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Surgical Strategies in the Management of Raynaud's Phenomenon: Comparative Analysis of Trends and Effectiveness Incorporating New Clinical Data

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Abstract

Introduction and objective

Raynaud's phenomenon is a condition of unknown origin and complex pathophysiology, characterized by an excessive sensitivity to vasoconstriction of arteries in the hands, feet, auricles and nose, leading to a characteristic constellation of symptoms with at least two phase course: pallor and cyanosis. The aim of this work is to review surgical techniques for treating

patients with Raynaud's phenomenon and to attempt to determine whether the results of current studies may support earlier initiation of surgical treatment.

Review methods

To prepare this review, the authors used PubMed and Google Scholar databases, searching the following keywords: "Raynaud's phenomenon", "Raynaud's phenomenon epidemiology", "Raynaud's phenomenon treatment", "Raynaud's phenomenon surgical management", "digital artery reconstruction" "sympathectomy", "arterial bypass", "venous arterialization". The search results were limited to studies from 2006 to 2024, as well as key studies from earlier years. Authors took into consideration articles originally written in English. In the end, 52 articles were included in this review.

Brief description of the state of knowledge

Currently, patients who are qualified for surgical treatment in the course of Raynaud's phenomenon are those who have symptoms or non-healing ulceration despite of an appropriate pharmacological treatment. Current therapy using calcium channel blockers, topical nitrates, selective serotonin reuptake inhibitors, angiotensin II receptor antagonists and pentoxifyllin does not bring full satisfaction to patients. Therefore, the search for optimal therapy continues, with a particular focus on the development of microsurgical treatment techniques.

Summary

The occurrence of Raynaud's phenomenon, especially the pain and discomfort associated with it, significantly reduces patients' quality of life. Due to advances in the field of microsurgery and the discovery of new mechanisms responsible for the development of Raynaud's phenomenon, earlier patient qualification for surgical procedures is becoming possible. This gives hope for further development of surgical approaches and improvements in treatment outcomes.

Keywords: Raynaud's phenomenon; sympathectomy; arterial bypass; venous arterialization

I. INTRODUCTION AND PURPOSE OF THIS WORK

Raynaud's phenomenon (RP) is defined as episodic vasospasm of the fingers, characterized by a typical course accompanied by pain, numbness and a change in the color of the affected area. It can be triggered by exposure to stress, vibrations, cold temperature or smoking cigarettes [1]. RP may occur as an isolated symptom of unknown cause (PRP- *primary Raynaud's phenomenon*) or as a part of underlying disease, such as scleroderma, dermatomyositis, systemic lupus erythematosus, mixed connective tissue disease, Sjögren's syndrome and rheumatoid arthritis (SRP- *secondary Raynaud's phenomenon)*. Current treatment methods

have not shown sufficient effectiveness neither in improving patients' quality of life nor preventing the development of complications of the disease [2]. The aim of this study is to review surgical treatment techniques for patients with Raynaud's phenomenon and to assess whether current research findings among surgically treated patients may support earlier inclusion of surgical intervention in the treatment protocols.

II. REVIEW METHODS

To prepare this review authors used PubMed and Google Scholar databases, searching the following keywords: "Raynaud's phenomenon", "Raynaud's phenomenon epidemiology", "Raynaud's phenomenon treatment", "Raynaud's phenomenon surgical management", "digital artery reconstruction" "sympathectomy", "arterial bypass", "venous arterialization". The search results were limited to studies from 2008 to 2024, as well as key studies from earlier years. Authors took into consideration articles originally written in English. In the end, 52 articles were included in this review.

III. DESCRIPTION OF THE STATE OF KNOWLEDGE

Introduction

The correlation between the occurrence of limb gangrene as a result of a vasospastic attack in response to cold and emotional stress was first described by Maurice Raynaud in 1862. Since then, there was a continuous research going on the etiology and effective treatment of this phenomenon, which has come to be known as Raynaud's phenomenon. The typical constellation of symptoms consists of the following sequence: an episode of vasoconstriction and pallor of the ischemic area, then stagnation of deoxygenated blood causing cyanosis, and finally, vasodilation and restoration of circulation that is associated with redness, swelling and pain [1]. The exact etiopathogenesis of this phenomenon has not yet been fully explained. Research is ongoing to determine the role of individual pro-inflammatory factors, genetic mutations and environmental influence in the onset of RP. A better understanding of these factors may help in the development of new therapeutic approaches aimed at improving patient quality of life and preventing complications. Current treatment tat includes the use of calcium channel blockers, topical nitrates, selective serotonin reuptake inhibitors, angiotensin II receptor antagonists and pentoxifyllin does not bring full satisfaction to the majority of patients.

