Carotid Sinus Syndrome: Historical Context, Clinical Classification, and Challenges in Management

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Abstract

Background: Carotid Sinus Syndrome (CSS) is a disorder involving an exaggerated response to the stimulation of carotid sinus baroreceptors, often resulting in syncope, particularly in older adults. Historically linked to ancient medical practices, CSS is now recognized as a manifestation of autonomic nervous system dysregulation, with significant clinical implications. This article provides a comprehensive review of CSS, focusing on its pathophysiology, diagnostic challenges, and current treatment strategies, particularly in the context of cardiac pacing. Methods: A thorough review of historical and contemporary literature was conducted, examining the pathophysiological mechanisms of CSS, its classification, and clinical presentation. The effectiveness of various diagnostic tools, including carotid sinus massage (CSM), and treatment approaches, particularly pacing and pharmacological interventions, were analyzed. Key studies were identified and synthesized to provide a detailed understanding of CSS and its management. Results: CSS is classified into three main types: cardioinhibitory, vasodepressor, and mixed, each with distinct clinical features. The condition primarily affects older males and is often triggered by external stimuli such as tight collars or neck movements. Diagnostic challenges persist, particularly in distinguishing CSS from other causes of syncope. Carotid sinus massage remains the gold standard for diagnosis, despite its risks. Treatment strategies vary, with cardiac pacing being most effective for cardioinhibitory CSS, while management of the vasodepressor form remains difficult due to the interplay between hypotension and hypertension. Pharmacological interventions, including fludrocortisone and midodrine, are limited by side effects and potential risks in hypertensive patients. Conclusion: Carotid Sinus Syndrome, though underdiagnosed, is a significant cause of syncope in older adults. While cardiac pacing is effective in preventing recurrences, managing the vasodepressor form of CSS poses ongoing challenges. Further research into new treatment options and a deeper understanding of autonomic dysregulation are essential to improving patient outcomes in CSS management.

Keywords: Carotid Sinus Syndrome, syncope, autonomic dysregulation, carotid massage, cardiac pacing

Significance | This review discusses Carotid Sinus Syndrome's historical roots, clinical classification, and challenges in managing its complex forms and triggers

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Editor Aman Shah Bin Abdul Majid, Ph.D., And accepted by the Editorial Board 15 December 2021 (received for review 23 November 2021)

Introduction

Carotid Sinus Syndrome (CSS) is a condition with deep historical roots, tracing back to ancient Assyrian practices where the carotid

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Please Cite This :
Bhaskaran Sathyapriya, Jayesh S Raghavendra et al. (2021), Carotid Sinus Syndrome: Historical Context, Clinical Classification, and Challenges in Management, Journal of Angiotherapy, 5(2), 1-5, 2145

sinus was manipulated to dull pain during rituals such as circumcision (Ask-Upmark, 1935). This ancient understanding of the carotid sinus's influence on consciousness has evolved into a modern recognition of CSS as a significant cause of syncope, particularly in the elderly. The carotid sinus, located at the bifurcation of the internal and external carotid arteries, houses baroreceptors that are critical in regulating heart rate and blood pressure. Carotid sinus hypersensitivity (CSH) occurs when there is an exaggerated response to stimulation of these baroreceptors, leading to a marked decrease in heart rate and blood pressure (Munster et al., 2016). CSH often precedes the development of CSS, a condition most commonly associated with syncope in older adults.

CSS is categorized into three distinct forms: cardioinhibitory, vasodepressor, and mixed (Figure 1). Each type presents unique clinical features and challenges for patient management. Cardioinhibitory CSS is the most prevalent form and is characterized by bradycardia or transient asystole, typically induced by carotid sinus massage (CSM) (Shojaa et al., 2009). Vasodepressor CSS is primarily marked by a significant drop in systolic blood pressure, often resulting in unexplained falls in older patients. Mixed CSS combines features of both cardioinhibitory and vasodepressor types, leading to both bradycardia and hypotension, making it a more complex variant that requires careful diagnostic and therapeutic strategies.

