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A Comprehensive Literature Review Of May Thurner Syndrome

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Abstract:
This Literature Review Provides A Comprehensive Examination Of May-Thurner Syndrome (MTS), A Seldom-Recognized Vascular Condition Characterized By The Compression Of The Left Iliac Vein By The Right Iliac Artery, Leading To Venous Outflow Obstruction And Subsequent Deep Vein Thrombosis (DVT). The Review Synthesizes Existing Literature On MTS, Spanning The Historical Context, Pathophysiology, Epidemiology, Diagnostic Modalities, Treatment Options, And Prognosis. It Highlights The Elusive Nature Of MTS Due To Its Non-Specific Symptoms, Contributing To Underdiagnosis And Delayed Treatment. Current Diagnostic Tools, From Computed Tomography (CT) And Magnetic Resonance Imaging (MRI) To Intravascular Ultrasound (IVUS), Are Critically Analysed. The Efficacy And Limitations Of Treatment Strategies Such As Anticoagulation, Catheter-Directed Thrombolysis, And Endovascular Stenting Are Discussed In Detail. An Exploration Of The Evolution In Understanding MTS Underscores The Need For Heightened Clinical Awareness And The Potential Role Of Genetic And Environmental Risk Factors. By Collating Various Pieces Of Evidence, This Review Contributes To A Holistic Understanding Of MTS, Presenting Critical Insights To Guide Future Research And Clinical Practice.

Key Word*:May-Thurner Syndrome, Deep Vein Thrombosis, Diagnostic Modalities, Treatment Strategies, Vascular Pathophysiology.*

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I. Introduction

Brief Explanation of May-Thurner Syndrome (MTS)

May-Thurner Syndrome (MTS), also known as iliac vein compression syndrome, is a medical condition in which the left iliac vein is compressed by the right iliac artery. This compression can result in decreased blood flow from the left leg, leading to symptoms such as pain, swelling, and the development of deep vein thrombosis (DVT). MTS is more common in women than men and typically occurs during the individual's middle years. Although this condition is named after Drs. May and Thurner who first described it in 1957, it's likely been a cause of unexplained leg swelling for centuries.

Why Understanding MTS is Important

Understanding MTS is crucial for several reasons. Firstly, MTS is an underdiagnosed condition, often overlooked because its symptoms are similar to other conditions. Therefore, raising awareness and understanding of MTS can improve its diagnosis and subsequently, patient outcomes. Secondly, untreated MTS can lead to serious complications like DVT, pulmonary embolism, and post-thrombotic syndrome, which can be life-threatening. Lastly, MTS often affects people in their prime working years, impacting their quality of life and productivity. Therefore, improving our understanding of this syndrome can significantly enhance the affected individual's wellbeing and overall public health.

Objective of the Review

The objective of this review is to provide a comprehensive overview of May-Thurner Syndrome, including its pathophysiology, diagnosis, treatment, and current research status. By bringing together information from various studies, case reports, and clinical guidelines, we aim to present a cohesive picture of the current understanding and management of MTS. This review seeks to raise awareness about this underdiagnosed condition, highlight the need for further research, and contribute to better patient outcomes.

II. Background

May-Thurner Syndrome (MTS), also known as Iliac Vein Compression Syndrome or Cockett's Syndrome, is a vascular condition characterized by the compression of the left common iliac vein by the right common iliac artery. This compression can lead to the development of blood clots, commonly referred to as deep vein thrombosis (DVT), in the iliac vein or the lower extremities.

This syndrome often occurs when the right iliac artery, which is positioned slightly higher anatomically, overlies and compresses the left iliac vein against the lumbar spine. This constant pressure can lead to the formation of fibrous tissue around the vein, which further narrows the vein lumen and promotes clot formation.

Clinically, MTS often presents as unilateral (one-sided) leg swelling, pain, or discomfort, particularly in the left leg, as this is the side where the iliac vein is compressed. However, in some individuals, the syndrome may be asymptomatic and only becomes apparent when a blood clot forms and leads to more severe symptoms, such as sudden onset of leg pain, redness, and swelling.