Etiology and epidemiology

A global meta-analysis conducted in 2014 found the prevalence of primary Raynaud's phenomenon to range from 1.6% to 7.2% in various populations, with nearly twice the incidence in women, especially in those under 40 years of age. Risk factors for developing Raynaud's phenomenon include female gender, a positive family history, frequent exposure to cold, and cigarette smoking [3, 8]. The etiopathogenesis of Raynaud's phenomenon has not yet been fully understood. Primary Raynaud's phenomenon (approximately 80% of cases) refers to a symptom occurring without any underlying disease that could explain its onset. Secondary Raynaud's phenomenon is the most common clinical manifestation of systemic sclerosis and may precede the onset of other symptoms. It may also occur in the course of dermatomyositis, systemic lupus erythematosus, mixed connective tissue disease, Sjögren's syndrome, and rheumatoid arthritis [3]. This phenomenon predominantly affects fingers and toes, as well as the tip of the nose and ears. This is most likely due to the different vascular structures in body areas responsible for regulating body temperature. These areas contain significantly more arteriovenous anastomoses [3]. These connections act as a bypass, allowing blood to flow directly from the arterial to the venous circulation, excluding the capillary bed. Unlike other blood vessels in the human body, arterioles and venules of the cutaneous circulation have a dual type of innervation - typical adrenergic innervation, which through its mediator (noradrenaline) causes vasoconstriction in response to cold, and sympathetic cholinergic innervation, which causes vasodilation in response to heat stress [4, 5]. In healthy individuals, exposure to cold leads to the stimulation of the adrenergic system leading to vasoconstriction and centralization of circulation. However, this process takes part in a controlled way, so despite the reduction of the total flow in the arteriovenous bed, it ensures a constant blood flow through the capillaries that nourish the skin [4]. In patients with Raynaud's phenomenon, even under normal thermal comfort, there is a reduced blood flow in the digits [5]. In the case of exposure to cold, there is further restriction of the already reduced blood flow in these patients [4, 5]. The degree of flow restriction varies depending on the etiology of the disease, with more severe symptoms and advanced circulatory impairment in the digits are observed in individuals with secondary Raynaud's phenomenon due to systemic sclerosis. This difference may result from the extent of endothelial dysfunction, which is more impaired in patients with SRP than in patients with PRP [5]. Endothelial damage plays a significant role in the pathogenesis of secondary Raynaud's phenomenon due to its function in the secretion of substances that have vasodilatory effects (nitric oxide, prostacyclin, endothelial-dependent relaxation factor [EDRF]) and vasoconstrictory effects (endothelin-1, angiotensin II), and its influence on the activity of

prothrombotic processes occurring in the vessel lumen [6]. A further consequence of endothelial damage is platelet activation, which results in the release of substances that affect vascular tonus, such as serotonin, platelet factor 4, beta-thromboglobulin [6]. In individuals with Raynaud's phenomenon, there is an imbalance in the substances produced by the endothelium, with increased production of vasoconstrictory endothelin-1 and angiotensin II, and decreased production of the vasodilatory nitric oxide and prostacyclin [6, 7, 8]. Due to the gradual thickening of the intima closing the vessel lumen observed in histopathological studies of patients with current RP who develop systemic sclerosis, some authors suggest a primarily vascular origin for the disease [7].

Symptoms

A typical feature of both primary and secondary Raynaud's phenomenon is the at least two-phase course of symptoms. Following the triggering factor (emotional stress, cold exposure), patients experience episodic pallor of one or more digits, the tip of the nose, ears or tongue due to the vasoconstriction. This pallor is characterized by a sharp demarcation and may occur bilaterally or, less frequently, unilaterally [1, 3, 9]. In most cases, the thumbs are not affected, and their involvement suggests a secondary nature to systemic sclerosis [9]. In the two-phase course of the phenomenon, after the ischemic episode, congestion occurs, leading to cyanosis of the digits due to anoxia. The least specific symptom is considered to be rubor resulting from reperfusion [3, 9]. Patients withs Raynaud's phenomenon complain of numbness and burning pain felt during the attack significantly reducing their quality of life [1, 9, 10]. Ischemic episodes usually last from 15 to 20 minutes and resolve after warming up [10]. The frequency of symptoms shows significant individual variability, with risk factors including female sex, frequent exposure to cold, smoking, and repeated mechanical trauma [11, 12]. Studies have shown a significant exacerbation of symptoms during the winter months, when the number of attacks doubled in the studied patients (1.5 vs. 2.9 attacks/day) [12]. Between attacks, symptom-free periods occur. Additionally, symptom differences may arise depending on whether the Raynaud's phenomenon is primary or secondary. Thus, patients with primary Raynaud's phenomenon are statistically younger (between 15 and 30 years of age), the dominant clinical sensations are numbness (93.7%) and tingling (53.2%), the level of reported pain is relatively low, and the thumbs are spared [13]. Complications such as ulceration and necrosis are also less common. The predominant symptom in patients with Raynaud's phenomenon in the course of systemic sclerosis is pain, which is associated with a greater degree of tissue ischemia due to more impaired blood flow in the vessels [13]. Studies have not shown consistent data regarding

