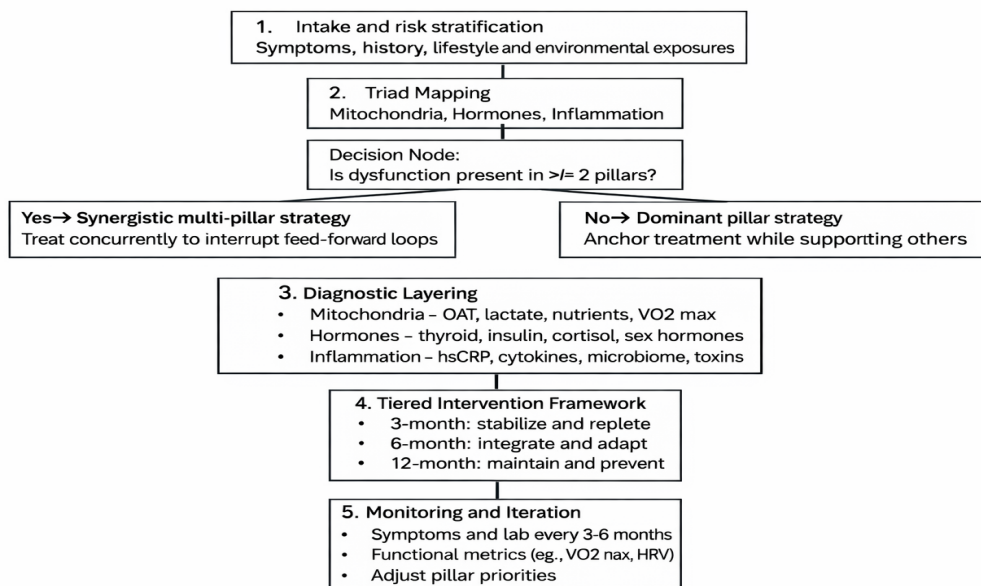


Figure 3: Longevity Triad Clinical Workflow and Decision tree for Precision Longevity Care

This figure depicts a stepwise clinical workflow for implementing the Longevity Triad in practice. Care begins with intake and risk stratification, followed by triad mapping across mitochondrial, hormonal, and inflammatory domains. A decision node guides prioritization: multi-pillar intervention is initiated when two or more pillars are dysfunctional, while a dominant-pillar approach is used when one pathway predominates with concurrent system support. Diagnostics are layered based on triad mapping, and interventions are delivered in tiered phases (3-, 6-, and 12-month) with ongoing monitoring using symptoms, laboratory markers, and functional outcomes to support iterative, personalized longevity care.

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ABSTRACT

Introduction: Non-communicable diseases (NCDs), including cardiovascular diseases (CVDs), contribute significantly to global mortality, accounting for over 70% of deaths worldwide. Recent advancements in Trans-dermal Optical Imaging (TOI) technologies, such as the Lifesten app, offer innovative approaches to blood pressure measurement. This study compares the accuracy of the Lifesten app to traditional cuff-based methods for measuring blood pressure.

Methods: A cross-sectional study was conducted in Kigali, Rwanda, targeting adults aged 18–45, including high-risk individuals that were identified through social media, community outreach, and targeted advertising. Participants underwent blood pressure measurements using both the Lifesten app and a traditional hand-cuff device. Data were analyzed using SPSS software to compare the two methods.

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Results: Among the 384 participants, 59.63% were male (n=229) and 40.37% were female (n=155), with the majority aged 18–27 years. The mean scores measured using the Lifesten app for systolic and diastolic pressures were 111.45 mmHg and 74.75 mmHg, respectively, compared to 116.78 mmHg and 75.71 mmHg using the traditional device, showing differences of 4.56% and 1.27%. In a subgroup of 12 hypertensive individuals, the app recorded lower systolic (114.17 mmHg) and diastolic (75.67 mmHg) readings than the traditional device (140.17 mmHg and 80.00 mmHg). The app's systolic MAE was 11.68 mmHg (MAPE: 9.63%), while diastolic MAE was 8.66 mmHg (MAPE: 11.63%).

Conclusion: The Lifesten app demonstrated potential for hypertension screening in resource-limited settings. However, algorithm

improvements are necessary to enhance its accuracy and ensure reliable clinical use.

Keywords: AI, digital health, NCDs, hypertension, Lifesten, Rwanda.

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I. INTRODUCTION

Non-communicable diseases (NCDs) are a global public health emergency, accounting for 74% of global deaths annually, as reported by the World Health Organization (WHO) [1]. Of the 41 million lives claimed by NCDs every year, over 15 million involve individuals aged 30 to 69, with 85% of these deaths occurring in low- and middle-income countries (LMICs). Among these, cardiovascular diseases (CVDs) are the primary contributor, causing 17.9 million deaths annually [1], [2]. These figures underscore the need for urgent and innovative interventions, especially in resource-limited settings where access to healthcare services remains inadequate

In Rwanda, the rising prevalence of NCDs, particularly CVDs, poses significant challenges to the health system [3]. The Ministry of Health estimates that NCDs account for 44% of all deaths in the country, with cardiovascular diseases contributing 14% to this total. Between 2012 and the latest STEPS survey, the prevalence of CVDs has increased from 15% to 16.8% [4]. Behavioral and environmental factors such as tobacco use,

Urbanization and the adoption of Western lifestyles further compound the problem, highlighting the need for tailored solutions to address these risk factors effectively [5], [6].

Efforts to combat NCDs in low- and middle-income countries (LMICs) are hindered by systemic barriers, including limited healthcare infrastructure and accessibility, particularly in remote areas [7], [8], [9]. As consequences, many individuals face delays in diagnosis and treatment, which exacerbates the burden of these conditions [10]. In addition, traditional healthcare delivery methods often struggle to meet the needs of underserved populations [11]. Therefore, introducing cost-effective, scalable, and locally relevant health technologies is essential for bridging these gaps [12], [13].

One of promising solution is transdermal optical imaging (TOI) technology, a ground breaking approach to cardiovascular health monitoring. This technology uses a smartphone's camera to analyze subdermal blood flow and oxygenation levels by processing light reflected from the skin [14], [15], [16]. The Lifesten app integrates this TOI technology with personalized health education programs designed to improve users' physical, mental, and nutritional well-being. By providing accessible tools for health monitoring and guidance, the app empowers individuals to take proactive steps toward better cardiovascular health [17].

The potential impact of innovative digital health solutions is particularly profound in low- and middle-income countries (LMICs) such as Rwanda, where they can serve as valuable complements to existing healthcare infrastructure. Mobile health (mHealth) platforms offer capabilities for real-time monitoring, early detection, and personalized interventions, thereby minimizing the need for frequent visits to healthcare facilities [18], [19]. These technologies are both cost-effective and scalable, making them especially suitable for resource-constrained settings [20]. However, the successful adoption of health technologies like the Lifesten app necessitates rigorous evaluation of their accuracy and reliability. This study seeks to compare the

Lifesten app with the conventional cuff-based device in measuring blood pressure and screening for hypertension, addressing critical aspects of its performance and clinical applicability.

II. METHODOLOGY

2.1 Study Design and Setting

This cross-sectional study was conducted across the three districts of Nyarugenge, Gasabo, and Kicukiro in Kigali City, Rwanda, targeting adults aged 18 to 45, with a particular focus on individuals who have limited access to healthcare services. The study primarily aimed to screen individuals at heightened risk for cardiovascular diseases, such as those with sedentary lifestyles, poor dietary practices, and habits involving tobacco and alcohol use. Participants were selected based on criteria including age, occupation, and specific lifestyle behaviors, ensuring a representative sample of the population.

2.2 Sample Size and Sampling

The sample size for this study was determined using Cochran's formula, which calculates the appropriate number of participants needed for a specified level of confidence and margin of error (Equation 1). For this study, a confidence level of 95% and a margin of error of 5% were applied, with an estimated population size of 300,000.

$$n = (Z^2 * p * (1 - p)) / E^2 \quad (\text{Equation 1})$$

In this equation, n represents the sample size, Z corresponds to the z-score for the desired confidence level, p is the estimated proportion of the population exhibiting the characteristic of interest, and E is the margin of error. Drawing from prior studies, the proportion p was assumed to be 0.5, which is commonly used in the absence of prior data, and the margin of error E was set to 0.05. With a 95% confidence level, the z-score value was 1.96. Substituting these values into the formula resulted in a calculated sample size of 384. To ensure the sample was representative of the population, purposive sampling was utilized, allowing for the inclusion of participants from various backgrounds and risk groups.

2.3 Eligibility Criteria

The inclusion criteria for this study were adults aged 18 to 45 who were primarily underserved by the current healthcare system in Kigali, including young individuals and those with high-risk lifestyles. Participants were required to be proficient in using smartphone applications, have access to the internet, and be at high risk of developing cardiovascular diseases due to factors such as poor dietary habits, tobacco use, and alcohol consumption. The exclusion criteria, on the other hand, included individuals under the age of 18 or over the age of 45, those already receiving regular medical treatment for cardiovascular diseases, and individuals who were either unable or unwilling to use smartphone applications or lacked internet access. Furthermore, individuals who did not meet the high-risk criteria for cardiovascular diseases, as identified through screening and assessment tools, were also excluded from participation in the study.

2.4 Study Procedure

Participants for the study were recruited through social media, community outreach, and targeted advertisements. Screening for hypertension was conducted using both the Lifesten app and a traditional cuff-based blood pressure measurement device. New participants were continuously enrolled and screened using both methods. They were given access to the Lifesten app, with training and ongoing support to help them understand cardiovascular disease risk factors and perform remote diagnostic tests.

Regular follow-ups tracked participant engagement and usage of the app. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software to compare Lifesten app with traditional cuff-based blood pressure measurement device in screening for hypertension.

2.5 Ethical Considerations

Ethical approval was obtained from the Rwanda national research and ethics committee with the IRB number being IRB 0001497 of IORG0001100 and with issuing number 148/RNEC/2023. Informed consent was appropriately obtained at every stage of data collection, and the confidentiality of respondents' identities was fully ensured.

III. RESULTS

3.1 Characteristics of Participants

The study included a total of 384 participants, of whom 59.63% (n=229) were male and 40.37% (n=155) were female. The majority (94%) were between 18 and 27 years of age. Regarding marital status, 369 participants were single. Geographically, most respondents resided in Gasabo District (n=166), followed by Nyarugenge District (n=76). Educational attainment revealed that 60% (n=230) of the participants had achieved college or university education. Socioeconomic data indicated that 250 respondents belonged to the middle-income class, while 119 were categorized as low-income earners (Table 1).

Table 1: Characteristics of Participants

Study Variable	Responses	Frequency	%
Gender	Male	229	60.0%
	Female	155	40.0%
Age	18 – 27	361	94.0%
	28 – 37	18	4.7%
	38 – 47	3	0.8%
	48 - 57	2	0.5%
Marital Status	Married	14	3.7%
	Separated/Divorced	1	0.3%
	Single	369	96.0%
Residence	Gasabo	142	37.0%

	Kicukiro	166	43.0%
	Nyarugenge	76	20.0%
Education Level	College/University	230	60%
	No formal education	1	0.3%
	Postgraduate	26	7.0%
	Primary	14	3.7%
	Secondary	113	29.0%
Social Economic Status	High Earning Class	15	4.0%
	Low Earning Class	119	31.0%
	Middle Earning Class	250	65.0%

3.2 Comparing Lifesten app and Conventional Handcuff Methods for Blood Pressure Screening in General Individuals

A comparative analysis of blood pressure screening revealed that the mean systolic pressure measured using the traditional device was 116.78 mmHg, whereas the application recorded a lower mean of 111.45 mmHg, representing a difference of 4.56%. For diastolic pressure, the traditional

device recorded a mean of 75.71 mmHg compared to 74.75 mmHg from the application, yielding a smaller difference of 1.27% (Table 2 and Figure 1). These findings indicated that the application tended to produce slightly lower readings, particularly for systolic pressure, although the overall differences between the two methods remained minimal.

Table 2: Comparison of Lifesten App and Conventional Handcuff Methods for Blood Pressure Screening in General Individuals

	N	Mean(machine)	Mean (App)	Percentage difference
measurements				
Systolic blood pressure	384	116.78	111.45	4.56%
Diastolic blood pressure	384	75.71	74.75	1.27%
Valid N (listwise)	384			

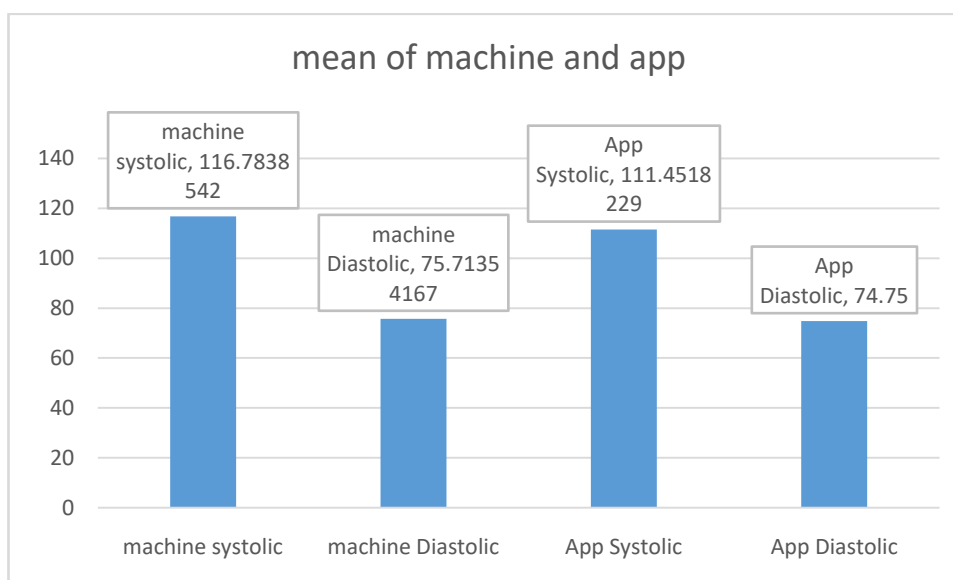


Figure 1: Difference between Lifesten App and Traditional Machine in Measuring Blood Pressure in General Individuals

3.3 Comparing Lifesten App and Conventional Handcuff Methods for Blood Pressure Screening in Hypertensive Persons

In a subgroup of 12 hypertensive individuals, conventional handcuff methods recorded a mean systolic blood pressure of 140.17 mmHg, reflecting elevated level consistent with hypertension, and a mean diastolic pressure of 80.00 mmHg,

positioned at the upper threshold of the normal range. In contrast, the mobile application reported a lower mean systolic pressure of 114.17 mmHg and a mean diastolic pressure of 75.67 mmHg (Table 3 and Figure 2). This indicated a tendency for the application to record lower blood pressure values compared to the traditional method, particularly for systolic measurements.