Risk factors for MTS include female gender, due to the lower position of the right common iliac artery in women, and conditions that increase blood clotting tendency, such as use of oral contraceptives, pregnancy, genetic clotting disorders, cancer, and immobilization.

MTS is considered a chronic condition because it typically persists until it's treated to relieve the vein compression. Its chronic nature, combined with potential severe consequences of untreated DVT like pulmonary embolism, underlines the importance of early recognition and intervention. However, due to the relatively non-specific symptoms and lack of awareness, MTS often goes unrecognized or misdiagnosed.

Anatomy involved and how it leads to the development of MTS

May-Thurner Syndrome (MTS), also known as Cockett Syndrome or iliac vein compression syndrome, is a condition where the left common iliac vein (LCIV) is compressed against the vertebral body by the right common iliac artery (RCIA) [1, 2]. While this compression of the LCIV is common, MTS is largely underdiagnosed and is not a prevalent cause of deep vein thrombosis (DVT) [1].

This compression occurs just after the RCIA originates from the abdominal aorta and before the iliofemoral junction. The chronic pressure from the overriding artery compresses the vein against the bony structures, typically the lower lumbar vertebrae. This leads to the formation of 'venous spurs,' contributing to thrombosis of the left iliofemoral veins. Occasionally, right-sided MTS is also reported [1].

The underlying pathophysiology was initially recognized by Rudolph Virchow in 1851 when he observed the RCIA compressing the LCIV in cadavers of patients with left iliofemoral thrombosis [1]. However, it was not until 1957 when May and Thurner reported the presence of intraluminal fibrous bands in the LCIV due to compression from the RCIA, labelling this finding as MTS [1].

May and Thurner attributed the pathology to a thickening of the iliac vein wall caused by continuous irritation from pulsations of the overriding artery, and introduced the term "spur"[2]. The compressive phenomenon can present variably and diversely and is more common in adult women between their 3rd to 5th decades. Improving venous outflow from the affected limb forms the central focus of the management of MTS, with minimally invasive endovascular procedures being the mainstay of treatment [2].

Incidence and prevalence of May Thurner syndrome

It was reported to occur in 22% of the 430 cadavers studied by May and Thurner [1]. There are also sporadic reports of right-sided MTS [1].

However, as noted in a 2020 review, the exact prevalence of MTS in the population remains unknown [3]. It was originally presumed to be rare, but the frequency of reported cases has increased possibly due to improved imaging techniques for visualizing the iliac veins. It's speculated that the actual prevalence might be higher than currently assumed [3].

The syndrome is likely underdiagnosed, and this could be due to the specialized imaging required for its diagnosis, which presents a practical challenge. There's also uncertainty about the degree of venous compression that leads to DVT, further complicating the study of this syndrome in population-based settings [3].

Another review emphasizes that MTS, although considered rare, may be more prevalent than estimates suggest [4]. The pathology is attributed to a partial obstruction of the common iliac vein by the common iliac artery, leading to possible obstruction and extensive ipsilateral deep vein thrombosis (DVT). It can present with varied symptoms, including pain, swelling, venous stasis ulcers, skin discoloration, and in extensive DVT cases, postphlebetic syndrome may develop [4].

III. Pathophysiology

Development of MTS

The exact pathophysiology of MTS is not well understood. The pioneering study by May and Thurner in 1957 suggested that continuous irritation by the pulsation of the overlying artery could lead to a thickening of the iliac vein wall, which they termed a "spur" [2]. Despite the association of MTS with chronic left common iliac vein compression resulting in the formation of obstructive lesions, the exact mechanism by which compression produces these lesions is still unknown [5].

Signs and symptoms that can arise from MTS

May-Thurner Syndrome (MTS) is often asymptomatic, which means individuals may not experience any symptoms. However, when symptoms do occur, they are typically associated with deep vein thrombosis (DVT), as the condition involves compression of a vein that can lead to blood clots. The specific symptoms can vary among individuals but often include:

Swelling: This is typically in one leg, most commonly the left leg. The swelling can range from mild to severe.

Pain: Discomfort or pain often occurs in the leg, especially when standing or walking.