the difference in the frequency of attacks and the primary and secondary RP [11, 13]. Systemic symptoms that may occur in patients with RP secondary to concomitant rheumatic disease include photosensitivity, skin rash, joints pain, hair loss, dryness of mucous membranes and mouth ulcers development [1, 13].

Diagnosis

The currently recognized diagnostic criteria for Raynaud's phenomenon are the result of an international consensus of experts in the field and consist of a three-step approach.

Table 1. International Consensus Criteria for the Diagnosis of Raynaud's Phenomenon [14].

The patient must respond positively to both screening questions: 1. Screening question: Are your fingers usually hypersensitive to cold? 2. Color assessment: Assessment of whether there is at least a two-phase course of symptoms (pallor and cyanosis/white and blue)
Risk calculation - ≥3 out of 7 criteria must be met: a) Symptoms are triggered by factors other than cold (e.g. emotional stress) b) Symptoms involve both hands, even if they are asynchronous or asymmetric c) Symptoms are accompanied by numbness and/or paresthesis d) During the occurrence of the symptom, the skin with a altered color is clearly demarcated e) The patient provided photos strongly suggesting the diagnosis of RP f) Symptoms sometimes occur in other regions of the body besides the hands (e.g. nose, ears, feet, aureolas) g) A three-phase course of color change during the episode (white, blue, red)

In order to set a diagnosis of primary Raynaud's phenomenon, in addition to meeting the criteria presented in the table above, it is also necessary to: (1) demonstrate the absence of changes in capillaroscopic examination (2) confirm the absence of physical findings suggestive of a secondary cause (such as ulcers, tissue necrosis, sclerodactyly, calcinosis, or skin fibrosis), (3) rule out a positive history of connective tissue disease (4) negative OR low titer ANA (e.g. 1:40 by indirect immunofluorescence) [14].

Nailfold capillaroscopy

This is a non-invasive examination for visual assessment of capillaries in the nailfolds. It is performed using a conventional capillaroscope or video capillaroscope. Due to the parallel arrangement of capillaries in the nailfolds, their morphology can be accurately assessed. If it is impossible to assess the nailfolds, the examination can be performed on the toes. Before the assessment, a 15-30 minute acclimatization period to the room's thermal conditions is necessary, and it should be ensured that the patient has not taken any medications affecting vasoconstriction or smoked in the 4-6 hours preceding the examination [10, 15]. In order to ensure the required sensitivity and specificity of the examination, all 8 fingers of both hands (excluding the thumbs) should be assessed [15]. According to EULAR, changes observed in the capillaries may appear as: (1) normal capillaries (harpin shaped, usually present in people with primary Raynaud's phenomenon), (2) nonspecific image (tortuous or crossing capillaries with diameter <20μm), (3) dilated capillaries (capillaries with a diameter ranging from 20 μm to 50μm and irregular course), (4) giant capillaries (uniformly dilated capillaries ≥50μm with a normal loop shape), (5) microhaemorrhages (hemosiderin deposits), (6) abnormal shape (e.g. ramified capillaries, non-covex head of capillaries, neoangiogenesis), (7) reduced capillary density (<7 per linear mm) [15].

Perfusion scintigraphy

Perfusion scintigraphy is a functional assessment method for blood flow using a radioactive tracer (e.g. Technetium-99m pertechnetate), the flow of which is monitored using a gamma camera [16]. Before the examination, the more symptomatic hand of the patient is assessed. Then, the process of cooling this hand in 4°C water is carried out, followed by a recovery period before the final injection of the radioactive isotope. Afterward, a series of images are taken using a gamma camera, providing data on two types of parameters: dynamic blood flow (finger-to-palm ratios), which helps to assess whether the patient has Raynaud's phenomenon, and static blood pool phase studies, whose results help differentiate primary from secondary Raynaud's phenomenon. Positive result of perfusion scintigraphy is indicated by the ratio of the finger blood-pool count of the chilled hand to that of the ambient hand <0.8 (normal>0.8) [16].

