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Circadian Syndrome: Definition and Its Relationship to Abdominal Fat

Definition of Circadian Syndrome

Circadian Syndrome is a relatively new concept that expands upon the traditional Metabolic Syndrome by incorporating circadian rhythm disruption as a central underlying etiological factor[1]. It was formally proposed in 2019 by researchers who suggested that the Metabolic Syndrome should be renamed the "Circadian Syndrome" to better reflect the growing evidence connecting disturbances in circadian rhythm with metabolic disorders[1] [2].

The Circadian Syndrome is defined as a cluster of cardio-metabolic risk factors and comorbidities that convey high risk of both cardiovascular disease and type 2 diabetes, with circadian disruption as the proposed common underlying mechanism[1] [2] [3]. This syndrome encompasses not only the traditional components of Metabolic Syndrome but also includes associated comorbidities that have been linked to circadian rhythm disturbances[1].

Components of Circadian Syndrome

The Circadian Syndrome includes the following components:

1. **Traditional Metabolic Syndrome Components**:
   - Elevated waist circumference (abdominal obesity)[1] [4]
   - Elevated triglycerides[1]
   - Reduced HDL cholesterol[1]
   - Elevated blood pressure[1] [5]
   - Elevated fasting glucose[1] [5]
2. **Additional Comorbidities**:
   - Sleep disturbances[1] [6]
   - Depression[1] [6]
   - Nonalcoholic fatty liver disease (NAFLD)[1] [7]
   - Cognitive dysfunction[1]

This expanded definition provides a more comprehensive framework for understanding the clustering of these risk factors and comorbidities, suggesting they share a common etiology related to disruption of the body's circadian system[1] [2].

Relationship Between Circadian Syndrome and Abdominal Fat

There is a strong relationship between Circadian Syndrome and excess abdominal fat (visceral adiposity). Research indicates that:

Mechanistic Connections

1. **Circadian Regulation of Adipose Tissue**: Adipose tissue possesses its own intrinsic circadian rhythm that regulates insulin sensitivity, lipid metabolism, and adipocyte function[8] [9]. Studies have shown that subcutaneous fat has an internal clock that regulates insulin sensitivity, with sensitivity peaking around noon and decreasing by more than 50% by midnight[8].
2. **Disruption Effects on Fat Distribution**: Circadian rhythm disruption promotes preferential accumulation of visceral fat[10] [11]. Chronic circadian misalignment, such as that experienced during shift work, leads to adipocyte hypertrophy (enlarged fat cells), particularly in visceral fat depots, along with adipose tissue inflammation and fibrosis[11] [12].
3. **Molecular Mechanisms**: The core clock genes (BMAL1, CLOCK, PER, CRY) regulate adipocyte differentiation, lipogenesis, and lipolysis[9] [13]. When these clock genes are disrupted, it leads to dysregulation of adipose tissue metabolism and promotes obesity[13] [14].
4. **Thermogenic Fat Regulation**: Circadian rhythms also regulate thermogenic fat (brown and beige adipose tissue), which has the capacity to burn excess energy as heat[14] [13]. Disruption of circadian rhythms can impair this thermogenic capacity, contributing to fat accumulation[14].

Clinical Evidence

1. **Shift Work Studies**: People who work night shifts or rotating shifts show higher rates of abdominal obesity compared to day workers[10] [12]. This is attributed to the misalignment between their internal circadian clock and their sleep-wake/feeding cycles[10].
2. **Experimental Models**: Animal studies demonstrate that circadian disruption through altered light-dark cycles or genetic manipulation of clock genes leads to increased visceral adiposity and metabolic dysfunction[13] [11]. For example, mice with mutations in the CLOCK gene or deletion of BMAL1 develop obesity and features of metabolic syndrome[13].
3. **Human Studies**: Research in humans has found that circadian misalignment alters adipose tissue gene expression and metabolism, promoting inflammation and insulin resistance in fat tissue[11] [15]. These changes are more pronounced in visceral fat compared to subcutaneous fat[8] [11].

Implications for Health

The relationship between Circadian Syndrome and abdominal fat has significant health implications:

1. **Cardiovascular Risk**: Circadian Syndrome has been found to be a stronger predictor of cardiovascular disease than the traditional Metabolic Syndrome[4] [16]. The combination of

circadian disruption and abdominal obesity significantly increases cardiovascular risk[5] [16].

2. **Diabetes Risk**: Disruption of circadian rhythms in adipose tissue contributes to insulin resistance and increased risk of type 2 diabetes[15] [9]. The circadian regulation of glucose metabolism is particularly affected by disruptions in the sleep-wake cycle[5].
3. **Mortality Risk**: Recent research indicates that Circadian Syndrome is associated with increased all-cause mortality risk[17]. This relationship appears to be dose-dependent, with more components of Circadian Syndrome correlating with higher mortality risk[17].

Conclusion

Circadian Syndrome represents an expanded understanding of metabolic disorders that incorporates circadian rhythm disruption as a central etiological factor[1] [2]. There is substantial evidence linking this syndrome with excess abdominal fat through multiple mechanisms, including direct effects on adipose tissue metabolism, adipocyte differentiation, and fat distribution[9] [10] [11].

Understanding this relationship provides new insights into the pathogenesis of metabolic disorders and suggests potential therapeutic approaches targeting circadian rhythms for the prevention and treatment of abdominal obesity and its associated metabolic complications[1] [14] [13]. Interventions such as timed eating, proper light exposure, regular sleep schedules, and circadian-aware medication timing may help address both circadian disruption and abdominal obesity[1] [18] [10].

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