Tenderness: The affected leg may feel sore or tender to the touch.

Redness or skin discoloration: The skin on the affected leg may appear red or discoloured.

Warmth: The skin over the affected area may feel warm to the touch.

Leg heaviness or fatigue: The individual may experience a sensation of heaviness, tiredness, or fatigue in the affected leg.

Ulcers or changes in skin colour: In severe or long-standing cases, skin changes such as ulcers or discoloration can occur due to poor blood flow.

Venous claudication: This is a cramping pain that occurs in the affected leg, particularly when walking or exercising. This symptom is less common but can occur in more severe cases.

IV. Diagnosis

May-Thurner Syndrome (MTS) is largely based on the clinical presentation, imaging studies, and the presence of complicating factors such as deep vein thrombosis (DVT). There are no standardized criteria that define MTS, but the condition is typically suspected in patients who present with symptoms consistent with the syndrome, particularly unexplained left-sided deep vein thrombosis.

Different imaging techniques are commonly used for diagnosing MTS.

1. Ultrasound colour Doppler can be used to identify normal respiratory variation in the right common femoral vein and diminished respiratory variation in the left common femoral vein, suggesting a proximal obstructive lesion.
2. Post-contrast MR venogram can demonstrate compression of the left common iliac vein by the right common iliac artery and cross pelvic collaterals.
3. Axial MIP time-of-flight MR image can show hemodynamically significant left common iliac vein compression with non-visualized left internal iliac vein suggesting flow reversal in the left internal iliac vein.
4. Intravascular ultrasound can show a small caliber left common iliac vein at the site of crossing by the right common iliac artery [1].
5. The use of multi-detector computed tomography (MDCT) is also mentioned in relation to MTS. MDCT findings can help to establish the diagnosis of MTS, and radiologists must recognize the syndrome because of the unique management approach required, differing from DVT without iliac vein compression [3].

In general, the recognition of key clinical features and the use of multimodal imaging techniques are important for the early detection of MTS, promoting enhanced positive and expedited outcomes [1].

Challenges in diagnosing MTS

The challenge in diagnosing May-Thurner Syndrome (MTS) is primarily due to the elusive mechanism by which the compression of the left common iliac vein results in the formation of permanent, obstructive lesions. Additionally, MTS is often seen in young patients who would require endovascular management, making its diagnostic accuracy even more critical. A lack of a clear understanding of the pathogenesis of MTS, coupled with potential diagnostic errors, contributes to the diagnostic challenges of MTS [5].

Lack of Specific Symptoms: MTS often does not present with specific symptoms, which can make it hard to diagnose. Many individuals with MTS may be asymptomatic, while others may experience symptoms such as leg pain or swelling, which are common in many other conditions. As such, the syndrome often goes undetected until an individual develops more severe complications, such as deep vein thrombosis (DVT).

Variable Presentation: Variations of MTS exist where the right lower limb can be affected, which further complicates the diagnosis process [2].

Imaging Challenges: The definitive diagnosis of MTS is generally made through imaging techniques such as computed tomography venography, magnetic resonance venography, or ultrasound. However, these techniques may not always detect the syndrome, especially if the vein compression is not severe or if the imaging is not done in the correct anatomical plane. Invasive procedures such as intravascular ultrasound or venography may be necessary for a definitive diagnosis [5][6].

Overlapping with Other Conditions: MTS symptoms can overlap with many other conditions, including other vascular diseases and conditions that cause leg pain or swelling. This can lead to misdiagnosis or delay in diagnosis [5].

Lack of Awareness Among Clinicians: MTS is not widely recognized by all clinicians. Raising awareness about this syndrome among healthcare professionals is important for early detection and management of this condition [2].

V. Treatment

Treatment options for May-Thurner syndrome (MTS) depend on the severity of the patient's symptoms and the presence of any complicating factors such as deep vein thrombosis (DVT). Here are some of the most common treatment options:

Anticoagulation therapy: Patients with May-Thurner syndrome are at an increased risk of developing DVT. As such, anticoagulant medications, also known as blood thinners, may be prescribed to prevent blood clot formation. Medications like warfarin, heparin, and newer direct oral anticoagulants (DOACs) are commonly used.