Thermography

Thermography is an indirect method of assessing blood flow within a specific area. It is based on the assumption that the vessels present in the hand and fingers play an important role in the body's thermoregulation, and therefore, disturbances in their flow are associated with a

significant changes in limb temperature. In order to perform the test, a room with strictly controlled temperature and humidity, along with a specialized thermal camera that captures infrared radiation (i.e., heat) from the skin, is required [17]. The results obtained in patients with primary and secondary Raynaud's phenomenon differ. In patients with primary Raynaud's phenomenon, an abnormally slow rewarming process is observed after cooling the hand compared to healthy individuals, though rewarming eventually occurs completely. In contrast, in patients with secondary Raynaud's phenomenon, such as those with systemic sclerosis, the same examination often shows that complete rewarming does not occur within the standardized examination time [17, 18]. Another form of using a thermal camera to distinguish patients with PRP from SRP is the heat challenge test. During this examination, the presence of a persistent temperature gradient between one (or more) fingertips and the dorsal surface of the hand in a room with a constant temperature of 30°C (the 'distal dorsal difference') suggests the presence of connective tissue disease in a given patient [17, 18].

Laser Doppler imaging (LDI)

LDI is an imaging method using the Doppler effect. It allows determination of blood flow by flux (flow through a particular area) [18, 19]. This non-contact system is based on dividing the scanned area into scaled perfusion units, in which the concentration of blood cells and their mean blood flow speed are assessed. This enables precise measurement of perfusion in a given part of the body. The method is quick due to the ability to perform line scanning with a laser across the skin, which is a crucial aspect for monitoring dynamic stimulation in tissue [19]. The use of the Laser Doppler technique allows for distinguishing patients with primary and secondary Raynaud's phenomenon from a healthy control group [18, 19].

Computed tomography angiography and magnetic resonance angiography

Computed tomography angiography (CTA) is the gold standard for diagnosing ischemic changes in the upper limb. It allows for precise imaging of the vessels anatomy and serves as the basis for planning surgical procedures. In patients with Raynaud's phenomenon, the obtained images are characterized by gradually progressing stenosis the proper digital arteries, often accompanied by contrast stagnation in the capillaries of the fingertips [20]. Despite its widespread use, in the experience of the authors of the cited publications, CTA shows lower accuracy compared to magnetic resonance angiography (MRA) in patients with systemic connective tissue disease [20, 26]. Additionally, it has been proven that the contrast used during standard angiography may further exacerbate vasospasm in patients with Raynaud's

phenomenon. Considering the higher accuracy of small vessels imaging, the lower risk of inducing vasoconstriction by administration of a contrast agent and the baseline higher risk of contrast-induced nephropathy in patients with systemic sclerosis, MRA should always be considered as an imaging test in patients with Raynaud's phenomenon [20, 26].

Treatment

So far, pharmacological therapy has been the cornerstone of treating Raynaud's phenomenon. Surgical treatment is reserved for patients in whom, despite exhausting all therapeutic options of pharmacological treatment, resolution of digital ulcers and necrosis has not been achieved. With advancements in microsurgical techniques, surgical treatment may play an important role for a broader group of patients.

Thoracoscopic sympathectomy (proximal sympathectomy)

The rationale for performing thoracoscopic sympathectomy results from the proven excessive activation of the adrenergic sympathetic system in the pathogenesis of the symptom. Indications for treatment include persistent tissue ischemia despite optimal pharmacotherapy. The procedure is performed under general anesthesia, and the access methods differ significantly in the available literature [21, 22, 23]. After intentionally collapsing the apex of the lung on the operated side, the sympathetic trunk can be visualized on the posterior chest wall, covered by the parietal peritoneum. The stellate ganglion is then localized and sympathectomy is performed in relation to the ribs at a level between T1 and T4 (depending on the source) using diathermy, a thoracoscopic scalpel or a harmonic knife. As the incision level increases, the effectiveness of the procedure improves, but the risk of complications, particularly compensatory sweating, also increases [24]. The incision is extended by 2 cm along the rib to cut additional nerve fibers [22, 23]. A retrospective study of 34 patients who underwent thoracoscopic sympathectomy showed recurrence of symptoms in 60% of patients during a 40-month follow-up, despite initial resolution of symptoms in 83%. Lack of treatment effects and complications in the form of excessive sweating were the reasons why as many as 43% (including 29% of patients with severe ischemic symptoms) of the operated patients regretted undergoing the procedure [22]. However, all patients with existing ulcers healed [22]. The short-term effectiveness of this method is also supported by two studies involving a small group of patients who underwent classic and single-port sympathectomy, in whom 100% satisfaction was achieved within the first month after the procedure and a significant decrease in the frequency and severity of ischemic attacks was achieved [23, 24]. After 6 months, in 66% of patients the frequency of