Table 3: Comparison of Lifesten App and Conventional Handcuff Methods for Blood Pressure Screening in Hypertensive Individuals

Measurements	N	Mean (machine)	Mean (App)	Percentage difference
Systolic blood pressure	12	140.17	114.17	18.55%
Diastolic blood pressure	12	80	75.67	5.41%
Valid N (listwise)	12			

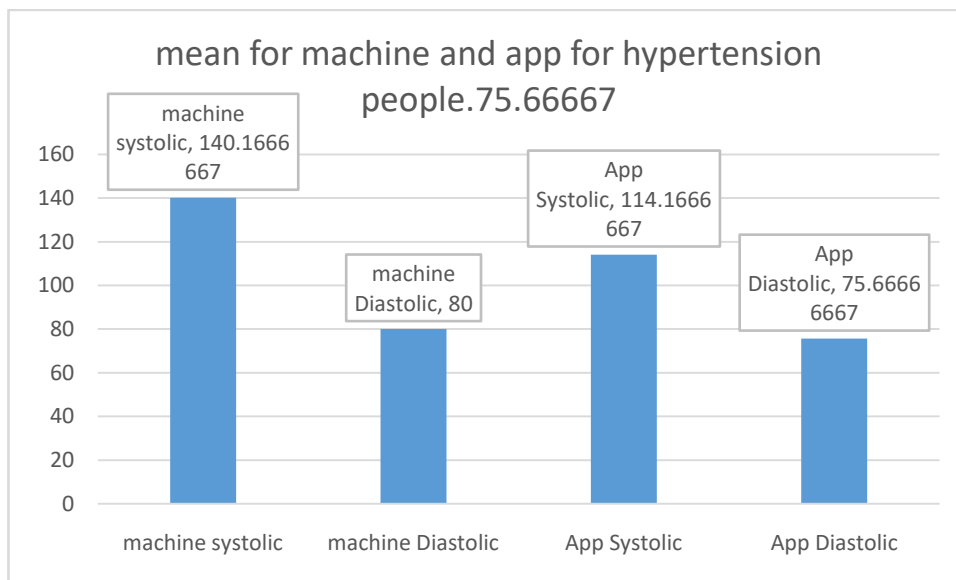


Figure 2: Difference between Lifesten App and Traditional Machine in Measuring Blood Pressure in Hypertensive Individuals

3.4 Accuracy of Lifesten App in Blood Pressure Screening Compared to Conventional Way

The comparison of systolic and diastolic blood pressure readings between the Lifesten app and the traditional machine revealed modest variations in accuracy. For systolic measurements, the Mean Absolute Error (MAE) was calculated to be 11.68 mmHg, indicating an average deviation of this magnitude from the traditional machine's values. This suggests that while the app demonstrated a degree of accuracy, its readings showed noticeable differences when compared to the reference method. Additionally, the Mean

Absolute Percentage Error (MAPE) for systolic measures was 9.63%, meaning that the app's systolic readings were, on average, within approximately 10% of the machine's measurements. This represents a respectable level of precision, particularly for a non-invasive and portable tool, but highlights the presence of some variability that requires attention for improved performance in clinical practice.

For diastolic readings, the MAE was lower, calculated at 8.66 mmHg, which reflects a smaller absolute deviation compared to systolic measurements. However, the relative accuracy of

the app's diastolic measurements was slightly lower, as indicated by a MAPE of 11.63% (Table 4). This higher percentage of error suggests that the app's diastolic readings are relatively less consistent when compared to the machine's values. While the app's performance for diastolic measurements showed some promise, the larger

relative error underscores the need for further refinement. These findings indicate that while the Lifesten app performs adequately for diastolic readings, there remains room for improvement to enhance its reliability and accuracy in both systolic and diastolic measurements.

Table 4: Accuracy of Lifesten App in Blood Pressure Screening Compared to Conventional Way

	Mean Absolute error. (MAE)	Mean Percentage error. (MAPE)
Systolic (Machine and App)	11.67578	9.633785451
Diastolic (Machine and app)	8.65625	11.6253

IV. DISCUSSION

This study compared blood pressure screening using transdermal optical imaging through the Lifesten app and a conventional cuff-based machine among high-risk young adults in Kigali. The results showed that the Lifesten app recorded lower systolic and diastolic blood pressure values in both general participants and those with hypertension. These findings suggest that while the Lifesten app can be a useful tool for blood pressure screening, its readings tend to be lower than those from the traditional cuff machine. This highlights the need to refine the app's algorithms to enhance its accuracy and bring it in line with the standard measurements provided by conventional blood pressure devices.

Even though there is no specific study on Lifesten app, different authors compared different transdermal optical imaging-based apps with standard reference to understand apps' effectiveness and accuracy. Schoettker *et al* conducted a comparison between smartphone-based blood pressure measurements taken from 50 participants using the OptiBP app and traditional auscultatory readings for systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) in an ambulatory setting. The differences in BP measurements (mean \pm standard deviation) between the two methods were within the ISO 81,060–2:2018 standards, with SBP at -0.7 ± 7.7 mmHg, DBP at -0.4 ± 4.5 mmHg, and MBP at -0.6 ± 5.2 mmHg [21]. This demonstrate that the transdermal optical imaging-based apps can accurately measure blood pressure and has the potential to

be an effective tool for detecting hypertension, particularly in low-income countries where smartphones are widely available, but healthcare access is limited.

After employing an advanced machine learning algorithm to develop computational models predicting reference systolic, diastolic, and pulse pressure based on facial blood flow data from 1,328 normative individuals, Luo et al found that the predicted blood pressure measurements were within 5 ± 8 mmHg of the reference values, indicating a minimal deviation from standard measurements [14]. In a separate study, after analyzing 353 paired recordings from 91 subjects, Degott *et al* found that the differences between OptiBP and reference blood pressure recordings were 0.5 ± 7.7 mmHg for systolic blood pressure (SBP) and 0.4 ± 4.6 mmHg for diastolic blood pressure (DBP), with an OptiBP acceptance rate of 85%, when evaluating OptiBP against AAMI/ESH/ISO universal standards for blood pressure measurement. The smartphone-based OptiBP cuffless mobile application met the validation criteria outlined by AAMI/ESH/ISO universal standards for blood pressure measurement in the general population, further demonstrating its potential for use in blood pressure screening [22].

The Lifesten app, while demonstrating effectiveness in measuring blood pressure and screening for hypertension, exhibits accuracy limitations when compared to the standard cuff-based method. For instance, among 12 hypertensive individuals whose mean systolic blood pressure was recorded as 140.17 mmHg using the traditional method, the app measured a

significantly lower mean of 114.17 mmHg, reflecting an 18.55% difference—the largest discrepancy observed across all screenings. Furthermore, the app consistently reported lower blood pressure readings in all other measurements compared to the reference. This raises concerns about the potential for underdiagnosis of hypertension, particularly in cases where blood pressure values are near the upper threshold of normal. These findings underscore the necessity of enhancing the Lifesten app's algorithm to improve its measurement accuracy and diagnostic reliability.

Cardiovascular health digital interventions such as Lifesten app, if implemented on a larger scale, holds substantial promise for supporting Rwanda's national cardiovascular disease prevention efforts, particularly in resource-limited settings where traditional healthcare access may be constrained. By delivering accessible, digital health education and screening directly to users' smartphones, the app can reach a broad demographic, including individuals who may otherwise face barriers to routine cardiovascular care. As demonstrated, the app effectively measured blood pressure with no much difference compared to the reference, demonstrating its potential of this new technology in screening of hypertension. If adopted nationally, the Lifesten app could provide a scalable and cost-effective tool to combat cardiovascular disease, reducing the burden on healthcare facilities while enabling early intervention through education screening and self-monitoring. Furthermore, the app's success in Rwanda could serve as a model for other low- and middle-income countries, highlighting how digital health solutions can enhance public health in settings with limited resources and infrastructure.

V. CONCLUSION

The Lifesten app, utilizing transdermal optical imaging technology to measure blood pressure, represents an effective tool for hypertension screening and monitoring. Its potential is particularly significant in underserved populations where conventional methods of cardiovascular health monitoring are often

inadequate. However, the app consistently recorded lower blood pressure values compared to the standard cuff-based device. Enhancing the app's algorithm to improve its accuracy is crucial to ensuring reliable hypertension detection and effective integration into clinical and community health settings.

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Optimal Surgical Treatment of Hiatal Hernias of Types II-IV

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ABSTRACT

Hiatal hernias of types II-IV have anatomical features that cause a displacement of the abdominal organs into the mediastinum through the hiatal opening of the diaphragm parallel to the esophagus without or together with it (paraesophageal component), which is an absolute indication for surgical treatment, since it is the cause of life-threatening conditions (acute intestinal or gastric, esophageal obstruction, strangulation and further necrosis of the organs located in the hernial sac). The recurrence rate of hiatal hernias of types II-IV reaches 20-40% and even 60%, underscoring the need for analysis and search for new solutions to this problem. The article analyzes the long-term results of treatment of 150 patients with hiatal hernias of types II-IV hernias, operated in the thoracic surgery department of the P. A. Bayandin Murmansk Regional Clinical Hospital in the period from 2013 to 2017, which made up a retrospective group (standard surgical treatments). Based on the assessment of the treatment results, changes were made to the surgical intervention tactics used.

Keywords: esophageal hernia, hiatal hernia, gastroesophageal reflux disease, diaphragmatic plastic surgery, cruroraphy, fundoplication.

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Optimal Surgical Treatment of Hiatal Hernias of Types II-IV

Stanislav A. Skriabin^α, Maria V. Korelskaya^σ, Dmitrii I. Vasilevskii^ρ & Tatyana P. Volkova^ω

ABSTRACT

Hiatal hernias of types II-IV have anatomical features that cause a displacement of the abdominal organs into the mediastinum through the hiatal opening of the diaphragm parallel to the esophagus without or together with it (paraesophageal component), which is an absolute indication for surgical treatment, since it is the cause of life-threatening conditions (acute intestinal or gastric, esophageal obstruction, strangulation and further necrosis of the organs located in the hernial sac). The recurrence rate of hiatal hernias of types II-IV reaches 20-40% and even 60%, underscoring the need for analysis and search for new solutions to this problem. The article analyzes the long-term results of treatment of 150 patients with hiatal hernias of types II-IV hernias, operated in the thoracic surgery department of the P. A. Bayandin Murmansk Regional Clinical Hospital in the period from 2013 to 2017, which made up a retrospective group (standard surgical treatments). Based on the assessment of the treatment results, changes were made to the surgical intervention tactics used. From 2018 to 2024, 180 patients with hiatal hernias of types II-IV underwent surgery in the same unit, forming a prospective study group (optimal surgical treatments). A comparison of these groups was carried out. The research evaluates the perception of certain factors, primarily shortening of the esophagus, as objective conditions with the transformation of surgical tactics allowing for achieving significantly better results. Good or satisfactory treatment outcomes were achieved in 73.7% of cases in patients of the retrospective group, and poor outcomes were achieved in 26.7%. In patients of the prospective group, these results were 88.6% and 11.4%, respectively. The research confirms that with shortening of the esophagus in type III hernias,

its high mobilization does not allow to reliably prevent repeated displacement of the stomach into the chest; the use of prostheses to correct the esophageal hiatus in case of shortening of the esophagus is an ineffective method of preventing relapse of the disease; the formation of a fundoplication cuff in the mediastinum in case of shortening of the esophagus should be considered an effective method of preventing relapse; in case of hernias of types II-IV and normal length of the esophagus, the use of prosthetic materials to correct the size of the hiatal opening is justified and allows to reduce the frequency of unsatisfactory treatment results.

Keywords: esophageal hernia, hiatal hernia, gastroesophageal reflux disease, diaphragmatic plastic surgery, cruroraphy, fundoplication.

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I. INTRODUCTION

Surgical treatment of hiatal hernias of types II-IV is a separate surgical problem that has been discussed for many years. Given the high long-term disease recurrence rate, unsatisfactory

surgical outcomes are reported according to various sources in 20-40% of cases. [1, 3, 4, 7, 9]. The reasons for unsuccessful treatment outcomes are the large size of the hernial gate (esophageal hiatus) and the destruction of the ligamentous apparatus that holds the organs of the abdominal cavity (primarily the stomach) in the abdominal position. Another factor influencing the tendency of this type of hernia to relapse is the primary or secondary (due to various pathogenetic influences) shortening of the esophagus. [2, 5, 11]. Over the long history of surgical treatment of hiatal hernias of types II-IV, many ways have been proposed to improve the results of surgical interventions, which are ideologically divided into several options. The first category includes techniques aimed at improving the reliability of plastic surgery of the hiatal opening: the use of a circular ligament of the liver, and patches made of biological or polymer prosthetic materials, to correct its size. The second group of techniques is aimed at strengthening the abdominal position of the stomach, and is called "gastropexy" in the literature. The essence of all surgical options is to fix the stomach to the anterior or lateral abdominal wall, preaortic fascia, etc. The third category of operations is aimed at correcting the shortening of the esophagus: its high mobilization

in the mediastinum, intersection of the vagus nerves, esophagogastroplasty (lengthening of the esophagus due to the small curvature of the stomach) [3, 6, 7, 8, 9]. Unfortunately, the vast majority of these techniques have significant negative consequences and have not been widely used in clinical practice. Thus, to date, the issue of increasing the effectiveness of surgical treatment of hiatal hernias of types II-IV remains open.

II. MATERIALS AND METHODS

The long-term treatment outcomes of 150 patients with hernias of the esophageal orifice of the diaphragm operated in the Department of thoracic surgery of the P.A. Bayandin Murmansk Regional Clinical Hospital (Russia) in the period from 2013 to 2017 were analyzed. These patients formed a retrospective group (standard surgical treatments). The results obtained led to changes in the tactics used for surgical interventions. From 2018 to 2024, 180 patients with hiatal hernias of types II-IV, who made up the prospective study group (optimal surgical treatments), were operated on in the same unit.

The groups were comparable in age and gender composition (Figure 1).

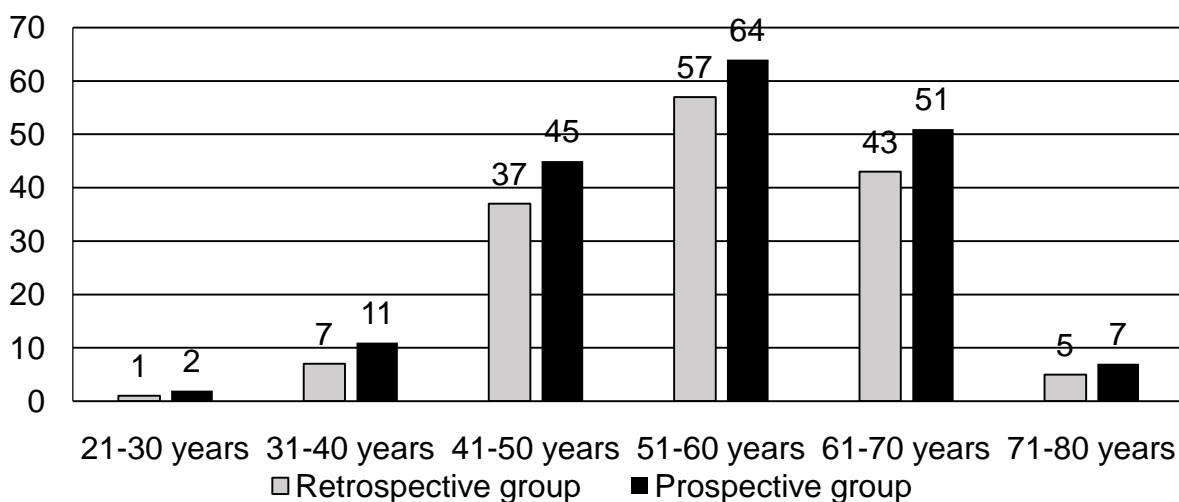


Figure 1: Distribution of Patients in the Retrospective and Prospective Groups by Gender and Age

The clinical signs of the disease in patients of both groups were similar and consisted of manifestations of gastro-esophageal reflux (heartburn, belching, regurgitation, chronic cough, hoarseness of voice, cardiac arrhythmias, etc.) in type III hernias.

Another category of symptoms (pain behind the sternum or in the abdomen, often worse after eating, vomiting, shortness of breath) was caused by a disruption in the passage of contents through the organs of the abdominal cavity displaced into the mediastinum. The reason for such changes in

function in hernias of types II-III was the formation of a “gastric valve” – the rotation of the part of the stomach located in the chest in different planes. In type IV hernias, the symptoms were caused by rotation or compression in the hiatal opening of the colon.

The method of instrumental diagnosis of the type of hiatal hernias in patients of both groups was the upper digestive tract radiography with contrast agent (BaSO₄) (Table 1.).

Table 1: Types of Diaphragmatic Hernias in Patients of the Retrospective and Prospective Groups

Type of Hiatal Hernia	Number of Patients, Absolutely . (%)	
	Retrospective Group (Standard Surgical Treatments)	Prospective Group (Optimal Surgical Treatments)
Paraesophageal Hernias (Type Ii)	17 (11,3%)	25 (13,9%)
Mixed Hernias (Type Iii)	131 (87,3%)	152 (84,4%)
Hiatal Hernias (Type Iv)	2 (1,3%)	3 (1,7%)
Total	150 (100%)	180 (100%)

In type II hiatal hernias, X-rays showed that the fundus, and sometimes a part of the stomach body, displaced into the mediastinum. In these cases, the gastroesophageal junction was located in the abdominal cavity. In mixed hernias, the findings were similar, except for the displacement of the gastro-esophageal junction into the chest. In type IV hernias, the imaging revealed a displacement of not only the stomach but also other organs into the mediastinum, creating additional radiographic shadows.

with a water-soluble contrast agent was performed. A “gastric valve” in patients of the retrospective group was detected in 13 (76.4% with this type of anatomical changes) with paraesophageal and 93 (71.0%) with mixed hernias. In the prospective group, 16 (64.0%) and 106 (69.7%) patients were affected, respectively. In type IV hernias, the colon was visualized in two people in the retrospective and three in the prospective group.