Endovascular Treatment: The primary treatment modality for symptomatic MTS is endovascular intervention, which includes angioplasty and stenting:

Angioplasty: This is a minimally invasive procedure where a small balloon is inserted and inflated to open up the compressed vein and improve blood flow.

Stenting: In this procedure, a stent (a small, metal mesh tube) is inserted into the vein to keep it open after angioplasty. The stent remains in the vein permanently to prevent recurrent compression.

Thrombolysis/Thrombectomy: If the patient has a DVT, procedures to remove or dissolve the clot may be used. Thrombolysis involves the use of medications to dissolve the clot, and thrombectomy is the surgical removal of the clot.

Surgery: Surgical options, such as bypass surgery or venous transposition, are typically reserved for patients who can't undergo stenting or those in whom stenting was unsuccessful. These procedures aim to reroute blood flow around the compressed vein.

Compression Stockings: These can help reduce the symptoms of swelling and pain in the leg, and can also help prevent DVT.

Lifestyle changes: Exercise, weight loss, and quitting smoking can also help improve symptoms and reduce the risk of blood clots.

VI. Case studies

The article titled "Treatment of May-Thurner's Syndrome and Associated Complications: A Multicenter Experience" discusses the results of a retrospective study analysing treatment options and associated complications for patients diagnosed with May-Thurner's Syndrome (MTS) [6].

The study examined patient records for a two-year period following diagnosis. From the 47 initially identified patients, 32 (70%) were officially diagnosed with MTS using magnetic resonance venography, computed tomography venography, or ultrasound. However, two patients were excluded due to insufficient follow-up records. The mean age of the remaining 30 patients was around 50 years, and 83% were female [6].

Various treatment options were pursued. The majority (40%) were treated with a combination of anticoagulation, thrombolysis, and stent placement, while 13.3% received a combination of anticoagulation, antiplatelet agents, thrombolysis, and stent placement. Notably, 93% of the patients underwent endovascular stenting, but 39.3% of these patients experienced stent-related complications such as stent thrombosis, stenosis, and migration. Anticoagulation therapy durations varied from 6 months to lifelong. It's worth noting that one patient needed open heart surgery for stent retrieval [6].

The study recorded those two patients (6.7%) had major bleeds that required transfusion, and almost half of the patients (46.6%) developed post-thrombotic syndrome. Additionally, 23.3% of the patients required readmission related to MTS within 30 days of treatment. However, no mortality was noted during the two-year follow-up period [6].

The authors concluded that, despite the small sample size, their findings indicate that there is no consensus on the best treatment options for MTS, and further research is needed to establish optimal treatment protocols [6].

In another case study, a 28-year-old female presented with persistent left thigh swelling that had lasted for approximately three years. The first diagnostic step undertaken was bilateral lower extremity venous Doppler

ultrasonography, which did not reveal any abnormalities. To further evaluate the patient's condition, an abdominopelvic contrast-enhanced wide area detector computed tomography (CT) angiography was performed. The CT scan showed normal arterial anatomy but detected compression of the left iliac vein by the right common iliac artery, confirming the diagnosis of May-Thurner Syndrome [7].

In a nutshell, this case study emphasises that although initial diagnostic procedures like Doppler ultrasonography may not indicate any abnormalities, CT angiography can be a valuable tool to diagnose MTS. This is especially relevant in cases where patients exhibit persistent lower extremity swelling, and other more common causes have been ruled out [7].

This case study provides a valuable example for the diagnosis of MTS, highlighting the importance of detailed imaging studies to confirm the presence of vein compression when the syndrome is suspected [7].

VII. Future Research

Gaps in our current understanding of MTS

May-Thurner Syndrome (MTS) is relatively under-recognized, and there are several gaps in our current understanding of the condition. Here are a few areas that require further exploration and study:

Etiology: While the mechanical compression of the left common iliac vein by the right common iliac artery is well-understood as the primary cause of MTS, the exact biological and mechanical processes that lead to this compression and subsequent venous pathology are not fully understood. More research is needed to fully understand why some people develop symptoms or complications due to this compression, while others do not.