attacks increased again, and the dosage of medications needed for symptom management returned to preoperative levels. Initially healed digit ulcers returned in 44.4% of the examined patients [24]. After one year, 66.6% of patients felt they had undergone surgery unnecessarily. Only one woman maintained a therapeutic effect comparable to that immediately after surgery [24]. Potential complications following thoracoscopic sympathectomy include compensatory excessive sweating in various body regions, a subjective feeling of swelling of the hand, and rarely, Horner's syndrome, subcutaneous emphysema, pneumothorax and haemothorax [22, 23, 24]. Due to the higher recurrence rate compared to local digital artery sympathectomy and the possibility of complications, thoracoscopic sympathectomy is not the preferred form of surgical treatment for Raynaud's phenomenon [12].

Local digital sympathectomy (distal sympathectomy)

The sympathetic innervation of the arteries in the wrist and hand is provided by sympathetic nerves originating from the second and third thoracic ganglia of the sympathetic trunk [25]. The fibers run run along the nerves of the forearm (in greater quantity in the median nerve than the ulnar nerve), dividing along with the branching of these nerves and accompany the corresponding arteries. Along their course, the nerves give off branches to the forearm and hand arteries, forming a sympathetic plexus that wraps around the arteries in the adventitia [26]. The procedure is performed under general anesthesia or local axillary block. The rationale for performing sympathectomy is supported by the restoration of the physiological color of previously ischemic fingers after the use of axillary block anesthesia. The preferred access is obtained through two incisions with maintaining a distance between them -transverse incisions of 1-1.5 cm in length made proximally to the finger flexion crease, and longitudinal incisions made through the center of the palm and extended along the course of the ulnar nerve. Recent data suggest that this approach results in a lower incidence of necrosis of the skin flap and ensures better wound healing [26]. The length of the performed sympathectomy is always the subject of an individual assessment of ischemic changes in a given patient. In a study comparing 20 patients with ulcerations present on a total of 42 fingers, the therapeutic effects of isolated digital periarterial sympathectomy versus general periarterial sympathectomy were evaluated [27]. The authors considered isolated digital sympathectomy to be a circumferential sympathectomy of the affected common digital arteries up to the initial fragment of both proper digital arteries over a length of 3 cm. General sympathectomy has been described as an extension of the procedure to include the removal of 1 cm of the adventitia of both radial and ulnar arteries in the wrist, superficial palmar arch and the common digital vessels to the

proximal portion of digital arteries [27]. This study found no statistically significant difference in the therapeutic outcomes between the two techniques. After 90 months, 15 out of 20 patients achieved complete healing of ulcers or a reduction in their total number. Among the 42 fingers assessed during the study, 11 required amputation [27]. In another study evaluating the efficacy of sympathectomy in 22 patients with a history of ulcers in the course of secondary Raynaud's phenomenon, 18 patients experienced improvement in terms of pain reduction and a subjective feeling of improved ulceration healing. The procedure in this study was performed according to the rules of general periarterial sympathectomy approach [28]. The most radical method of the procedure was presented by O'Brien and Merritt, in a retrospective study on the long-term results of extended periarterial sympathectomy from 2017 [26, 29, 31]. As a result of many years of experience in the surgical management of patients with Raynaud's phenomenon, it was concluded that attempts to limit the procedure to isolated digital periarterial sympathectomy are associated with the frequent need for reoperation with the use of more aggressive margins [26, 29]. A possible cause of this is suspected to be the systemic nature of sympathetic dysregulation, due to which the lack of supply to the proximal parts of the arteries causes that despite the achievement of dilation of the distal vessels, the inflow to them remains reduced due to insufficient inflow. Therefore, the common consensus recommends performaning adventectomy of the dorsal branch of the radial artery starting from the anatomical snuffbox to its division in the interosseous spaces. The ulnar artery is treated up to 8-10 cm proximally from the wrist crease, including the superficial vascular arch and volar arteries, which connect to the deep arch. After this, adventectomy of the proper digital arteries is performed, up to 5 mm from the common volar bifurcation. Additionally, the proper digital arteries are treated up to the interphalangeal joint [26, 31]. The authors emphasize the important role of performing the procedure in the bifurcation area, due to the exceptionally rich innervation of these areas [26, 29]. Early intervention on vessels at high risk of occlusion prevents further development of symptoms and complications, while the application of botulinum toxin (Botox) to the arterial surface ensures prolonged vasodilation effect [26]. In order to demonstrate effectiveness its effectiveness, a retrospective study was conducted involving 337 patients with ischemia or digits ulceration present who, underwent distal sympathectomy. A significant reduction in pain was noted in 94.7% of patients, and complete ulcers healing occurred in 73% of subjects. Complication in the form of amputation occurred in 28%, while 24.1% of patients experienced other complications [30]. Similar data were obtained in a 2017 evaluation, which showed a 94.8% reduction in pain among patients who underwent extended periarterial sympathectomy, with 78% of patients with ulcers achieving complete healing [31]. However, these data are