To clarify the nature of anatomical disorders, diagnose the “gastric valve” in hernias of types II-III, or determine the organ displaced to the chest in hernias of type IV, computed tomography

During endoscopic examination of the upper digestive tract, changes in the mucous membrane of the esophagus and stomach were noted in some patients of both groups (Table 2).

Table 2: Endoscopic Changes of the Upper Digestive Tract in Patients of the Prospective Group

Patient Groups	Number of Patients, Absolutely . (%)		
	Erosive Esophagitis	The Cylindrical Cell Metaplasia	Erosive Gastritis
Retrospective Group (Standard Surgical Treatments)	86 (57,3%)	19 (12,7%)	110 (73,3%)
Prospective Group (Optimal Surgical Treatments)	110 (61,1%)	16 (8,8%)	101 (67,3%)

Pronounced erosive esophagitis and cylindrical cell metaplasia of the esophageal epithelium in patients of both groups were observed mainly in type III hernias characterized by gastroesophageal reflux. Erosive gastritis was detected in the part of

the stomach displaced to the chest in patients of both groups with paraesophageal and mixed hernias.

The indications for surgical treatment in patients of both the retrospective and prospective groups were *identical*: the presence of clinical manifestations of the disease and the risk of developing life-threatening conditions (ischemia and necrosis of abdominal organs located in the chest or their acute obstruction).

III. RESULTS

All patients of both the retrospective and prospective groups underwent laparoscopic removal of esophageal hernias of types II-IV. Neither group required conversion of surgical access.

The basic principles for mobilizing the necessary anatomical formations in both groups were identical. The abdominal organs located in the chest were moved to the abdominal position, while the frontal was straightened along the axis and a probe with a diameter of 45 Fr was inserted into its lumen for anatomical orientation. The hernial sac mobilized in the chest, bluntly and acutely, and separated from the hiatal pedicels. After that, the sac was acutely separated from the

abdominal part of the esophagus and the proximal part of the stomach, and excised.

After the mobilization was completed, the main anatomical conditions influencing the choice of reconstruction option and predicting the long-term results were evaluated: the length of the abdominal esophagus and the size of the hiatal opening (Table 3).

The performance of the reconstructive stage in patients of the retrospective and prospective groups was fundamentally different in cases of esophageal shortening (with type III hernias). It is this issue that has led to the evolution of views on tactical approaches to the treatment of hernias of the esophageal orifice of the diaphragm following the initial analysis of long-term results.

In the retrospective group, when the esophagus was shortened (the length of the abdominal region was less than 2.0 cm), its high mobilization in the mediastinum (up to the level of the middle thoracic part) was performed. It was assumed that this technique would reduce the likelihood of recurrence of a hiatal hernia (Table 4).

Table 3: Length of the Esophagus and Size of the Hiatal Opening in Patients of The Retrospective and Prospective Groups

Type of Hiatal Hernia	Number of Patients, Absolutely . (%) P					
	The Normal Length of the Esophagus			Shortening of the Esophagus		
	Size of Hiatal Opening			Size of Hiatal Opening		
	before 5 cm	more 5 cm	more 8 cm	before 5 cm	more 5 cm	more 8 cm
Retrospective group Hernias (type II)	4 (23,5%)	11 (64,7%)	2 (11,8%)	-	-	-
Prospective group Hernias (type II)	13 (52,0%)	7 (28,0%)	5 (20,0%)	-	-	-
Retrospective group Hernias (type III)	5 (3,8%)	13 (9,9%)	6 (4,5%)	2 (91,5%)	79 (60,3%)	26 (19,8%)
Prospective group Hernias (type III)	12 (7,9%)	17 (11,2%)	2 (1,3%)	7 (4,6%)	95 (62,5%)	19 (12,5%)
Retrospective group Hernias (type IV)	-	-	2 (100%)	-	-	-
Prospective group Hernias (type IV)	-	-	3 (100%)	-	-	-

Table 4: Types of Surgical Interventions in Patients of the Retrospective and Prospective Groups

Type of Hiatal Hernia	Number of Patients, Absolutely . (%)					
	Plastic Surgery of the Hiatal Opening with Own Tissues		Plastic Surgery of the Hiatal Opening with the Installation of a Prosthesis Behind the Esophagus		Plastic Surgery of the Hiatal Opening with the Installation of a Prosthesis behind and an Front of the Esophagus	
	Circular Fundoplication of the R. Nissen Type	Posterior Fundoplication of Type A. Toupet	Circular Fundoplication of The R. Nissen Type	Posterior Fundoplication of Type A. Toupet	Circular Fundoplication of The R. Nissen Type	Posterior Fundoplication of Type A. Toupet
Retrospective group Hernias (type II)	4 (23,5%)	-	11 (64,7%)	-	1 (5,9%)	1 (5,9%)
Prospective group Hernias (type II)	13 (52,0%)	-	-	7 (28,0%)	-	5 (20,0%)
Retrospective group Hernias (type III)	7 (5,4%)	-	85 (64,9%)	7 (5,3%)	29 (22,1%)	3 (2,3%)
Prospective group Hernias (type III)	133 (87,5%)	-	-	17 (11,2%)	-	2 (1,3%)
Retrospective group Hernias (type IV)	-	-	-	-	-	2 (100%)
Prospective group Hernias (type IV)	-	-	-	-	-	3 (100%)

In the prospective group, when the esophagus was shortened, a fundoplication cuff in the mediastinum was initially assumed to form. In such situations, circular reconstruction of the R. Nissen type (360) was always performed with suture fixation of the cuff to the gastroesophageal junction area. This type of fundoplication is most resistant to destruction when displaced into the chest. Prosthetic materials were not used to correct the size of the hiatal opening during the formation of the cuff in the mediastinum.

In patients with a normal length of the esophagus, the reconstructive stage in the retrospective and prospective groups was identical. With small sizes of the esophageal orifice of the diaphragm (up to 5 cm) and full-fledged muscular legs, the hiatal orifice was plasticized with its own tissues. With its large size or hypotrophy of the diaphragm legs, posterior crural surgery was performed to strengthen the suture line with a mesh prosthesis. In cases of severe tissue tension (the size of the

esophageal orifice of the diaphragm is more than 8 cm), posterior and anterior surgery was performed with reinforcement with a prosthesis. "Heavy" polypropylene implants were used ("Prolen", "Esfil", "Uniflex"), U-shaped or of linear shape, which were located no closer than 2-3 mm from the inner edge of the radial hole and fixed with a stapler or nodal seams. To prevent damage to the esophagus by the edge of the prosthesis, a fundoplication cuff was placed between them.

There were no statistically significant differences in the incidence of intraoperative complications between the two groups. In patients of the retrospective group, undesirable effects occurred in 13 (8.6%) cases: gastric perforation - in 2 (1.3%), bleeding - in 3 (2.0%), pneumothorax - in 8 (5.3%). In patients of the prospective group, complications were noted in 16 (8.9%) cases: gastric perforation - in 2 (1.1%), esophageal perforation - in 1 (0.6%), bleeding - in 2 (1.1%),

pneumothorax – in 11 (6.1%). All complications were classified into categories I-II on the Clavien-Dindo scale and were eliminated during surgery. The duration of operations in both groups was comparable: in the retrospective group, 107-189 minutes (on average, 132 minutes), in the prospective group, 105-176 minutes (on average, 127 minutes). Complications in the early postoperative period were observed with equal frequency in both groups: 5 (3.3%) and 8 (4.4%), respectively. There were no deaths in the retrospective and prospective groups.

The hospital stay after surgery in the retrospective group ranged from 4 to 11 days (on average – 6 days), whereas in the prospective group – it ranged from 4 to 12 days (on average – 5 days).

The long-term results of surgical treatment of hernias of types II-V over a period of two to five years were studied and compared in 116 (77.3%) of 150 patients in the retrospective group and 132 (73.3%) of 180 patients in the prospective group (Fig. 2).

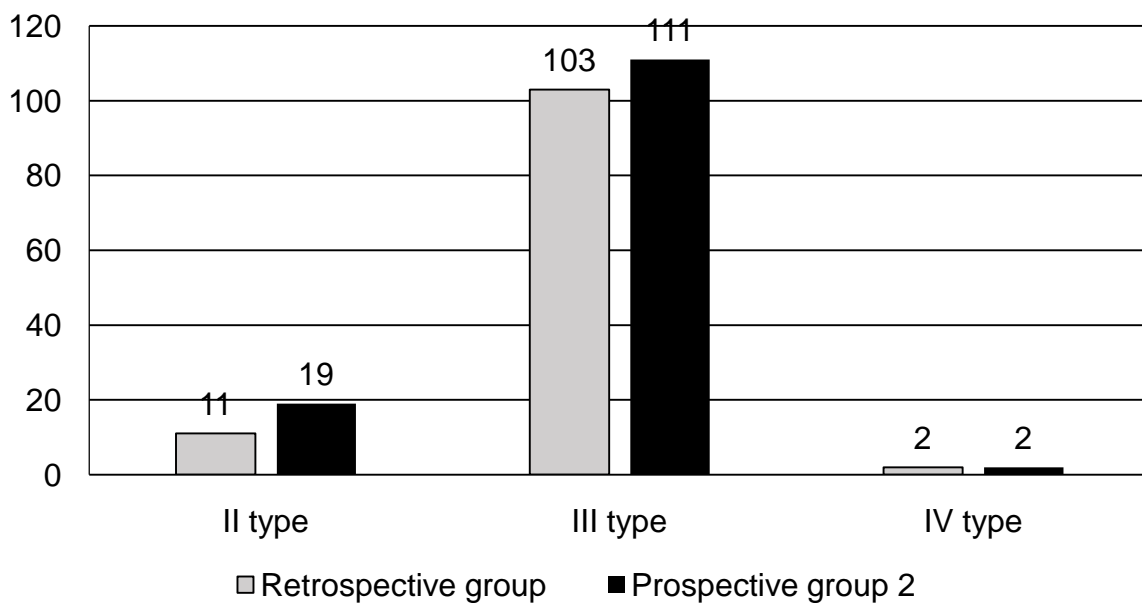


Figure 2: Number of Patients in the Retrospective and Prospective Groups with Studied Long-Term Treatment Outcomes

The analysis of the treatment results included the evaluation of clinical symptoms, as well as upper digestive tract X-ray data studies with BaSO₄, and esophago gastroduodenoscopy.

A good or satisfactory long-term treatment outcome was found in 85 (73.7%) of 116 patients in the retrospective group and 117 (88.6%) of 132 in the prospective group. Unsatisfactory - in 31 (26.7%) and 15 (11.4%), respectively (Table 5).

The result was considered good in the absence of clinical symptoms of hiatal hernia, manifestations of gastroesophageal reflux and erosive gastritis, as well as the preservation of anatomical relationships established during surgery between the esophagus, stomach, and diaphragm. A satisfactory outcome was the absence of clinical and endoscopic manifestations of the disease, despite radiological signs of minimal displacement of the stomach into the thoracic cavity. The unsatisfactory results included clinical and anatomical recurrence of diaphragmatic hernia.

Table 5: Results of Treatment of Patients in the Retrospective and Prospective Groups

Type of Hiatal Hernia	Number of Patients, Absolutely . (%)	
	Good or Satisfactory	Unsatisfactory
Retrospective group Hernias (type II)	9 (81,8%)	2 (18,2%)
Prospective group Hernias (type II)	17 (89,5%)	2 (10,5%)
Retrospective group Hernias (type III)	74 (71,8%)	29 (28,2%)
Prospective group Hernias (type III)	98 (88,3%)	13 (11,7%)
Retrospective group Hernias (type IV)	2 (100%)	-
Prospective group Hernias (type IV)	2 (100%)	-

The differences were statistically significant.

IV. DISCUSSION

Surgical treatment of hiatal hernias of types II-IV, according to most experts, remains a separate and far from being solved problem of practical medicine. [1, 4, 6, 7, 9].

The main reasons for the high frequency of unsatisfactory surgical results in this type of hernia are two anatomical factors: shortening of the esophagus and the large size of the hiatal opening. Additional physiological effects include propulsive contractions of the digestive tract, of which the esophagus is a part, and respiratory excursions of the diaphragm, leading to a displacement of the organs relative to each other. [1, 2, 3, 4,10].

Unfortunately, the current level of knowledge and technical capabilities does not allow us to overcome these factors conceptually, and the search for ways to reduce the recurrence rate of type II-IV hiatal hernias after surgical treatment, as in many other areas of practical medicine, is still developing along the path of finding reasonable compromises [1, 4, 6, 7, 9].

The conducted research reflects this approach and illustrates its effectiveness. The desire to maximize the restoration of natural visceral anatomy, as realized in patients of the retrospective group, enabled very average treatment results consistent with the literature. On the contrary, the perception of certain factors, primarily the shortening of the esophagus, as

objective conditions with the transformation of surgical tactics makes it possible to achieve significantly better results. A good or satisfactory treatment result in patients of the retrospective group was achieved in 73.7% of cases, and a poor result in 26.7%. In patients of the prospective group – in 88.6% and 11.4%, respectively.

Significant differences in treatment outcomes in the retrospective and prospective groups were achieved with mixed (type III) hiatal hernias. It is with this type of disease that a decrease in the length of the esophagus often occurs. Unfortunately, its high mobilization, contrary to the available evidence, as shown by the analysis of surgical interventions in patients of the retrospective group, is not always effective in preventing the recurrence of hiatal hernias. Disease recurrence in the retrospective group was detected in 28.2% of cases.

The formation of a fundoplication cuff in the mediastinum in such situations, as recommended by some researchers, turned out to be a simple and fairly reliable technical procedure that gives a good long-term functional result. The frequency of unsatisfactory outcomes of surgical interventions in patients of the prospective group was 11.7%. An additional confirmation of the leading role of esophageal shortening in the recurrence of type III hiatal hernias is the multiple times more frequent use of prostheses to strengthen the plastic of the hiatal opening in

patients of the retrospective group, compared with the prospective group (124 cases versus 19), with much more modest long-term results [2, 5, 11]. On the contrary, with a normal length of the esophagus (hernias of types II and IV, sometimes type III), the use of polymer implants should be considered an important option to increase the reliability of reconstruction, since in such situations the key cause of disease recurrence is the leading one. This opinion is supported by some experts, and the comparable treatment results obtained in the study in patients of the retrospective and prospective groups allow us to consider it justified (recurrence of 18.2% and 10.5%, respectively) [2, 5, 11].

A sufficiently large number of observations (173 people in the retrospective and prospective groups) and a long time to evaluate long-term results (from two to five years in both groups) in this study allows us to consider the use of prostheses to safely correct the size of the diaphragm's food-water opening. There are no undesirable consequences associated with the use of this technology. The indications in the literature of a high incidence of complications have not been confirmed [1, 2, 3, 4, 10].

V. CONCLUSIONS

1. Surgical treatment of hiatal hernias of types II-IV remains far from solving the problem of practical medicine. The disease recurrence rate exceeds 10%.
2. When the esophagus is shortened in type III hernias, its high mobilization does not reliably prevent the stomach from moving back into the chest.
3. The use of prosthetics to correct the hiatal opening during esophageal shortening is an ineffective way to prevent recurrence of the disease.
4. The optimal surgical treatment of hernias includes the following conclusions based on a comparative study: the formation of a fundoplication cuff in the mediastinum with shortening of the esophagus should be considered an effective way to prevent recurrence of hiatal hernia;
5. In cases of hernias of types II-IV and normal esophageal length, the use of prosthetic materials to correct the size of the hiatal opening is reasonable, and reduces the frequency of unsatisfactory treatment results.

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Between Vocation and Burnout: Working Conditions, Training, and Career Prospects for Cardiologists in Argentina

Diego S. Novielli, Horacio Pomes Iparraguirre, Fernando J. Sokn, Ruben Kevorkian, Carlos Rapallo, Alberto Caccavo, Anibal Picrell, Nestor Pérez Baliño, Osvaldo H. Masoli & Jorge E. Tronge

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ABSTRACT

Introduction: The practice of cardiology in fragmented healthcare systems faces increasing structural pressures related to heavy workloads, inadequate compensation, and limited professional recognition. These factors negatively affect physician well-being, contribute to burnout, and pose challenges to workforce sustainability. In parallel, demographic changes characterized by the aging specialist population and the reduced influx of young physicians are generating concern regarding the future availability of qualified cardiovascular professionals.