The pathophysiology of CSS revolves around an exaggerated carotid sinus reflex, involving afferent signals from the carotid sinus to the glossopharyngeal nerve, which then projects to the nucleus tractus solitarius. The efferent signals, mediated by the vagus nerve in cardioinhibitory CSS, result in bradycardia and potential asystole (Paré, 1649). In vasodepressor and mixed forms, sympathetic withdrawal leads to arterial hypotension (Hillier Parry, 1799). Interestingly, histological findings in CSS patients often reveal normal intima and nerve terminals, suggesting that the syndrome may be more related to autonomic dysregulation, especially in older individuals with heightened cardiac sympathetic activity (Koch, 1924). This autonomic dysregulation can be exacerbated by chronic denervation of the sternocleidomastoid muscles, further increasing the sensitivity of the baroreflex arc and contributing to CSH (Sollman & Brown, 1912; Hering, 1923, 1927).

Diagnostic approaches for CSS rely heavily on the carotid sinus massage (CSM), which remains the gold standard. A 10-second CSM, performed sequentially on both sides while monitoring electrocardiographic activity and blood pressure, can confirm the diagnosis if it induces prolonged asystole (de Castro, 1928). However, differentiating CSS from other causes of syncope, such as vasovagal syncope, remains challenging due to overlapping symptoms and the presence of underlying cardiovascular conditions in many CSS patients. The condition is often triggered by external stimuli such as tight collars or neck movements, which compress the carotid sinus, but it can also occur without any identifiable local triggers.

Treatment strategies for CSS have evolved over time, with initial approaches focusing on carotid sinus massage (Weiss & Baker, 1933). Cardiac pacing emerged as a more accepted treatment, particularly for cardioinhibitory CSS (Voss & Magnin, 1970), although managing the vasodepressor form has proven more difficult due to the complex interplay between hypotension and hypertension (Mandelstamm & Lifschitz, 1928). Pharmacological interventions such as fludrocortisone and midodrine have been used, but their effectiveness is limited, especially in hypertensive patients (Braun & Samet, 1928). Newer drugs like droxidopa offer some promise, but more research is needed to establish their efficacy (Shen et al., 2017).

CSS is an underrecognized yet significant cause of syncope, particularly in older males. While cardiac pacing is the most effective treatment for preventing recurrences, managing the vasodepressor form remains a challenge due to the complex nature of the condition. Further research into pharmacological treatments and a deeper understanding of autonethicsomic dysregulation in CSS patients are needed to improve outcomes in the future.

Classification of Carotid Sinus Syndrome

CSS can manifest in three distinct forms, each with its own clinical characteristics and implications for patient management:

Cardioinhibitory CSS

The most prevalent form of CSS, cardioinhibitory CSS, is characterized by bradycardia—a slow heart rate—or temporary asystole, which is a cessation of heart activity. In patients with this condition, carotid sinus massage (CSM) can induce asystole lasting more than three seconds (Shojaa et al., 2009). This type of CSS primarily involves the vagal activation that leads to decreased heart rate.

Vasodepressor CSS

Vasodepressor CSS, while sharing clinical features with the cardioinhibitory and mixed forms, is primarily marked by a decrease in systolic blood pressure. Older patients often present with unexplained recurrent falls, which are more frequent in this form than in others. The pathophysiology involves sympathetic inhibition, leading to hypotension without significant changes in heart rate.

Mixed CSS

Mixed CSS is a combination of the cardioinhibitory and vasodepressor forms. Patients with this type experience both bradycardia and hypotension, making it a more complex variant that requires careful diagnostic and therapeutic approaches.