difficult to interpret unequivocally due to the extended scope of the procedure which included vein graft reconstruction in 31 of 46 patients who suffered arterial occlusions. Another study supporting the efficacy and safety of distal sympathectomy is a retrospective analysis of 17 patients (26 hands) who underwent this procedure. This study showed a reduction or complete resolution of pain in 92.3% of cases, with recurrence of ulcers only in two cases (7.7%) after a follow-up of 6 months to 4.5 years [32]. A recent 2023 study also demonstrated a significant reduction in pain levels in all patients with Raynaud's phenomenon who underwent selective digital sympathectomy and a reduction in the duration of attacks from 19.33 min (±1.79 min) in the control group to 9.47 min (±0.31 min) in the operated group [33]. Complications of distal sympathectomy include potential delayed wound healing, infections, and flexion contracture [30, 31, 32].

Venous arterialization

In approximately 14-20% of patients diagnosed with changes affecting small peripheral arteries, angiographic examination reveals occlusion of arteries without patent distal vessels, which excludes the possibility of reconstructive treatment [34, 35]. Venous arterialization is an option to improve the local condition and reduce ischemia in patients with diseases affecting the distal part of the arterial tree, in whom pharmacological therapy does not bring the intended effects [36]. The general assumption of the procedure is to enable the flow of arterial blood, rich in oxygen and nutrients, to the distal part of the hand and digits. This goal is achieved by performing arteriovenous anastomosis, which enables high-pressure arterial blood flow to the venous bed and subsequently through arteriovenous shunts to the capillary bed. A key role in the planning phase of the surgery is the Doppler ultrasound examination of the forearm veins, especially the cephalic vein, which is most commonly used during the procedure [37]. The course of the cephalic vein is marked with a marker along the desired section. In most patients, the cephalic vein remains patent despite multiple intravenous punctures in this area. In case of doubt, the basilic vein can be used as an alternative [37, 38]. The most commonly used method of anaesthesia is local anaesthesia with brachial plexus block, which produces an analgesic effect and interferes the conduction of sympathetic impulses, resulting in vasodilation of the upper limb arteries [37, 39]. The choice of anastomosis site depends on the individual assessment, based on imaging studies (Doppler ultrasound, high-resolution magnetic resonance angiography, computed tomography angiography), the severity of stenosis, present atherosclerosis or further occlusion of the arteries, as well as the experience of the operator. There is no consensus in this area among surgeons. Thus, in the presented publications, Kind,

Chloros and Peters seem to prefer performing distal anastomoses for their patients [35, 36, 40]. In this case, the most distal part of the radial or ulnar artery with preserved flow is identified, then an incision is made to expose and dissect the cephalic vein up to the mid metacarpal level, along with dissecting the artery proximal to the site of its occlusion. Permanent vascular clips are placed on the branches of the cephalic vein between the arterial anastomosis and the metacarpophalangeal joints and they are transected before the vascular anastomosis to direct the inflow to the main venous channels [35, 36, 40]. Leaving temporary vascular clips on the cephalic vein guarantees access for performing valvulotomy. This is the process of removing venous valves that could cause obstruction of arterial blood flow in the cephalic vein after the successful anastomosis creation. It is typically done using a valvulotome, which is mostly limited to veins on the dorsum of the hand due to the size of the device and the small diameter of the vessels distally to this site. If there is complete or nearly complete occlusion of small veins on the dorsal hand and further distally, open valvulotomy may be necessary, with an incision at the valve site and excision of the valve leaflets [36]. Next, a proximal end-to-end or end-to-side anastomosis of the cephalic vein and artery is created. Literature reviews repeatedly emphasize the importance of leaving an adequately long segment of the cephalic vein to rotate it to the level of the artery without causing any tension [35, 36, 37, 39]. Authors who opt for creating an anastomosis at the level of the brachial artery justify their approach with the fact thet it results in higher blood pressure flowing into the venous bed with this type of connection. Higher blood pressure ensures continuous flow through the veins on the back of the hand and more distally, where the small caliber of the vessels did not allow the use of a valvulotome. In this case, the remaining unremoved valves are incompetent and do not disturb the flow [37, 39]. After performing an anastomosis and removing the clips from the vessels, a strong palpable pulse and audible Doppler signal in the cephalic vein should be present [36, 37, 39]. Due to the very limited review of the literature available on venous arterialization, statistical data on its effectiveness are of questionable value. A review conducted in 2019 showed that among all patients undergoing arterialization, a significant reduction in ischemic pain was noted [41]. These data are consistent with the studies presented by Kind, who performed arterialization in 3 patients, achieving pain relief in all of them when assessed at 8 and 16 months after the procedure [36]. In addition to pain reduction, in a follow-up after 6.8 months, Peters reported complete ulcerations healing and improvement in sensation and mobility of the hands of all patients (n=8) [40]. A case report published in 2023 describes a 62-year-old woman with a 10-year history of worsening ischemic pain in both hands who underwent bilateral arterialization. In a 14-month follow-up, ulcer healing and reduced pain were noted, without the accompanying