Objective: The aim of this study was to evaluate cardiologists' perceptions of working conditions, income satisfaction, professional recognition, training pathways, and future career expectations, as well as to explore their association with demographic and occupational characteristics.

Keywords: cardiology. healthcare workforce. working conditions. professional burnout. health policy.

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Between Vocation and Burnout: Working Conditions, Training, and Career Prospects for Cardiologists in Argentina

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Objective: The aim of this study was to evaluate cardiologists' perceptions of working conditions, income satisfaction, professional recognition, training pathways, and future career expectations, as well as to explore their association with demographic and occupational characteristics.

Methods: An observational, analytical, cross-sectional study was conducted using an anonymous, self-administered survey distributed nationwide between June and September 2023. The questionnaire, validated by an institutional ethics committee, consisted of 16 items grouped into three domains: relationship with scientific societies, professional recognition, working conditions, and continuing medical education. Demographic and occupational variables were also collected. Data analysis was performed with descriptive statistics and Pearson or Spearman correlation coefficient analysis, as appropriate, using Python 3.1.

Results: A total of 404 responses were analyzed, predominantly from more experienced cardiologists, reflecting an aging workforce. Younger professionals reported a heavier weekly workload, with a significant inverse correlation observed between age and hours worked ($r = -0.41$). Economic dissatisfaction was highly prevalent: over 70% of respondents expressed dissatisfaction with their income, and 95% felt that their remuneration did not adequately reflect their workload. Nearly half anticipated a worse economic situation within the next five years. Satisfaction with current income showed a positive correlation with future economic expectations ($r = 0.23$). Medical residency remained the preferred training pathway, while support for professional recertification was moderate and positively associated with greater economic satisfaction.

Conclusions: The practice of cardiology in fragmented healthcare systems is characterized by excessive workload, widespread economic dissatisfaction, and unfavorable future prospects, particularly among younger professionals. These conditions contribute to professional burnout and threaten workforce retention and generational renewal. It is essential to implement comprehensive health policies that address remuneration models, professional recognition, training structures, and physician well-being to ensure long-term sustainability of cardiovascular care in diverse healthcare settings.

Keywords: cardiology. healthcare workforce. working conditions. professional burnout. health policy.

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I. INTRODUCTION

Argentine cardiology is going through a critical period characterized by profound structural tensions, resulting from the interaction of demographic, economic, labor, and organizational factors. Within a historically fragmented healthcare system (1) (comprising public, social security, and private subsystems), there are coexisting heterogeneous care models that differ substantially in resource availability, financing schemes, and professional employment conditions. This fragmentation generates inequities in access to care, discontinuities in care processes, and increasing pressure on specialized human resources, particularly cardiologists, key players in the care of cardiovascular diseases, the leading cause of morbidity and mortality in Argentina.

Over the last decade, various reports from different scientific societies (2,3) have pointed to a progressive deterioration of working conditions in cardiology, evidenced by loss of purchasing power, the precariousness of contractual

relationships, and the increase in multiple job-holding. These are associated with higher levels of professional burnout, job dissatisfaction, and burnout syndrome, compromising the well-being of professionals, patients, and the sustainability of the healthcare system.

In parallel, there is sustained aging of the cardiology workforce and a lower rate of new generations entering the specialty, (4,5) a phenomenon that poses medium-and long-term risks. In this context, it is essential to systematically analyze cardiologists' perceptions of their work, economic, and educational realities, with the aim of generating evidence to guide healthcare policies for planning and holding human resources, and strengthening cardiovascular care in the country. (6)

II. METHODS

An observational, analytical, and cross-sectional study was conducted to evaluate different dimensions of cardiologists' professional practice in Argentina.

The study population consisted of cardiologists and cardiology residents who voluntarily completed an anonymous survey between June and September 2023. The questionnaire was self-administered and distributed via the Argentine Society of Cardiology (SAC) institutional email, as well as through social media and instant messaging channels (WhatsApp). Data collection was performed using the REDCap platform, in accordance with the SAC institutional recommendations.

A structured questionnaire, validated by the SAC Ethics and Research Committee, was used. It comprised 16 items organized into three domains:

1. Cardiologist relationship with the Scientific Society (5 questions),
2. Quality and professional recognition of cardiological practice (7 questions), and
3. Continuing medical education (4 questions).

Most questions used five-point Likert-type ordinal response scales (7). Additionally, demographic variables (age, gender) and employment variables

(weekly workload, perceived income) were collected to explore their association with the different domains evaluated.

Data analysis was performed using Python version 3.1. Qualitative variables were expressed as absolute frequencies and percentages, while quantitative variables were described using mean and standard deviation. Pearson or Spearman correlation coefficients were used to assess associations and correlations between variables, depending on the distribution and nature of the data.

The survey is available at the following link: <http://redcap.sac.org.ar/redcap/surveys/?s=HEWTKTPEKR978KJF>.

III. RESULTS

A total of 404 responses were recorded. The study population consisted of 398 (95%) cardiologists and 60 (14.9%) cardiology residents. Among the total number of respondents, 141 (34.9%) were female. Mean age was 54.6 ± 12.6 years. Nearly three-quarters of respondents (307, 76%) had more than 10 years of experience, and only 45 (11.1%) had up to 5 years, reinforcing the hypothesis of sustained aging of the specialized human resource. See Table 1.

Nearly half of respondents (195, 48.3%) practiced in metropolitan areas, reflecting a concentration of supply and resources, while peripheral regions remained underrepresented in this survey. Regarding the professional practice setting, the private sector accounted for the majority of professional activity ($\approx 68\%$), with residency programs being relevant but not universal (49.3% of centers offered cardiology residency). The majority of cardiologists (424, 105%) considered that the scope of care should focus on primary (prevention and promotion of cardiovascular health) and secondary (diagnosis and treatment of cardiovascular diseases) care. It should be noted that this question allowed for multiple responses, and only 36 (9%) replied that they should work exclusively in critical care areas. And although slightly more than half (209, 51.7%) were not part of a myocardial infarction care network, it was

observed that over 96% agreed with promoting such networks.

The economic satisfaction analyses revealed a strikingly homogeneous phenomenon: 285 (70.5%) respondents expressed dissatisfaction with their income, and approximately 384 (95%) disagreed with the statement that remuneration adequately reflects the amount of work performed. The population surveyed showed an average of 40 hours/week, with no significant differences in reported hours between women (42.2 hours/week) vs. 40.5 hours/week for men. The majority of respondents worked between 30 and 60 hours per week (approximately 65%), but a subgroup of at least 28 physicians (7%) worked more than 60 hours per week, with younger cardiologists exhibiting the highest working hours. This pattern was particularly evident in the boxplot of hours worked by age group (Figure 1). Almost half of the cardiologists surveyed (178, 44.8%) believed their economic situation will worsen in the next five years, and only one in fifteen (26, 6.5%) anticipated an improvement. Both women and men showed a high level of dissatisfaction. The assessment of adequate social and professional representation revealed that 377 respondents (93.3%) thought that cardiologists were underrepresented. See Table 2.

In relation to academic training, residency was considered the gold standard choice (363, 94%) with the current classic system consisting of one year of internal medicine plus three years of cardiology (260, 65.3%) while the choice of a post-basic system was relegated to 5 responses (1.3%). Concerning certification, only half of cardiologists (216, 54%) fully supported recertification, and 1 in 5 (21.6%) were against it. It could be interpreted that, in the case of income satisfaction and recertification, economic dissatisfaction was associated with greater rejection of recertification, but it predominated at all professional levels dissatisfied with their income. (Figure 2).

IV. DISCUSSION

The results of the study reveal a complex and multifactorial network that affects the

professional well-being of Argentine cardiologists. The structural element underlying most of these findings is the disconnection between workload and remuneration conditions in a fragmented healthcare system that forces professionals, especially younger ones, to hold multiple jobs in order to earn a reasonable income.

The association between age and working hours shows a significant negative correlation ($r = -0.41$), which expresses how increasing age is accompanied by a progressive decrease in weekly hours. This finding is not circumstantial, but rather reflects the way cardiology practice is structured in Argentina, where young professionals must have multiple jobs to achieve minimum income levels in a fragmented and outdated compensation system. (8,9) The correlation empirically supports a perception already documented in qualitative studies: working more does not improve the subjective sense of well-being. (10) This is also linked to the theory of physician burnout, which indicates that the uncoupling between effort and reward is one of the strongest predictors of emotional exhaustion and the idea to migrate or abandon clinical practice. In CONAREC's work (Argentine Council of Cardiology Residents), (11) 35% of residents met positive criteria for burnout, and a more recent survey of SAC cardiologists, including all ages, revealed that professionals under 40 and/or with less than 10 years in the specialty have significantly more burnout than their older colleagues: approximately 50% of those under 40 reported burnout vs. 28% of those over 40. (12) This situation, accompanied by the virtually unanimous perception of wage injustice, operates as a central determinant of professional discontent and is closely related to expectations. (13) In contrast, Argentine physicians of all ages continue to prefer residency as the best training system, despite its slow economic development due to the type of contract, salary and mainly the time that must be prioritized for study. (14,15)

In this regard, the correlation analysis between present satisfaction with income and future economic expectations showed a moderate positive coefficient ($r = 0.23$), indicating that present economic perceptions strongly influence

subjective projections of career development. Those who are currently more dissatisfied tend to anticipate deterioration in the next five years, a finding that has been observed in previous studies of the 2015 SAC policies area. (16) It is well known that this increases the risk of doctors leaving for countries with more favorable conditions, which hinders the possibility of structural reorganization of the medical system.

Another critical element of the study is the relationship between acceptance of recertification and economic satisfaction. The positive correlation found ($r = 0.13$) suggests that recertification, understood as a process of professional recognition, is more highly valued by those who perceive their economic situation as relatively more stable, which are mostly those with more than 20 years of cardiology practice. This relationship is important for the design of professional policies, as it shows that the legitimacy of recertification mechanisms depends in part on the professional's economic context.

V. CONCLUSIONS

The results of this national survey reveal a complex and worrying prospect regarding the professional practice of cardiology in Argentina. Quantitative evidence shows a consistent pattern: the profession operates in a context of excessive workload, widespread financial dissatisfaction, and predominantly negative perspectives regarding future income growth. (17) There is clear evidence that younger cardiologists work longer hours, often as a result of the need to hold multiple jobs to compensate for the frailty of the remuneration system. However, this intensification of work is not associated with an improvement in economic perception, which reinforces the feeling of structural devaluation and increases the risk of emotional burnout. Evidence of economic dissatisfaction directly affects the subjective projection of the profession, generating a vicious circle in which present precariousness fuels future pessimism. (18) This phenomenon, widely documented in healthcare environments in crisis, constitutes a vulnerability factor for the retention of specialists and the

incorporation of new professionals into the discipline.

At the same time, the relationship between acceptance of recertification and economic satisfaction shows that professional evaluation and updating processes cannot be considered in isolation from the work context. Where financial and symbolic recognition is insufficient, recertification runs the risk of being interpreted as an additional requirement with no actual benefit. These conclusions suggest that any recertification policy must be accompanied by professional development strategies, wage improvements and institutional support mechanisms, given that these are not currently required in healthcare institutions.

Another key finding is the aging of the cardiology workforce. The low representation of young professionals, coupled with their heavy workload and lower financial satisfaction, projects a scenario of risk for the future availability of specialists, particularly in regions with lower

jobs, devaluation, and lack of prospects may lead to an increase in medical emigration or a shift toward non-healthcare activities, thus deepening the generational gap.

Overall, the results of this survey highlight the urgent need to reconsider the conditions of professional practice in cardiology in Argentina. The implementation of fee reforms, the strengthening of union representation, the development of integrated healthcare networks, the expansion of quality training programs, and the establishment of professional welfare mechanisms are essential measures to ensure the sustainability of the specialty. Similarly, it is essential to generate active policies that encourage the entry and retention of young cardiologists, ensuring adequate generational turnover and equitable distribution of human resources throughout the country. This study is a valuable contribution to the design of such policies and to the construction of a more just, efficient, and humane healthcare system.

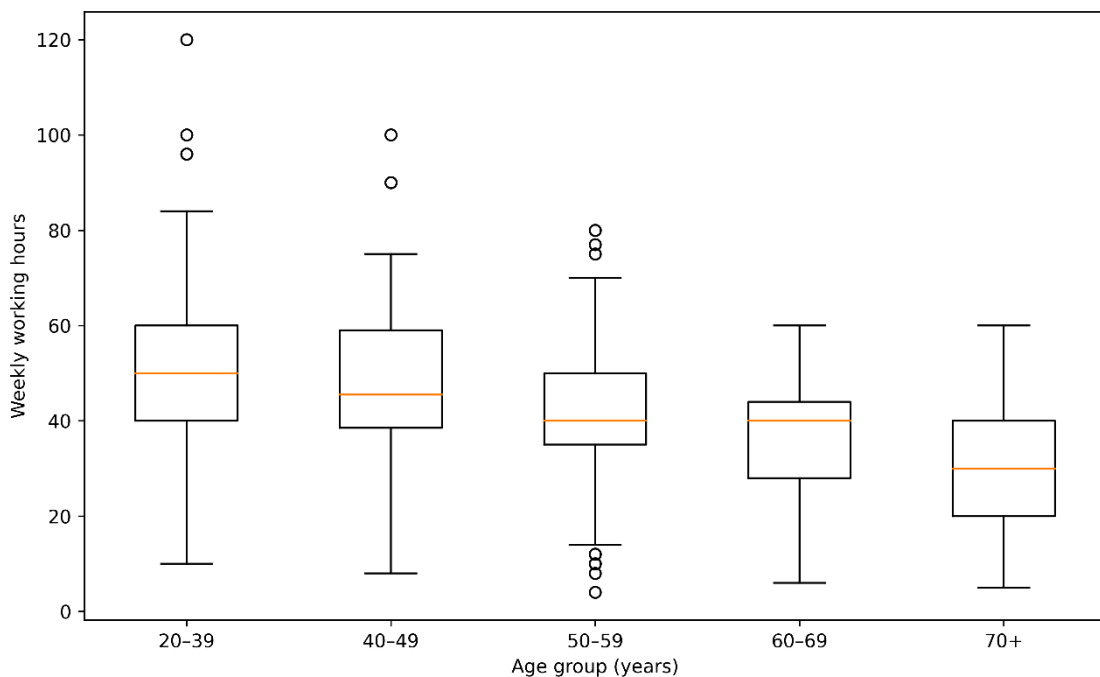


Figure 1: Boxplot of weekly hours per age group

Description: Professionals between 20–39 years of age present the highest workloads (median 50 h/week).

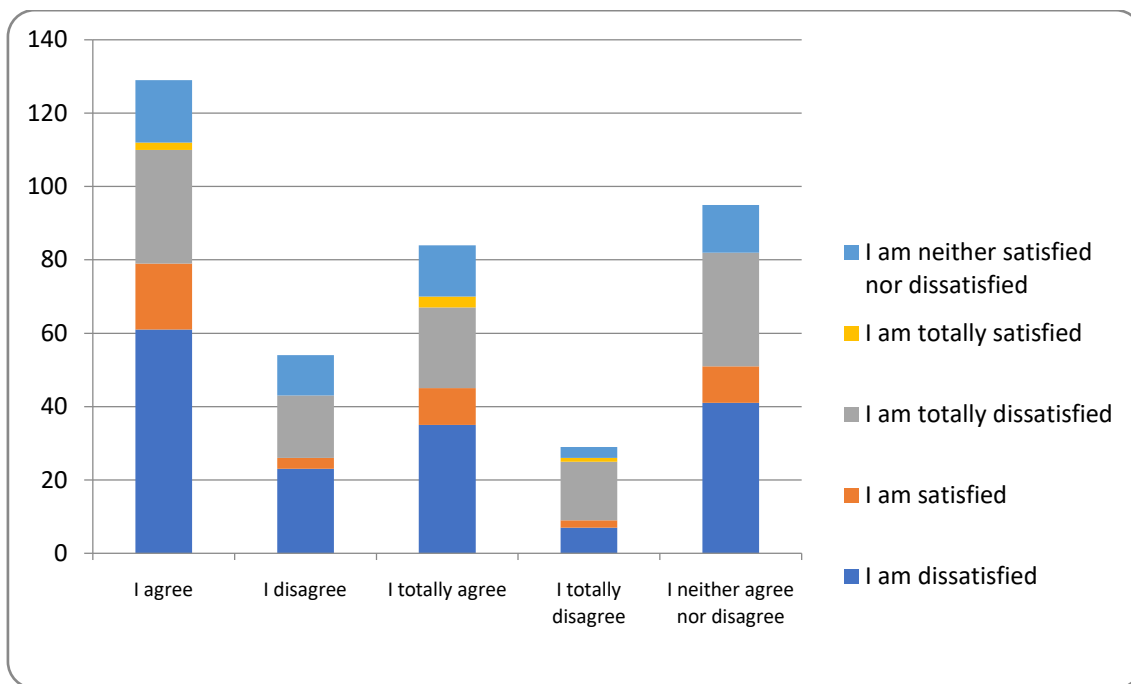


Figure 2: Relationship between certification and economic satisfaction

Description: Professionals who recertify are more economically satisfied.