Pathophysiologic Mechanisms

Reflex Pathways and Neural Involvement

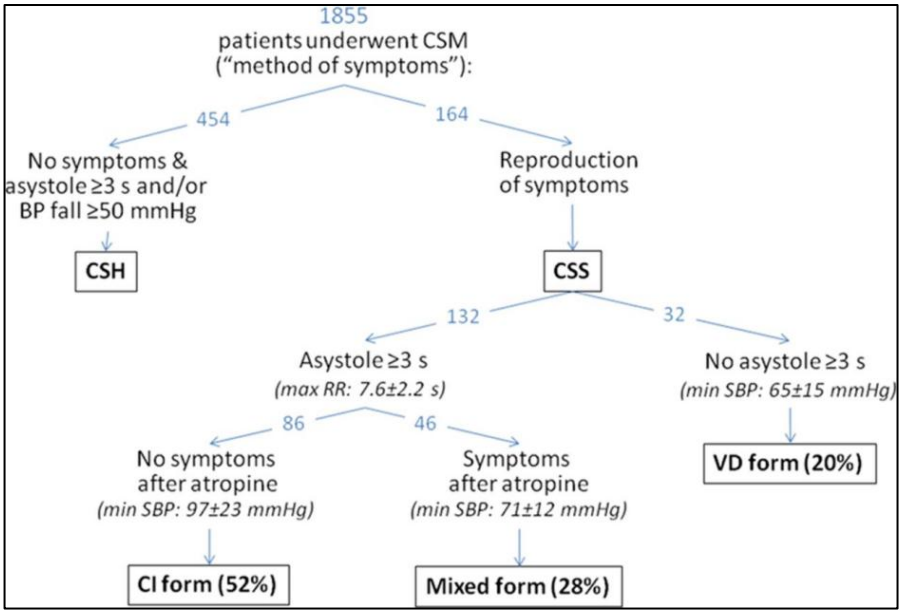

Figure 1. Types of CSS

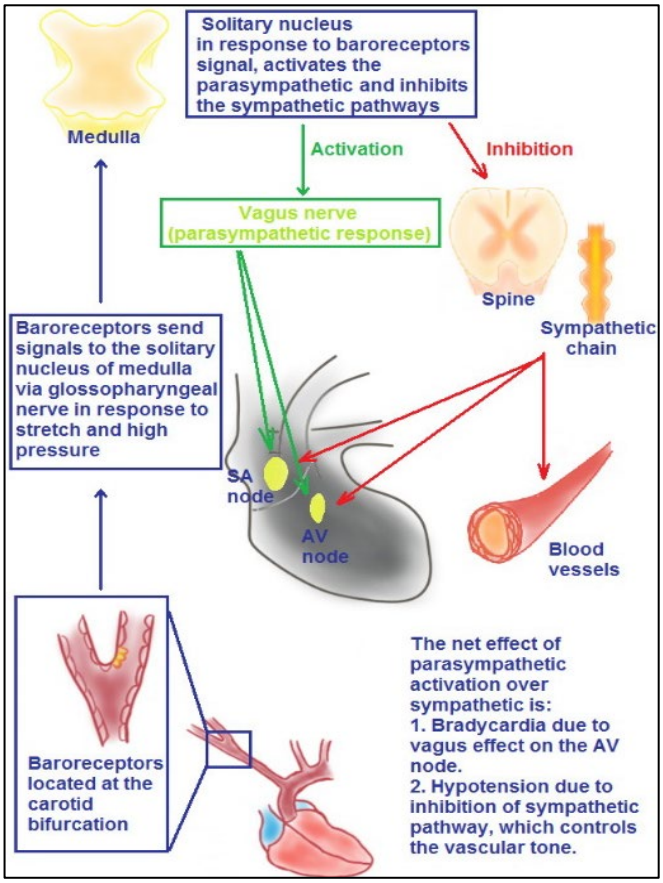

Figure 2. Pathophysiology for Carotid Sinus Syndrome

The pathophysiology of CSS is centered around the exaggerated response of the carotid sinus reflex. This reflex involves the afferent signals transmitted from the carotid sinus via Hering's nerve to the glossopharyngeal nerve, which then projects to the nucleus tractus solitarius (Sharafkandi, 1987). The efferent signals are mediated by the vagus nerve in the case of cardioinhibitory CSS, resulting in bradycardia and potential asystole (Paré, Ambroise). In vasodepressor and mixed forms, sympathetic withdrawal leads to arterial hypotension (Hillier Parry, 1799).

Histological Findings and Autonomic Dysregulation

Histological examinations have shown that the intima and nerve terminals in CSS patients are typically normal (Waller, 1862), suggesting that the condition is not due to structural abnormalities in the carotid sinus itself. Instead, CSS appears to be linked to autonomic dysregulation, particularly in older individuals, where there is increased cardiac sympathetic activity (Koch, 1924). This dysregulation may be exacerbated by chronic denervation of the sternocleidomastoid muscles, which can heighten the sensitivity of the baroreflex arc and contribute to CSH (Sollman & Brown, 1912; Hering, 1923, 1927).