complication of increased venous pressure in the hands [42]. According to the data presented by Thibaudeau in the group of 12 patients who underwent arterialization, 100% of them noted a reduction in pain intensity, and 75% of patients with ulceration present before the procedure experienced healing or improvement [38]. The most common complication occurring after the procedure is hand swelling, occurring in 30.8% of patients [38].

Arterial bypass

The treatment involving venous bypass is a widely accepted method for treating ischemia in the lower limbs. A key condition for qualifying a patient with pharmacologically resistant hand ischemia for this treatment is the segmental nature of the occlusion in the radial or ulnar artery, or the dorsal hand arteries, as visualized in imaging studies, with the presence of a distal "run-off" in the common digital arteries [43, 44]. The procedure is usually performed under an axillary block, with or without general anesthesia, which interrupts the impulsation of the sympathetic nerves that leads to arterial vasodilation in the upper limb. The surgical procedure may vary depending on the location of the stenosis. Short stenosis of the ulnar artery in Guyon's canal is typically addressed with a short vein graft, sutured end-to-end in front of the stenosis in the distal forearm and to the distal ulnar artery just before to the superficial arch. Radial artery stenosis can be treated with an end-to-end (or end-to-side) vein graft anastomosis to the patent portion of the radial artery in the forearm and distally to the distal radial artery fragment, deep palmar arch, or the princeps pollicis artery [43, 44, 45]. The most challenging case is segmental stenosis within the superficial palmar arch, which may require a vein graft implanted end-to-end to the ulnar artery on the distal forearm and end-to-side anastomoses connecting the common digital arteries to the vein graft [43]. In the case of systemic diseases, the risk that type of vascular occlusion increases [43, 46]. The vein graft can be obtained from the cephalic vein, basilic vein [43, 47], or saphenous vein/great saphenous vein [44, 45, 46], with patency confirmed through preoperative Doppler ultrasound. To improve intraoperative visualization of the vein, authors recommend applying temporary tourniquet compression during the procedure [43]. Depending on the location of the stenosis, the surgical access may vary, but most authors agree that in patients with systemic disease, the entire superficial palmar arch should be revised. Extending the incision in this way allows for a full assessment of the arterial tree of the hand and, if needed, enables local distal sympathectomy or application of botulinum toxin on the arterial surface [43, 44, 46, 47, 48]. After harvesting a vein with an appropriate length reserve, the site for distal anastomosis is prepared. Some authors do not rule out the possibility of starting with a proximal anastomosis, especially in the case of doubts about the quality of the harvested