Table 1: Demographic and working characteristics of the surveyed population

Variable	Result
Total number of surveyed cardiologists	404
Age, years (mean ± SD)	54.6 ± 12.6
Age group	
≤ 40 years	81 (20.0%)
> 40 years	323 (80.0%)
Gender	
Male	261 (64.6%)
Female	141 (34.9%)
Years of cardiology practice	
≤ 5 years	45 (11.1%)
6–10 years	52 (12.9%)
11–15 years	50 (12.4%)
16–20 years	67 (16.6%)
> 20 years	190 (47.0%)
Cardiologist in training	
Yes	20 (5%)
No	398 (95%)
Predominant working sector	
Public institution	132 (32.7%)
Private institution	119 (29.5%)
Mixed	153 (37.9%)
Geographical region of cardiology practice	
CABA	92 (22.8%)
Greater Buenos Aires	103 (25.5%)
Province of Buenos Aires	76 (18.8%)

Variable	Result
ANW	43 (10.6%)
ANE	28 (6.9%)
Cuyo Region	25 (6.2%)
Central Region	19 (4.7%)
Patagonia	18 (4.5%)
Working hours per week (mean ± SD)	40.9 ± 17.4

ANW: Argentine North Western Region; ANE: Argentine North Eastern Region

Table 1: Demographic and working characteristics of the surveyed cardiologists. The data are expressed as numbers and percentages or mean ± standard deviation, as appropriate.

Table 2: Perception of professional recognition, economic conditions and future expectations

Variable	Results
Perception of remuneration according to workload	
Agree / totally agree	8 (2.0%)
Neither agree nor disagree	7 (1.7%)
In disagreement / totally in disagreement	384 (95.0%)
Did not repond	5 (1.23%)
Level of income satisfaction	
Satisfied / totally satisfied	49 (12.1%)
Neutral	59 (14.6%)
Dissatisfied / totally dissatisfied	285 (70.5%)
Did not respond	11 (2.7%)
Expectation of future economic development	
It will improve	29 (7.2%)
It will be similar	98 (24.3%)
It will be worse	224 (55.4%)
Undefined	53 (1.1%)
Perception of economic, social and union representation	
Adequate	32 (7.9%)
Inadequate	318 (78.7%)
Does not know	54 (13.4%)

Table 2: Perception of professional recognition, economic conditions and future expectations of surveyed cardiologists. Results are expressed as numbers and percentages.

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"Bilateral Mastoiditis Complicated by Unilateral Zygomaticitis – Rare form, Challenging Diagnosis"

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ABSTRACT

Introduction: Bilateral mastoiditis complicated by unilateral zygomaticitis is an exceptional clinical entity, rarely described in the literature. Although the incidence of complications of acute otitis media has decreased significantly with the introduction of modern antibiotic therapy, atypical forms of bone extension remain a diagnostic challenge. The association of bilateral mastoid involvement with zygomatic bone involvement can cause a non-specific clinical picture, delaying diagnosis and the establishment of appropriate treatment.

Materials and Methods: In this case study we present a 41-year-old male patient who suffered bilateral mastoiditis complicated by unilateral zygomaticitis following a chronic rhinosinusal pathology in exacerbation. He presented with accusations of: pronounced headache, bilateral otodynia, suppurative otorhea, swelling in the projection of the zygomatic bone on the left, bilateral hearing loss. The patient underwent bilateral petromastoid clearance surgery with incision and drainage of the zygomatic collection on the left.

Keywords: mastoiditis, otorhea, zygomaticitis, hearing loss.

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Introduction: Bilateral mastoiditis complicated by unilateral zygomaticitis is an exceptional clinical entity, rarely described in the literature. Although the incidence of complications of acute otitis media has decreased significantly with the introduction of modern antibiotic therapy, atypical forms of bone extension remain a diagnostic challenge. The association of bilateral mastoid involvement with zygomatic bone involvement can cause a non-specific clinical picture, delaying diagnosis and the establishment of appropriate treatment.

Materials and Methods: In this case study we present a 41-year-old male patient who suffered bilateral mastoiditis complicated by unilateral zygomaticitis following a chronic rhinosinusal pathology in exacerbation. He presented with accusations of: pronounced headache, bilateral otodynia, suppurative otorrhea, swelling in the projection of the zygomatic bone on the left, bilateral hearing loss. The patient underwent bilateral petromastoid clearance surgery with incision and drainage of the zygomatic collection on the left.

Results: Epidemiological data from the literature indicate that acute mastoiditis in adults accounts for approximately 10–15% of all mastoiditis cases. The overall incidence is estimated at less than 0.5 cases per 100,000 adults annually in countries with access to modern health services. Although antibiotic therapy has dramatically reduced mortality associated with mastoiditis (from 20–30% in the pre-antibiotic era to less than 1% today), it remains a pathology with a significant risk of extracranial complications (subperiosteal abscess, apical-cervical mastoiditis, petrositis) and endocranial complications (meningitis, lateral sinus thrombosis, brain abscess). Although less

common, acute mastoiditis remains a pathology of current interest, with a significant impact on public health, requiring a multidisciplinary and updated approach to the new infectious challenges. We present a rare case of such an otic pathology in a 41-year-old male patient who suffered bilateral mastoiditis complicated by unilateral zygomaticitis as a result of enduring a chronic acute rhinosinusal pathology.

Conclusions: Acute mastoiditis, although rare in the age of antibiotics, continues to be an otological emergency, with significant potential for endocranial and extracranial complications, especially in cases not properly treated.

Keywords: mastoiditis, otorrhea, zygomaticitis, hearing loss.

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I. INTRODUCTION

Acute mastoiditis is one of the most common complications of acute otitis media, resulting from the spread of the infection to the mastoid cell system. Although predominantly affecting the pediatric population, adult cases account for approximately 10–15% of all reported cases of mastoiditis and present a distinct clinical profile [1, 2]. In countries with modern health systems, the overall incidence of acute mastoiditis has decreased significantly and is currently estimated at less than 0.5 cases per 100,000 adults per year, largely due to early diagnosis, widespread use of antibiotics, and vaccination programs [2, 3].

The introduction of antibiotic therapy has dramatically reduced mortality associated with mastoiditis, from 20–30% in the pre-antibiotic

era to less than 1% in contemporary clinical practice [1, 4]. However, acute mastoiditis remains a potentially serious condition with a significant risk of endocranial and extracranial complications. These include the formation of subperiosteal abscesses, cortical bone erosion, petrositis, thrombosis of the lateral venous sinus, meningitis, and intracranial abscesses [4, 5]. Given its rarity in adults and the possibility of an atypical presentation, acute mastoiditis continues to represent a diagnostic and therapeutic challenge, requiring prompt recognition and a multidisciplinary approach in management [1, 5].

From a contemporary otological perspective, atypical forms of mastoiditis are classified based on the topographic extension of the infectious process and the affected bone structures, each subtype presenting characteristic clinical manifestations and a specific profile of complications, which requires a differentiated diagnostic and therapeutic approach.

Zygomatocitis (zygomatic mastoiditis)- is an unusual spread of the suppurative process from the mastoid to the zygomatic process of the temporal bone. This type occurs when mastoid pneumatization extends anteriorly to the zygomatic root, allowing the infection to infiltrate the spaces near the zygomatic bone and the retroauricular subcutaneous tissue.

Affected Region- Zygomatic process and adjacent tissues of the temporal bone, preauricular and zygomatic region.

Clinical Manifestations- Edema and pain in the temporal-zygomatic region, preauricular or facial swelling, displacement of the pinna of the ear in the antero-inferior, hyperemia and possible palpable fluctuation. The diagnosis is confirmed clinically and by imaging (CT).

Complications- Abscess formation, tissue necrosis, bone erosion and extension of the suppurative process to the facial region, possibly mimicking other entities (e.g., parotitis). Surgically, the approach can be complex due to extracranial extension [6].

Squamitis (Squamous Mastoiditis)- The purulent-necrotic form in which the infection

spreads from the mastoid cell system to the squamous portion of the temporal bone. This can lead to destructive osteomyelitis located in the lateral region of the temporal bone.

Affected Region- The temporal bone scale, representing the external and lateral portion of the temporal bone above the external auditory canal.

Clinical Manifestations- Intense localized pain in the temporal region, edema and tenderness to palpation, possible local hyperthermia. The diagnosis is based on imaging (CT/MRI) which indicates extensive bone destruction.

Complications – Progressive bone erosion, deep infection and increased risk of intracranial or extracranial extension, requiring aggressive surgical approach [7, 8].

Petrositis Ppetrosal Mastoiditis/Gradenigo- petrositis is the purulentnecrotic infection of the apex of the petrous portion of the temporal bone, traditionally associated with the Gradenigo triad: *acute otitis media, trigeminal retroorbital pain and paresis of the abducens nerve (VI)*. This form represents the medial extension of the infectious process from the mastoid bone to the bony apex.

Affected Region- The petrous apex of the temporal bone, deep region of the base of the skull. *Clinical manifestations* – periorbital or retro-orbital pain, diplopia or paresis of the abducens nerve, persistent otorrhea, fever and otalgia. Neurological signs may precede the obvious signs of mastoiditis.

Complications- Increased risk of thrombosis of the lateral venous sinus, meningitis, intracranial abscesses (epidural, subdural, cerebral), and other cranial neuropathies [7, 8].

Cervical Apical Mastoiditis- (Bezold Abscess)- cervical apical mastoiditis-is an externalized form of mastoiditis in which purulent exudate extends from the tip of the mastoid process into the cervical plane, between the deep muscle planes, below the sternocleidomastoid muscle (Bezold abscess and similar variations).

Affected Region- The area of the mastoid tip and the deep cervical muscle spaces (under the

sternocleidomastoid muscle, parotid or in the parapharyngeal space).

Clinical Manifestations- Edema and pain in the upper cervical region, limitation of neck mobility, fluctuating subcutaneous swelling, stiffness of the cervical muscles, possible fever. Imaging can reveal purulent accumulations under the muscles.

Complications– Deep cervicofacial abscesses, skin fistulas, local sepsis, risk of extension to the parapharyngeal space or mediastinum, as well as systemic complications if treatment is delayed [9].

Although, in the age of antibiotics, the incidence of mastoiditis has decreased significantly, severe and complicated forms continue to be encountered, especially in the context of delayed or inadequate treatment. Bilateral mastoiditis is a rare and severe pathology, indicating an extensive infectious process, with an increased potential for endocranial and extracranial complications.

Zygomatocitis is a rare bone complication of mastoiditis, characterized by the propagation of the infectious process at the level of the zygomatic bone, through pneumatic cells or pathways of anatomical continuity. The occurrence of unilateral zygomatocitis in the context of bilateral mastoiditis underlines the unpredictability of the dissemination of infection and requires thorough clinical and imaging evaluation. This pathological association is particularly important from a diagnostic and therapeutic point of view, as it can mimic other inflammatory or tumoral conditions of the facial region.

Early recognition of complicated mastoiditis, as well as understanding the mechanisms of infection spreading to neighboring bone structures, are essential for instituting appropriate treatment and preventing intracranial and extracranial complications. In this context, this article aims to address the issues related to classification, pathogenic mechanisms and the importance of the correct diagnosis of bilateral mastoiditis complicated by unilateral zygomatocitis.

II. MATERIALS AND METHODS

In this case study we present a 41-year-old male patient who suffered bilateral mastoiditis complicated by unilateral zygomatocitis following a chronic rhinosinusal pathology in exacerbation. The patient presented with complaints of: pronounced headache, bilateral otodynia, vertigo, suppurative otorrhea, swelling in the projection of the zygomatic bone on the left, bilateral hearing loss, general weakness.



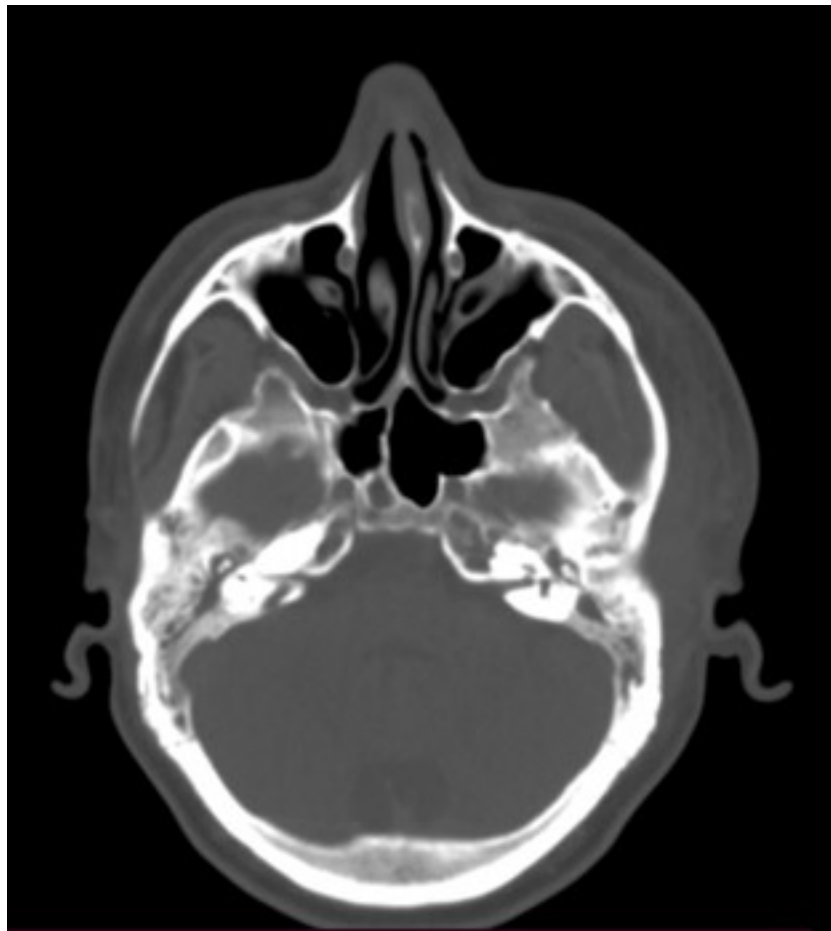
Figure 1: Clinical image (a, b)

The patient considers himself ill for about 3-4 weeks, when he presented the symptoms of a chronic rhinosinusal pathology in exacerbation, after a few days the rhinosinusal symptoms subsided, but pronounced headache, vertigo, bilateral progressive otodynia began, which was followed by abundant right ear otorhea, insignificant in US, and postural instability. The patient did not go to the doctor. He administered topical outpatient treatment with pic. Floxadex, the condition with worsening in dynamics. For about 2 days, swelling and hyperimia have been installed in the projection of the zygomatic bone on the left. He called the 112 service, the patient was redirected to IMSP SCR "T.Moşneaga", for the consultation of the ENT doctor and specialized treatment.

Otoscopically, narrowed UD – CAE was highlighted, abundant suppurated eliminations, at

aspiration of which the detachment of the posterior wall was highlighted, visible pulsation, TM is not visualized; US – narrowed, hyperemic CAE, MT is not visualized, the detachment of the posterior wall was highlighted. The suppurated eliminations were collected for bacteriological examination.