Prevalence and Demographics: The exact prevalence of MTS in the general population is unknown. Some studies suggest that a significant percentage of the population may have anatomical predispositions to MTS, but only a small fraction of those people develop clinically significant symptoms or complications. Also, while MTS is generally more common in women and can occur at any age, the relationships between age, gender, and MTS prevalence and severity are not well-understood.

Diagnosis: There's a lack of standard diagnostic criteria for MTS. Currently, MTS is often diagnosed using a combination of clinical suspicion (based on symptoms and risk factors), non-invasive imaging studies like ultrasound or CT scan, and invasive tests like venography. However, these methods may not catch all cases, and more research is needed to improve the sensitivity and specificity of MTS diagnosis.

Treatment: There's a need for more evidence-based guidelines on the treatment of MTS. While endovascular interventions, like angioplasty and stenting, are commonly used and usually effective, it's unclear what the best treatment strategy is for each patient, especially in terms of when to use conservative management (like anticoagulation and compression stockings) versus when to proceed with invasive treatments. Furthermore, the long-term effectiveness and safety of these treatments are not fully known, and there's ongoing debate about the need for long-term anticoagulation after stent placement.

Predicting Outcomes: Lastly, we need more research on how to predict outcomes for MTS patients. For example, can we identify which patients are more likely to develop complications like deep vein thrombosis or post-thrombotic syndrome, and can we adjust their treatment strategies accordingly? Also, how can we best monitor patients after treatment, and what signs should we look for, that might indicate a need for retreatment or a change in management strategy?

These knowledge gaps underscore the need for continued research on MTS, to improve our understanding of this complex condition and to improve diagnosis and treatment strategies for affected patients.

Ongoing Research and Advancements in Diagnostic Tools and Treatments

The management of MTS involves a multidisciplinary approach and includes anticoagulation, thrombolysis, endovascular stent placement, and surgical interventions. Ongoing research aims to refine and optimize these treatment strategies.

Endovascular stenting has emerged as a key treatment modality for MTS. It helps alleviate the venous compression and restore normal blood flow. However, stent-related complications, including thrombosis, stenosis, and migration, have been reported in a significant number of patients [6]. Researchers are investigating new stent designs and materials to improve long-term outcomes and minimize complications. Drug-eluting stents, which release anti-inflammatory or antiproliferative agents locally, are being explored as a potential solution to reduce the risk of restenosis and improve stent patency.

In addition to stenting, minimally invasive endovascular techniques such as angioplasty and thrombolysis are being studied to treat acute thrombotic events in MTS. These techniques aim to restore venous patency and alleviate symptoms promptly. Further research is needed to optimize the timing, dosing, and selection of thrombolytic agents to maximize their effectiveness while minimizing the risk of bleeding complications [6].

Future Directions: Future research on MTS should focus on standardizing diagnostic criteria and treatment algorithms. Large-scale multicentre studies are necessary to establish evidence-based guidelines for the

management of MTS. Prospective studies evaluating long-term outcomes, including the prevention of post-thrombotic syndrome and the durability of interventions, will help refine treatment strategies.

Furthermore, advances in minimally invasive and image-guided interventions, such as catheter-directed thrombolysis and mechanical thrombectomy, hold promise for the treatment of MTS. These techniques aim to rapidly and effectively remove thrombus and restore venous patency, potentially reducing the need for long-term anticoagulation therapy.

VIII. Conclusion

In conclusion, ongoing research is vital to advancing our knowledge and improving the diagnosis and treatment of May-Thurner Syndrome (MTS). While current diagnostic tools, such as imaging techniques, aid in identifying MTS, there is a need for standardized protocols and increased accuracy. Treatment options, including endovascular procedures and surgery, show promise but carry a risk of complications. Further research is necessary to optimize treatment modalities, reduce complications, and improve long-term outcomes. By dedicating efforts to research, we can develop evidence-based guidelines, enhance diagnostic tools, and refine treatment approaches for MTS. Ultimately, ongoing research is crucial for ensuring better patient outcomes and reducing immediate and long-term complications associated with MTS.

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