venous fragment [43]. To prevent twisting and kinking of the vein, it is marked and then sutured in a reversed (end-to-end or end-to-side) manner, ina way depending on the location of the obstruction that was explained above. Flow assessment after the procedure is performed using Doppler ultrasound, ideally after applying pressure to the ulnar artery if the procedure involved the radial artery and vice versa [44]. To evaluate the effectiveness of bypass procedures in the hand, a summary of 119 patients who underwent this procedure was prepared, with nearly half of whom were diagnosed with a systemic autoimmune disease. In this group, 91.7% avoided the development of ulcerations postoperatively, 93% of patients reported an improvement in the reduction of perceived pain, and healing of existing wounds took place in 88.6% of cases [41]. A retrospective study by Cornejo showed long-term effects at 12.1 months follow-up, with 23 out of 25 implanted vein grafts remaining patent. During this time, 72% of patients reported an improvement in the scope of experienced symptoms. Of the 44% of patients with existing ulcers, complete healing was achieved in all of them. Progression of ischemia and occurrence of new lesions occurred in 28% of the treated patients, and 12% (3 out of 35) required amputation [47]. The most common complications following arterial bypass were wound infection (24%), anastomotic dehiscence (12%), graft thrombosis (4%), hematoma and hemorrhage, which occurred in 13 patients in this study [47]. In the presented literature review, Thibaudeau found a reduction in pain in 100% (n=76) who underwent bypass surgery. Ulcer healing was achieved in 92.7% of patients, and complications such as hematoma and delayed wound healing were reported in 2.1% of the cases [38]. The issue under question is the long-term effect of arterial graft procedures. In the description of his clinical case of reconstruction using the patent deep vein perforator, Tomaino reported a long-term effect of pain reduction 1.5 years after the procedure, with documented blood flow in the digital arteries six months post-surgery [49]. Similarly, Frontario observed good reconstruction outcomes after three and twelve months in his patients, documenting patency of the grafts and proper wound healing [45]. Kwon, in the follow-up of two patients with Raunaud's phenomenon secondary to systemic sclerosis, demonstrated normal hand functionality with preserved blood flow in the digits and relief of symptoms after 26 and 28 months [46]. The recent large study published in August 2024 evaluated 79 digits in 57 patients with secondary Raynaud's syndrome who underwent reconstruction of digital artery with an interposition vein graft [50]. In 97.5% of cases, pain reduction was reported, and in 95.3%, ulceration resolution was observed. Symptoms recurrence occurred in 16 patients during follow-up, and the estimated 5-year risk of recurrence in the remaining patients group was 69.3%. The most important variables influencing this estimate were smoking and the performance of periarterial sympathectomy

during vein graft implantation [50]. This study may significantly influence the current approach to treating patients with Raynaud's phenomenon, demonstrating the effectiveness of vein graft implantation in alleviating pain and healing ulcers, especially if followed by periarterial sympathectomy.

Fat grafting

Another treatment option for patients with Raynaud's phenomenon who do not respond to conservative treatment is fat grafting. The efficacy and safety of autologous fat tissue transplantation, collected under local anesthesia, prepared appropriately in the laboratory and injected back into the subcutaneous tissue of each finger, were investigated in two separate trials conducted on patients with Raynaud's phenomenon [51, 52]. In both studies, preliminary results showed a reduction in symptom intensity in most patients, and in some cases, improved peripheral perfusion of the digits. The rationale for the effectiveness of this procedure is based on the belief that adipose tissue transplantation stimulates neovascularization due to the presence of stem cells in the transplanted tissue. However, further studies are needed to assess the efficacy and standardize this procedure [50, 51].

IV. SUMMARY

Due to the unsatisfactory results of Raynaud's phenomenon treatment in the opinion of patients, there is a continual need to develop new treatment methods. For this purpose, research is being conducted on both new forms of drug therapy and surgical techniques aimed at improving quality of life. Based on the latest studies on surgical treatment, which demonstrate both its safety and effectiveness, it may be necessary to amend the treatment protocols for patients with RP. This view is also supported by feedback from patients who underwent distal sympathectomy with or without the concurrent implantation of a vein graft. These patients, when expressing their opinion on the procedure during follow-up studies, considered the outcomes to be satisfactory and prompted to make an earlier decision on surgical treatment. In order to authenticate these findings, it is essential to continue research aimed at precisely understanding the pathophysiology of Raynaud's phenomenon and demonstrating the long-term effectiveness of and early initiation of surgical treatment in a larger patient population.

V. DATA

Authors' contribution:

Conceptualization: Aleksandra Cygnarowicz; Methodology: Negar Hosseinnejad, Mariola Turemka; Check, formal analysis: Karolina Sacher, Kinga Witowska; Investigation: Kinga Witowska, Aneta Mandziuk; Resources: not applicable; Data curation: Karolina Sacher, Krystyna Zabojska; Writing - rough preparation: Aleksandra Cygnarowicz; Negar Hosseinnejad; Writing - review and editing: Krystyna Zabojska, Mikołaj Biskupski, Aneta Mandziuk, Urszula Korotko; Visualization: Mariola Turemka, Aneta Klaudia Wojtas, Mikołaj Biskupski, Urszula Korotko; Supervision and project administration: Aleksandra Cygnarowicz;

All authors have read and agreed with the published version of the manuscript.

Declaration of the use of generative AI and AI-assisted technologies in improving the language and readability. In preparing this work, the author(s) used https://chatgpt.com for the purpose of improving the language and readability in English language. After using this tool/service, the author(s) have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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