When performing computed tomography of the temporal bones (middle and inner ear), the mastoid cells and the bilateral tympanic house were totally opaque, the ossicular chain preserved, the intercellular septa preserved, bone defect in the squamous region of the temporal bone on the left, thickening of the tissues in the zygomatic region on the left, diffuse hypodense opacity of the subcutaneous layer with the deletion of the normal planes. (Figures 2, 3).



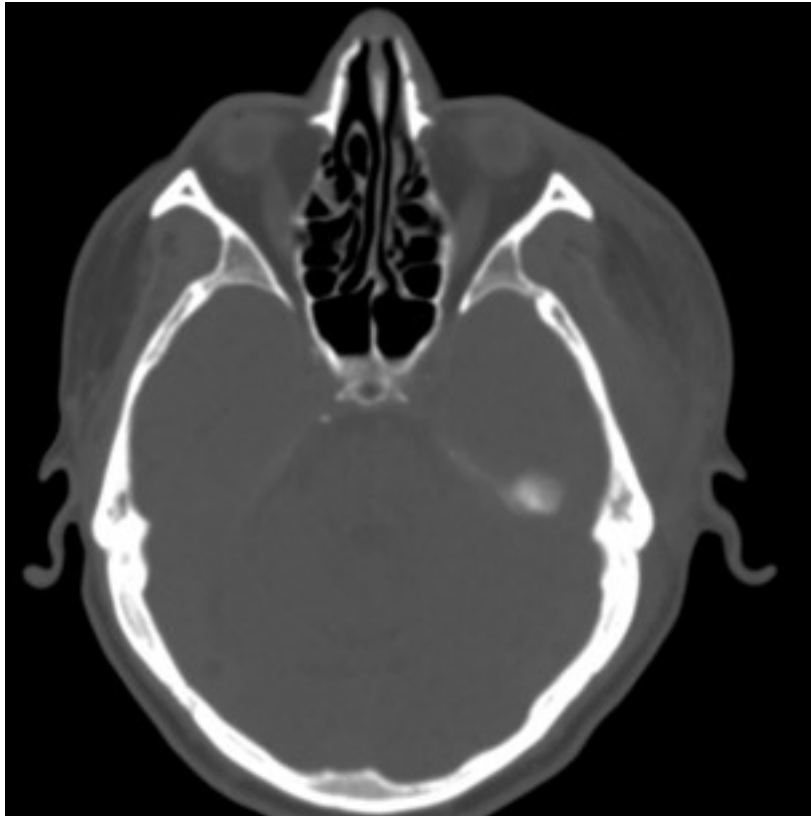


Figure 2 (a, b): Computed tomography of the temporal bones (middle and inner ear)





Figure 3 (a, b): Image in 3D reconstruction. Bone defect in the squamous region of the temporal bone on the left

Subsequently, the patient was evaluated by the neurologist, excluding intracranial complications, after which the consilium was carried out jointly with the head of the ENT department, the head of the department with the decision to intervene urgently, by performing bilateral petromastoid clearance surgery with incision and drainage of

the zygomatic collection on the left. Postoperatively, the patient was transferred to intensive care for monitoring, with the establishment of specific treatment - double antibiotic therapy according to the antibiogram, anti-inflammatory, corticosteroid, etc.



Figure 4: Intraoperative image-Incision and drainage of the zygomatic collection on the left

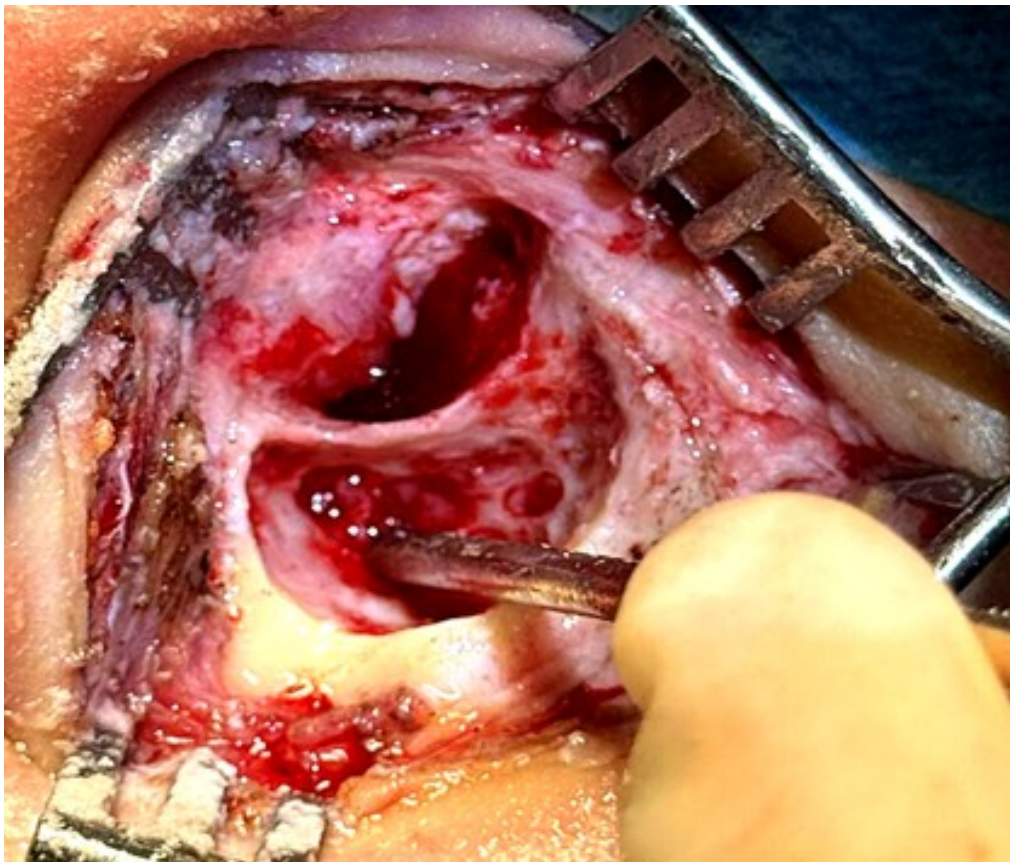
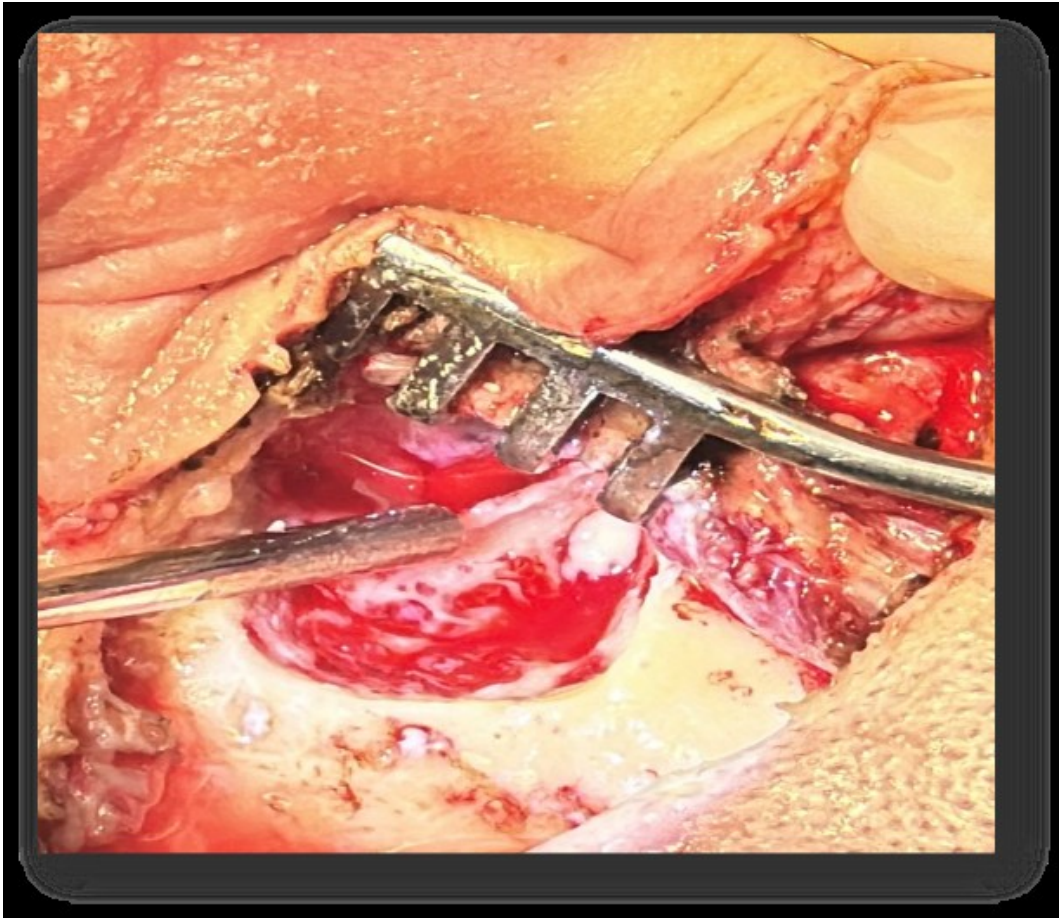


Figure 5 (a, b, c): Intraoperative (At the opening of the first cells - removal of purulent contents under pressure. At the opening of the antrum- polypoid inflammatory tissue).

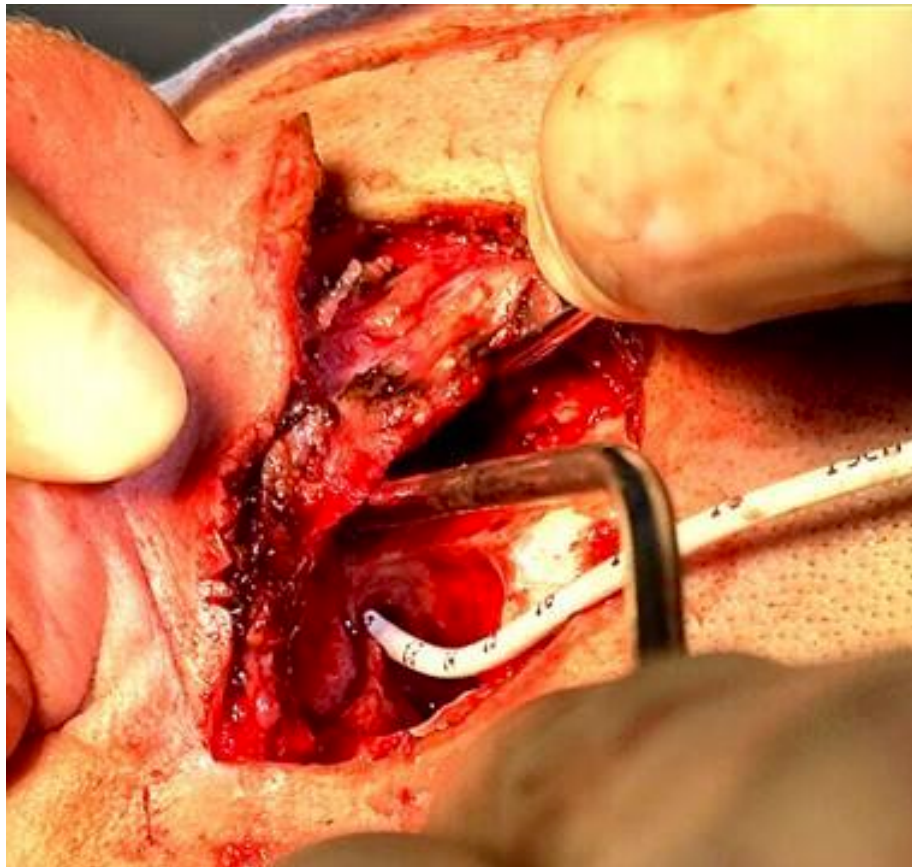


Figure 6 (a, b): Intraoperative (A defect of the bone wall was highlighted 0.5 cm above the antrum, with communication with the zygomatic and temporal region - a drainage tube was placed. The wound was kept open in order to avoid possible postoperative complications)



Bilateral Mastoiditis Complicated by Unilateral Zygomaticitis – Rare form, Challenging Diagnosis



Figure 7 (a, b, c): A 3-a zi postoperator

Daily aseptic dressing of the open wound was performed, with aspiration of the contents through the drainage tube, with subsequent wound washing. Subsequently, on the 7th day, secondary suturing of the retroauricular wound was performed.

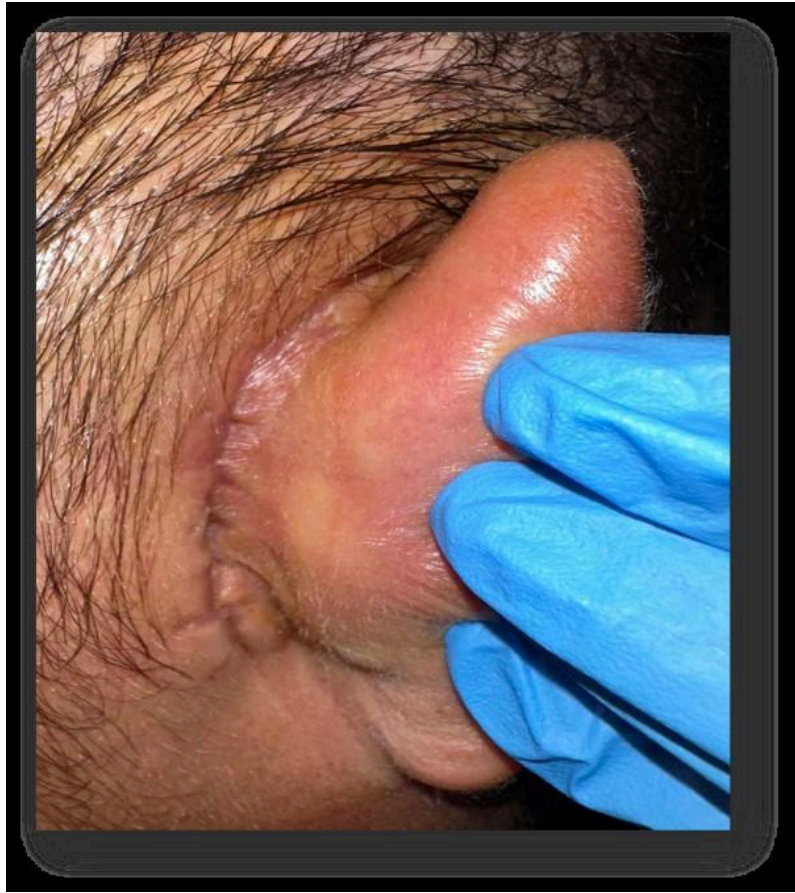




Figure 8 (a, b, c): O lună postoperator

III. DISCUSSION

Bilateral mastoiditis is an extremely rare condition, especially in adults, being most commonly seen as a complication of untreated acute otitis media. In the literature, cases of bilateral mastoiditis are reported sporadically, most of which are associated with compromised immunity, craniofacial malformations or persistent severe infections. Bilateral forms are considered challenging diagnoses due to the often non-specific symptomatology and initial subclinical evolution, which can delay early identification and appropriate treatment.

The complication of unilateral zygomaticitis, as observed in the case presented, is extremely rare and indicates the extension of the inflammatory process to the perimastoid and facial tissues. Zygomaticitis occurs as a result of the spread of

infection through continuity or through the cellular spaces of the face, which can lead to localized facial edema, pain and, in severe cases, risk of compromised nerve function or deep suppuration. This clinical peculiarity gives the diagnosis a high degree of difficulty, requiring a detailed imaging evaluation, preferably CT, to identify the extent of inflammation and any purulent collections.

From a microbiological point of view, bilateral mastoiditis and associated complications tend to be caused by resistant pathogens or polymicrobial infections, which requires the prompt initiation of broad-spectrum antibiotic treatment, subsequently adjusted according to the results of the cultures. Surgery, whether in the form of mastoidectomy or drainage of the zygomatic collections, remains an essential component in

the management of complicated cases, especially when there is a risk of dissemination to the deep or intracranial spaces.

The case presentation emphasizes the importance of maintaining a high degree of suspicion in the face of bilateral symptoms and signs of facial extension, even when the initial clinical signs are discreet. It also highlights the need for a multidisciplinary approach for optimal diagnosis and treatment.

In conclusion, bilateral mastoiditis complicated by unilateral zygomaticitis is a rare and provocative form of otological condition, with the potential for severe complications if not identified and treated early. Reporting these cases helps to raise clinical awareness and develop appropriate therapeutic strategies.