Diagnostic Approaches

Carotid Sinus Massage (CSM)

The gold standard for diagnosing CSS is a 10-second carotid sinus massage (CSM), performed sequentially on the right and left sides while monitoring electrocardiographic activity and blood pressure (de Castro, 1928). A prolonged asystole during CSM confirms the diagnosis of CSS (Heymans, 1929). However, the accuracy of the test can be influenced by factors such as the duration and position of the massage (Sunder-Plassman, 1930).

Differential Diagnosis and Challenges

Differentiating CSS from other causes of syncope, such as vasovagal syncope, can be challenging. Patients with CSS often present with minimal early signs, and the condition predominantly affects males with preexisting cardiovascular conditions, including sinus node disease and atrioventricular block. The use of delayed hysteresis pacemakers or implantable loop recorders has improved the detection of sinus arrest in these patients, but distinguishing CSS from other syncopal conditions remains difficult.

CSS Triggers and Clinical Presentation

Common Triggers

CSS is often triggered by external stimuli such as tight collars or neck movements, which compress the carotid sinus (Figure 2). Other, less common triggers include neck tumors, surgery, or radiation therapy. In some cases, CSS can occur without any identifiable local triggers, but it still results in recurrent syncope (Mehrmann, 1925).

Clinical Features

Patients with CSS typically present with syncope, which may occur without warning. Males over the age of 40 are most commonly affected, and there is often an underlying cardiovascular disease. The condition carries a significant risk of recurrence and was historically associated with high mortality rates. In cardioinhibitory CSS, arrhythmias such as sinus arrest without escape rhythm are observed in up to 72% of cases when monitored with advanced devices.

Treatment Strategies

Carotid Sinus Massage

Initially, treatment for CSS involved the use of carotid sinus massage, following established protocols of 5-10 seconds of bilateral, sequential CSM at the point of maximal carotid artery pulsation. The procedure was conducted first in a supine position, followed by a 70-degree head-up tilt position. While pacing treatment introduced in the 1970s offered some relief, it did not gain widespread acceptance due to the perceived dangers of CSM (Mandelstamm et al., 1928).

Pacing and Pharmacological Interventions

Cardiac pacing became a more commonly accepted treatment in later years, especially for patients with cardioinhibitory CSS. However, managing the vasodepressor form of CSS has proven more challenging. Increased fluid and salt intake was recommended to counteract hypotension, but the management of concurrent hypertension complicated the therapeutic approach (Roskam, 1930). The use of hypotensive medications could lower blood pressure during symptoms but risked causing dangerously high blood pressure levels during other times (Nathanson, 1933; Parry et al., 2000). First-line treatments often involve reducing or discontinuing hypotensive drugs (Weiss & Baker, 1933), with fludrocortisone and midodrine prescribed in some cases. However, these medications can be problematic in hypertensive patients, and midodrine carries additional side effects such as urinary retention in males (Parry & Kenny, 2005; Voss & Magnin, 1970). The development of newer drugs like droxidopa offers some hope, but evidence supporting their efficacy in CSS management is still lacking (Shen et al., 2017).

Conclusion

Carotid Sinus Syndrome is an underrecognized yet significant cause of syncope, particularly in older males. Diagnosis primarily relies on carotid sinus massage, which, despite its risks, remains a valuable tool in reproducing spontaneous symptoms. While cardiac pacing is the most effective treatment for preventing recurrences, managing the vasodepressor form of CSS remains a challenge due to the complex interplay between hypotension and hypertension. Further research into new pharmacological treatments and a better

understanding of autonomic dysregulation in CSS patients could improve outcomes in the future.

Author contributions

S.B. and R.J.S. conceived the presented idea. B.S., P.K., C.A., S.A.A., and S.D. All authors discussed the results and contributed to the final manuscript.

Acknowledgment

Author was grateful to their department.

Competing financial interests

The authors have no conflict of interest.

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