IV. CONCLUSIONS

1. Acute mastoiditis, although rare in the age of antibiotics, continues to be an otological emergency, with significant potential for endocranial and extracranial complications, especially in cases not properly treated.
2. Early diagnosis, based on thorough clinical evaluation and imaging investigations (CT, MRI), is essential to prevent complications and establish the indication for surgical treatment when necessary.
3. In the current context, marked by increased bacterial resistance and self-medication, atypical forms may become more and more frequent, requiring clinical vigilance and updating treatment protocols.
4. Interdisciplinary collaboration between ENT doctors, neurologists, imagingists, reanimatologists and surgeons is essential for the effective management of these complex cases.
5. Continuous medical education and correct information of patients about the complications of otitis media are essential steps in reducing the incidence of mastoiditis and its atypical forms.

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ABSTRACT

Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic vasculitis that predominantly affects small blood vessels and occurs in patients with asthma and tissue eosinophilia. The form associated with anti-neutrophil cytoplasmic antibodies (ANCA) is rarer. This case report presents a patient with late-onset asthma who initially presented with skin lesions (purpura), progressing to acute kidney injury, and subsequently diagnosed with glomerulonephritis. The difficulty and complexity of the clinical diagnosis and the importance of initiating appropriate and early therapy to minimize damage to target organs, improve prognosis, and avoid adverse effects motivated the presentation of this case and its literature review.

Palavras Chaves: churg- strauss, vasculite, eosinofilia, granulomatose eosinofílica com poliangiite.

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Diagnostic Challenges of Eosinophilic Granulomatosis with Polyangiitis: A Case Report

Desafios Diagnósticos Da Granulomatose Eosinofílica Com Poliangeíte:
Um Relato De Caso

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Gabriel Teixeira Junqueira^ϙ, Livia Tomazelli[¥], Mickaella Baldão Nechar^χ
& Tamires Carmo Cruz^v

RESUMO

A Granulomatose eosinofílica com poliangiíte (GEPA) é uma vasculite sistêmica que afeta predominantemente pequenos vasos sanguíneos ocorrendo em pacientes portadores de asma e eosinofilia tecidual. A forma relacionada ao anticorpo anticitoplasma de neutrófilo (ANCA) é mais rara. Este relato de caso apresenta um paciente asmático tardio que iniciou quadro com lesões cutâneas (púrpuras), evoluindo com injúria renal aguda, diagnosticado posteriormente com glomerulonefrite. A dificuldade e complexidade no diagnóstico clínico e a importância de iniciar terapia adequada e precoce a fim de minimizar lesão em órgãos-alvos, melhorar prognóstico e evitar efeitos adversos, motivaram a apresentação do caso e sua análise literária.

Palavras Chaves: churg- strauss, vasculite, eosinofilia, granulomatose eosinofílica com poliangiíte.

Objetivo Primário: Relatar um caso clínico de GEPA e a dificuldade em realizar e confirmar o diagnóstico, bem como tratamento precoce e desfecho favorável.

Objetivo Secundário: Relacionar o caso clínico com dados epidemiológicos e literários, para suspeita e diagnóstico, a fim de tratamento precoce.

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I. INTRODUÇÃO

A granulomatose eosinofílica com poliangiíte (GEPA) é uma vasculite rara que afeta vasos sanguíneos de pequeno calibre, estando associada a anticorpos anticitoplasma de neutrófilos (ANCA). (1) Descrita inicialmente por Churg e Strauss em 1951, a doença é caracterizada por vasculite necrotizante disseminada com granulomas extravasculares, ocorrendo exclusivamente em pacientes com asma e eosinofilia tecidual. A GEPA é classificada como uma vasculite de pequenos vasos e também está associada a síndromes hipereosinofílicas, nas quais a inflamação dos vasos e a proliferação eosinofílica contribuem para o dano orgânico. (2) (3).

Embora a etiologia da GEPA ainda seja considerada idiopática, a doença é classicamente vista como mediada por células Th2, com evidências emergentes sugerindo que os ANCA desempenham um papel direto na patogênese. (4) A doença evolui tipicamente através de três fases: uma fase prodrômica com asma e rinosinusite, uma fase eosinofílica com eosinofilia periférica e envolvimento de órgãos, e uma fase vasculítica com manifestações clínicas devido à vasculite de pequenos vasos. (5)

O diagnóstico da GEPA é baseado em critérios clínicos e laboratoriais, incluindo a presença de asma, eosinofilia e sinais de vasculite sistêmica. (6) A presença de ANCA, especialmente com padrão perinuclear (p-ANCA), é observada em cerca de 40-77% dos pacientes, mas não é essencial para o diagnóstico. A biópsia de tecidos

afetados pode revelar vasculite necrotizante e granulomas eosinofílicos, embora os granulomas extravasculares sejam raramente observados.

O prognóstico da síndrome de Churg-Strauss é geralmente bom com tratamento adequado, que inclui corticosteróides e, em casos mais graves, imunossupressores como ciclofosfamida. No entanto, agentes biológicos como rituximabe e mepolizumabe têm mostrado ser alternativas terapêuticas promissoras. (6)

II. MÉTODO

Este trabalho teve como finalidade demonstrar a dificuldade no diagnóstico da Granulomatose eosinofílica com poliangiite, bem como associar o caso clínico do paciente L.C.G. com dados epidemiológicos descritos na literatura sobre a doença.

A pesquisa pode ser classificada, quanto aos seus objetivos, em qualitativa, descritiva e indutiva, pois analisa dados coletados do caso clínico e se utiliza de artigos científicos para correlacionar as bases, sinais clínicos e métodos diagnósticos da patologia em questão.

Este estudo foi realizado em Ribeirão Preto-SP, com dados coletados na Santa Casa de Misericórdia, seguindo o protocolo do comitê de ética da instituição, com o termo de consentimento assinado pelo paciente e garantindo a confidencialidade do estudo.

II. RELATO DE CASO

L.C.G., sexo masculino, 62 anos, branco, previamente portador de asma diagnosticada aos 56 anos, procura atendimento médico em novembro de 2024 com queixa de lesão hiperemiada, dolorosa e com presença de hipertermia local em membro inferior direito, com evolução de 20 dias, tendo sido diagnosticado na ocasião com celulite no membro e orientado a tratamento com moxifloxacino. Retornou ao serviço hospitalar 8 dias após término de antibioticoterapia, com queixas de náusea e epigastralgia. Ademais, relatou novos sintomas, como perda ponderal de 14 quilos em 1 mês, associado a lesões cutâneas hiperemiadas

por toda a superfície corporal, em forma de petéquias, principalmente na face, membros e tórax, com prurido local. Negava outras queixas gastrointestinais, urinárias, respiratórias ou outras. Alegou não ter apresentado exacerbação de quadro asmático nos últimos 5 anos. À chegada, notou-se presença de cianose nas falanges distais de ambas as mãos, com duração efêmera, seguida de hiperemia local, sendo suspeitado de fenômeno de Raynaud.

O paciente foi internado para investigação clínica. Em hemograma admissional, apresentava níveis adequados de hemoglobina e plaquetas, porém com leucocitose sem desvio à esquerda e eosinofilia importante (Hemograma: hemoglobina: 14,7/hematócrito: 44,3/leucócitos: 25.000/bastonetes absolutos: 0/segmentados absolutos: 12.000/linfócitos absolutos: 1.500/eosinófilos absolutos: 10.250/plaquetas: 351.000).

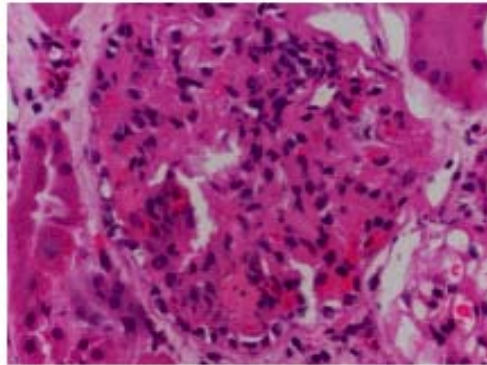
Diante do contexto, foi constatada síndrome hipereosinofílica cuja possível etiologia poderia ser vasculite sistêmica acometendo pequenos vasos. A exclusão de parasitoses e infecções bacterianas foi realizada com base nos exames laboratoriais e na avaliação clínica. Além disso, foram realizados alguns exames investigatórios, como Endoscopia Digestiva Alta, que demonstrou apenas gastrite enantematosa leve em antro; Tomografia Computadorizada de abdome sem contraste, que mostrou coeficiente de atenuação difusamente heterogêneo em ambos os rins, com áreas hipodensas segmentares, sugerindo diagnóstico diferencial entre processo inflamatório e/ou infeccioso e infarto renal; pesquisa de BCR- ABL cujo resultado negativo e dosagem de imunoglobulina E, com valor de 1.444 UI/ml.

Durante a internação, o paciente apresentou piora progressiva das lesões cutâneas, com disseminação das lesões hiperemiadas e petéquias em diversas áreas do corpo. Além disso, foi observada uma piora da função renal, com aumento exponencial dos níveis de creatinina e ureia. Em admissão, os valores de creatinina e ureia estavam dentro dos parâmetros de normalidade para a faixa etária do paciente, mas ao longo da internação o paciente evoluiu com

injúria renal aguda. Desta forma, foi indicada a realização de biópsia renal para definição etiológica, que possibilitou o diagnóstico de GEPA.

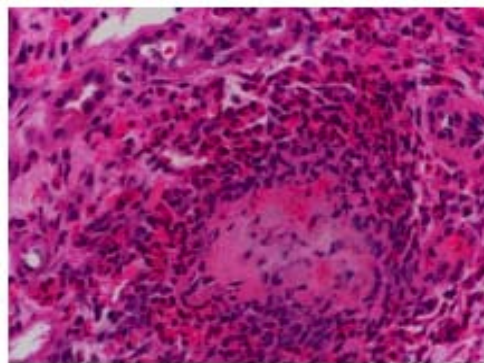
Em biópsia, foi evidenciado presença de hiper celularidade endocapilar por infiltração de leucócitos em glomérulos, com necrose fibrinóide segmentar, expansão do compartimento intersticial por fibroedema e intenso infiltrado

inflamatório com polimorfonucleares neutrófilos e especialmente rico em eosinófilos em túbulos e interstício, sendo esses achados, associado aos dados clínicos, sugestivo de glomerulonefrite pauci-imune, acompanhada de intenso infiltrado inflamatório túbulo intersticial rico em eosinófilos, sendo compatível com Granulomatose eosinofílica com poliangiite- Churg Strauss.



Fonte: Autores (2024)

Figura 1: Corte histológico corado pela hematoxilina-eosina e aumento de 40x mostra glomérulo renal com hiper celularidade endocapilar por infiltração de leucócitos.



Fonte: Autores (2024)

Figura 2: Corte histológico corado pela hematoxilina-eosina evidencia vasos em região medular, com necrose fibrinoide central, envolvida por intenso infiltrado inflamatório rico em eosinófilos

Enquanto aguardava-se o resultado do exame supracitado, foi iniciada a pulsoterapia com corticoide, já sendo notada uma melhora considerável da função renal e das lesões cutâneas. Após confirmação diagnóstica, foi iniciado pulsoterapia com ciclofosfamida e paciente recebe alta hospitalar para seguimento ambulatorial com reumatologista.

com reversão completa do quadro apresentado previamente. Foi realizado o segundo ciclo de ciclofosfamida em dezembro de 2024. Mantém seguimento da função renal, bem como de outros exames laboratoriais e podemos notar os valores de creatinina decrescendo de 3,77 mg/dl e ureia 155 mg/dl para 0,99 mg/dl e 54 mg/dl, respectivamente.

Atualmente, o paciente continua em acompanhamento e sem novas queixas clínicas,



Figura 3: Lesões purpúricas em dorso, sugestivas de vasculite. Fonte: autores (2024)



Fonte: autores (2024 - 2025)

Figura 4: A) lesões purpúricas em face previamente ao tratamento e B, após pulsoterapia, com remissão das lesões orais



Fonte: Autores (2024 -2025)

Figura 5: A) lesões em face previamente ao tratamento e B) com remissão completa após pulsoterapia

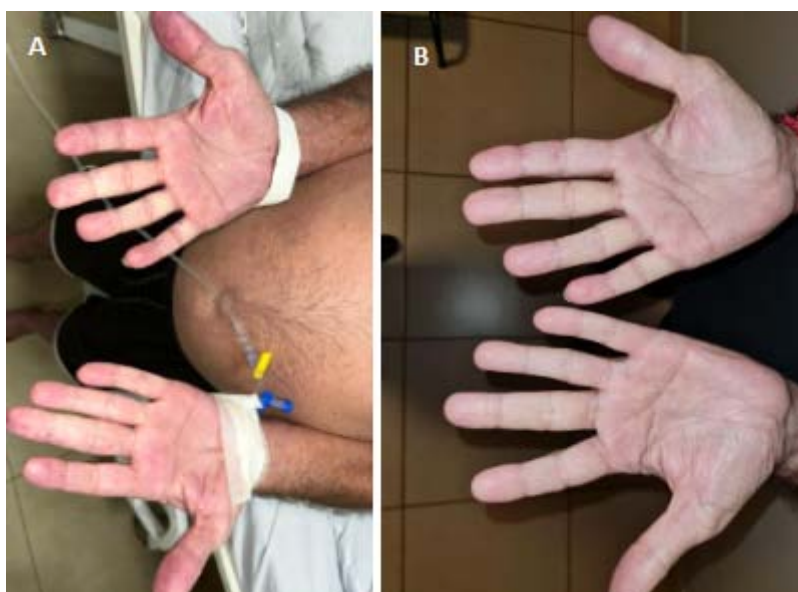


Figura 6: A) Imagem de mãos de paciente com presença de cianose de falanges distais, palidez em falanges médias, quadro sugestivo de Fenômeno de Raynaud. B) Após tratamento, sem evidência de novos fenômenos vasculares. Fonte: Autores (2024 -2025)

III. DISCUSSÃO

A granulomatose eosinofílica com poliangiite, conhecida como síndrome de Churg Strauss, é uma doença reumatológica rara, embora cada vez mais reconhecida nas últimas décadas (7). O quadro clínico tipicamente se inicia com rinite alérgica, polipose nasal e asma de início tardio. Essa fase pode durar anos e é normalmente seguida por hipereosinofilia e infiltrados pulmonares eosinofílicos (8). Com a evolução, a doença pode atingir diversos órgãos, sendo as formas mais graves aquelas com acometimento cardíaco, renal, gastrointestinal e de sistema nervoso central.

Diante de um quadro clínico suspeito para granulomatose eosinofílica com poliangiite, alguns exames complementares podem auxiliar no diagnóstico, como hemograma com achado de eosinofilia, principalmente quando excede valor maior que 10% na contagem diferencial de leucócitos (9); dosagem de ANCA, presente em 55-67% dos portadores; e nível elevado de IgE, o qual é sensível, porém pouco específico (7). Achados pulmonares ocorrem entre 27 a 93% dos casos e podem anteceder a fase de vasculite sistêmica. Os mais comuns são: infiltrados intersticiais bibasais, linhas septais, micronodulações difusas e espessamento hilar.

Em menor número de casos, pode haver derrame pleural bilateral com predomínio de eosinófilos (2).

Caso não identificada e devidamente tratada, a doença possui elevada taxa de mortalidade. A base do tratamento consiste em uso de glicocorticóides (prednisona, 1 mg/kg/dia, com redução progressiva da dose ao longo de 9 a 12 meses, desde que haja melhora clínica e laboratorial) (10). Em pacientes com vasculite grave, o que inclui sintomas de trato gastrointestinal, proteinúria (>1g/d), insuficiência renal (creatinina>1.5 mg/dL), alteração de sistema nervoso central e cardiopatia, é realizada associação de glicocorticóide com agente citotóxico, sendo a ciclofosfamida a mais utilizada (7). A taxa de remissão com tratamento adequado é de 80% com sobrevida de 79.4% e reatividade de 25% (2).

No presente relato, a suspeita diagnóstica da doença se iniciou frente a um quadro de síndrome consumptiva, fenômeno de Raynaud, lesões cutâneas do tipo vasculite e piora de função renal em um paciente que apresentava história clínica de asma de início tardio associada a níveis elevados de eosinófilos em hemograma. Para complementação diagnóstica, foi realizado dosagem de IgE, com resultado acima do valor de

referência. A tomografia de tórax não apresentava infiltrado intersticial pulmonar, achado mais comum dessa doença, porém apresentava espessamento brônquico, sugestivo de infiltrado eosinofílico. Devido a piora de função renal, procedeu-se com biópsia desse órgão, cujo resultado permitiu a confirmação diagnóstica de granulomatose eosinofílica com poliangiite. Então, foi iniciado tratamento com glicocorticóide e ciclofosfamida, que possibilitou a rápida melhora clínica e laboratorial com queda de eosinofilia e normalização da função renal.

IV. CONCLUSÃO

A granulomatose eosinofílica com poliangiite pode ser de difícil diagnóstico no início da apresentação, visto que os sintomas podem ser inespecíficos ou confundidos com outras patologias mais rotineiras. Diante do exposto, é importante salientar que, diante de quadro clínico e laboratorial compatível, esta vasculite deve ser considerada como hipótese diagnóstica e a instituição de tratamento adequado e precoce é de extrema importância para a boa evolução clínica da síndrome, visando minimizar complicações sistêmicas e atingir a remissão dos sintomas.

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Cervical Encirclage – A Boon for Mid- Trimester Pregnancy with Cervical Insufficiency

Dr. Vinutha M. Sharma, Ummu Kulsum, Divya Babu, Govinda Raju & Sandhya babu

INTRODUCTION

The human cervix is a complex structure that undergoes extensive changes throughout pregnancy and parturition to support the fetus and facilitate its expulsion. Cervical insufficiency is defined as the inability of the cervix to retain fetus, in the absence of uterine contractions owing to a functional or structural defect¹. The term “Cervical insufficiency” is now replaced by “cervical incompetence”. Epidemiologic studies suggest an approximate incidence of 0.5% in the general obstetric population and 8% in women with a history of previous mid-trimester miscarriages.

Cervical incompetence may be congenital or acquired. The most common congenital cause is a defect in the embryological development of Mullerian ducts. Ehlers-Danlos syndrome and Marfan syndrome are due to deficiency in collagen leading to incompetence. The most common acquired cause is cervical trauma such as cervical lacerations during childbirth, cervical conization, LEEP (loop electrosurgical excision procedure), or forced cervical dilatation during uterine evacuation².

Keywords: cervical cerclage, cervical insufficiency, mid-trimester pregnancy, preterm birth prevention, second trimester miscarriage, high- risk pregnancy.

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Cervical Encirclage – A Boon for Mid-Trimester Pregnancy with Cervical Insufficiency

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I. INTRODUCTION

The human cervix is a complex structure that undergoes extensive changes throughout pregnancy and parturition to support the fetus and facilitate its expulsion. Cervical insufficiency is defined as the inability of the cervix to retain fetus, in the absence of uterine contractions owing to a functional or structural defect¹. The term “Cervical insufficiency” is now replaced by “cervical incompetence”. Epidemiologic studies suggest an approximate incidence of 0.5% in the general obstetric population and 8% in women with a history of previous mid-trimester miscarriages.

Cervical incompetence may be congenital or acquired. The most common congenital cause is a defect in the embryological development of Mullerian ducts. Ehlers-Danlos syndrome and Marfan syndrome are due to deficiency in collagen leading to incompetence. The most common acquired cause is cervical trauma such as cervical lacerations during childbirth, cervical conization, LEEP (loop electrosurgical excision procedure), or forced cervical dilatation during uterine evacuation².

Incompetence often manifests silently, without uterine contractions or overt symptoms, and may rapidly progress once the internal os loses its competency.

The first report of cervical incompetence was done in 1658 by Cole, Culpeter and Rowland and a surgical approach of treatment emerged nearly 300 years later³. Indications of cervical encirclage are:

1. History indicated cervical encirclage is done in patients with history of one or more mid trimester pregnancy losses due to cervical incompetence.
2. An ultrasound indicated encirclage is done in patients with cervical length less than 25 mm before 24 weeks of gestation.
3. Rescue or emergency encirclage (physical examination indicated cerclage) is done in patients with silent cervical dilatation in the absence of uterine contractions⁴.

Cervical encirclage can be done by either transvaginal or transabdominal route. The Shirodkar suture is a transvaginal purse string suture inserted after bladder mobilization anteriorly and the rectum posteriorly above the level of the cardinal ligament, while the Mc Donald suture is inserted lower at the cervicovaginal junction, but without bladder mobilization. Transabdominal cerclage is usually done in patients with previous failure of transvaginal encirclage or anatomic limitations. Transabdominal cerclage is placed abdominally at the level of the cervico-isthmus junction and is consequently higher in the cervix than vaginally placed cerclages. It can be inserted laparoscopically or by laparotomy and can be placed pre-pregnancy or in the first trimester².

Prevention of preterm birth remains a significant challenge, especially in women with cervical incompetence.

This study aims to assess the obstetric and neonatal outcomes following history indicated, ultrasound indicated and rescue encirclages incorporating both singleton and twin pregnancies in a hospital setting, thus providing data to optimize intervention and enhance perinatal outcomes in cervical insufficiency.

II. AIM AND OBJECTIVES

The aim of the study is to determine maternal and fetal outcomes following history indicated, ultrasound indicated and rescue encirclages.

III. MATERIALS AND METHODS

This is a retrospective study conducted at Sandhya fertility and maternity hospital, Vellore, Tamil nadu. Details of patients who underwent cervical encirclage between November 2023 and October 2024 were collected and followed up upto 6 weeks postpartum.

Inclusion Criteria:

1. Pregnant women >18 yrs.
2. Pregnant women who underwent Mc Donald's cervical encirclage due to previous history of mid-trimester spontaneous miscarriage and/or preterm birth.
3. Pregnant women who underwent Mc Donald's cervical encirclage due to Transvaginal ultrasound showing cervical length <2.5 cm.
4. Pregnant women who underwent rescue Mc Donald's cervical encirclage due to silent and painless dilatation of the cervix with or without membrane bulging through the external cervical os through per speculum examination/ultrasound.

Exclusion Criteria

1. Prophylactic cervical encirclages.
2. Pregnant women who presented with active vaginal bleeding, preterm prelabour rupture of membranes, active labour.
3. Incomplete data.
4. Not willing to be a part of our study.

Informed written consent was obtained from all the women before encirclage. The study included 44 pregnant women and details on age, mode of conception, parity, single/twin gestation, previous history of mid-trimester miscarriages, preterm birth and h/o preterm prelabour rupture of membranes, other risk factors, history of any cervical surgery; indication for cervical cerclage, gestational age at cervical cerclage were obtained. Gestational age of delivery, interval between cervical encirclage and delivery, mode of delivery, neonatal survival, birth weight, APGAR score, NICU admission and postpartum complications was studied.

IV. RESULTS

Our study includes 44 antenatal patients who met the inclusion criteria. The median age group is found to be 29.5 years (20-39 years). 14 patients (31.8%) were primigravida & 30 (68.2%) were multigravida. Of these 30, 10 were grand multiparous (>gravida 3).

History indicated cervical encirclage was done in 15 patients (34.1%). Of this 4(26.7%) had previous 1 mid-trimester miscarriage, 8 (53.3%) had previous 2 mid-trimester miscarriage, 2 (13.3%) had previous 3 mid-trimester miscarriage, 1 (6.7%) had previous history of preterm birth at 30 weeks of gestational age. Ultrasound indicated cervical encirclage was done in 22 patients (50%). 3 patients (6.9%) had both history & ultrasound indicated encirclage. Of this all the 3 had previous 1 mid-trimester miscarriage. So, 18 of our patients had previous mid-trimester miscarriage (40.9%). 6 patients had previous miscarriage at around 16-20 weeks (33.3%) & 12 had at around 20-24 weeks (66.7%) of gestational age. 4 patients under went rescue encirclage at 18+1 to 22+2 weeks of gestational age. 1 patient in our study had cervical length less than 1.5 cm, 3 patients had 1.5 to 2 cm length & 25 patients had 2.1 to 2.5 cm length. The rest 15 patients had their cervical length > 2.5 cm but were included in our study as they had to undergo history indicated cervical encirclage. 10 patients had internal OS opened (2-4mm) & 4 patients (28%) had wide opened OS.

32 (72.7%) of our patients had their cervical encirclage electively done between 12-20weeks & we had 1 patients (2.3%) who underwent rescue encirclage at 18+1 weeks. 8 patients (18.2%) underwent elective encirclage between 20-26 weeks & 3 (6.8%) patients underwent rescue encirclage at 20+2,20+3, 22+2 weeks. Of the 4 rescue encirclage in our study 3 patients underwent spontaneous miscarriage at 26w, 21+2 weeks, 24+5 weeks of gestational age respectively & 1 patient who had encirclage at 20+3 weeks delivered vaginally at 36+5 weeks of gestational age. Of the total population 4 patients (10.5%) had early preterm delivery, 15 patients (39.5%) had late preterm delivery & 19patients (50%) had term delivery. Out of these 44 patients who underwent cervical encirclage, 5 (11.4%) had spontaneous miscarriage at 18 to 26weeks of gestational age, out of which 1 was ultrasound indicated encirclage, 1 was history indicated encirclage and 3 were rescue encirclages. All these women with failed cervical encirclage were advised abdominal encirclage before planning future pregnancies.

19 patients underwent vaginal delivery of which 9 had spontaneous onset of labour (8 late preterm & 1 early preterm). 3 patients underwent assisted vaginal delivery (2 late preterm & 1 term) the indication behind maternal exhaustion. 17 patients in our study underwent LSCS of which 9 were preterm & the rest were term.

Out of the 14 twin pregnancies, 4 (28.5%) had spontaneous onset of preterm labour and delivered normally, 3 (21.5%) had undergone term lower segment cesarean section due to failed induction, 7 (50%) underwent preterm lower segment cesarean section. The indication for preterm LSCS would go as 4 patients twin 1 with non- cephalic presentation with PROM, 1 patient each for severe preeclampsia , iugr with abnormal doppler and previous cesarean with PROM.Of the 25 singleton pregnancies 7 underwent LSCS and the indication were 2 patients with failed induction, 2 patients with breech with PPRM, 1 each for previous cesarean section , breech and severe pre eclampsia. All patients who delivered before 34 weeks of gestational age received atleast 1 dose of steroid before delivery. We didn't

encounter any cases of PPH, chorioamnionitis or eclampsia in our samples.

All the babies born to the women included in our study had APGAR score>7 at 1 minute and 5 minutes after birth. All the babies with birth weight >1.8 kg , <2.5kg were admitted in NICU in view of observation for few hours.

V. DISCUSSION

Our study analysed 44 antenatal patients, who underwent encirclage, including 14 twin pregnancies, we found a distribution of outcomes that highlights the importance of timing and indication of cervical cerclage. Out of the 44 women, 79.5% were between 20-35 years, similar to shilpi et al^[5], sandhyashree pk et al,⁽⁶⁾ Lu et al,⁽⁷⁾ where majority belonged to 20-35 years. 68.2% of encirclages were done in multigravida similar to Golbasi C et al,⁽⁸⁾ which included 68.3%of multiparous women and Indhu et al,⁽⁹⁾ where 64% were multigravida. In our study 40.9% women had previous mid-trimester miscarriage and 9% had previous preterm birth, 2 women had both mid-trimester miscarriage and preterm birth. A retrospective study conducted by Joanna, had 35% patients with history of preterm delivery, and 53% with previous mid-trimester losses. In our study, majority had ultrasound indicated encirclages followed by history indicated encirclages, only 4 patients underwent rescue encirclage. 72.7% of the encirclages were done electively between 12-20 weeks and 18.2 % underwent encirclage between 20-26 weeks. Early cerclage gave successful results for us. But none of the earlier studies demonstrated the effectiveness of early encirclage over delayed encirclages. A prospective observational study by Shruthi et al did history indicated encirclage at 12-14 weeks, ultrasound indicated encirclages at 14-24 weeks, rescue encirclage within 24 weeks¹⁰. Previous studies indicate that gestational age at the time of encirclage placement does not appear to impact the likelihood of preterm deliveries^{11,12}. But a study by Diamant H et al says that late mid-trimester cervical encirclages were still effective in prolonging the duration of pregnancy¹³.

Majority of the patients in our study (56.8%) had cervical length between 2.1 to 2.5 cm, only 1 patient had cervical length <1.5 cm. A meta analysis to determine the effectiveness of cervical encirclage depending on cervical length states that cerclage when done in women with cervical length <25 mm, with prior preterm birth reduced the chances of preterm birth <35 weeks¹⁴ and, post encirclage cervical length <25 mm need to be followed by serial ultrasound measurements, as it helps in predicting preterm labour^{15,16}.

Cervical dilatation at the time of encirclage is an important factor in determining the success of encirclage. In our study, the internal os was wide open in 4 patients, all these 4 patients underwent rescue encirclage and out of them, 3 underwent spontaneous miscarriage. It was found in our study that the effectiveness of encirclage was better in patients whose cervix was just open (2-4mm) than in patients whose cervix was wide open with bulging membranes. Several studies state that advanced cervical dilatation at the time of encirclage placement was associated with preterm birth^{17,18} and rescue encirclage showed poor outcomes and associated with high risk of chorioamnionitis and membrane rupture^{19,20}. The rescue cerclage in our study had notably poor outcomes. This underscores the importance of early screening and intervention.

In our study, 10.5% patients had early preterm delivery at 28-34 weeks, 39.5% late preterm delivery between 34+1 to 37 weeks and 50% had term delivery after 37 weeks. A ten year retrospective cohort on cervical encirclage states that the mean gestational age of delivery was 36.1 \pm 3.8 week in elective cerclage group and 31.4 \pm 5.6 weeks in emergency cerclage²¹. Another retrospective cohort study in a tertiary centre had 27.9 % preterm birth before 37 weeks and 69.1 % term deliveries with 2.9 % miscarriage²².

Previous studies have demonstrated that prophylactic cerclages tend to yield superior results compared to rescue encirclages^{10,23,24}.

Out of the 14 twin pregnancies in our study, none of the patients had spontaneous miscarriage or early preterm delivery. 11 patient underwent late

preterm delivery and 3 underwent term labour. A study on twin pregnancies with cervical encirclage had 41.5% patients with delivery before 32 weeks and 27.7% had delivery before 28 weeks²⁵ unlike our study. Another study on evaluating the impact of cerclage in twin pregnancies stated that 10.4% underwent preterm delivery in cerclage group compared to 28.2% preterm deliveries in group without cerclage²⁶. A cohort study on cervical cerclage in twin pregnancies with cervical dilation or shortening states that cerclage appears to prolong the gestational age at delivery and reduces the incidence of preterm birth and adverse perinatal outcome²⁷. Twin gestation per se is not an indication for cervical encirclage.

Out of 44 women, 22 women in our study had vaginal birth and 17 underwent LSCS due to obstetrics and fetal indications. A study on emergency cerclage and mode of delivery had 60% patients who delivered vaginally and 40 % delivered by cesarean section²⁸. Another descriptive study on mode and success of delivery following cervical cerclage resulted in 63.5% vaginal deliveries and 36.5 % cesarean section²⁹. Placement of cervical cerclage does not mandate caesarean section. Many patients with cervical cerclage undergo vaginal delivery with timely stitch removal with no obstetric and fetal complications.

Our neonatal outcomes were reassuring. 100% neonatal survival rate was seen with APGAR > 7, and when indicated newborns received appropriate NICU care. The neonatal survival in our study was more compared to neonatal survival of 78 %, 73.3% and 74% in studies by wafi et al²⁹, shalini et al³⁰, cecile et al³¹ respectively. Managing cerclage in cases of preterm premature rupture of membranes (PPROM) is challenging, as the benefit of prolonging the pregnancy versus the risk of chorioamnionitis should be meticulously thought.

V. CONCLUSION

Hence, we conclude that prolongation of period of pregnancy was higher in elective cervical cerclage compared to emergency cerclage and is associated

with favourable perinatal outcomes. History indicated cerclage is preventive and yields the best obstetric and neonatal outcome, ultrasound indicated cerclage for short cervix prolongs the gestational age if identified earlier, rescue encirclage has a high failure rate and twin gestations require selective use of cerclage.

Timely and appropriate encirclages can prolong pregnancy significantly and improve neonatal outcomes.

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