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Contraindications to Intermittent Pneumatic Compression: Between Lines of Recommendations

Dmytro Zaitsev¹, Svitlana Viktorivna Vasylyuk-Zaitseva²

- 1 Shupyk National Medical Academy of Postgraduate Education
- 2 National University of Life and Environmental Sciences of Ukraine

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Abstract

When exploring the contraindications for intermittent sequential pneumatic compression (ISPC), doctors should follow the manufacturer's recommendations for a specific pneumatic compression device model, while manufacturers tend to defer clinical decision-making to the doctor. Contraindications can be determined through expert assessments, leading to discrepancies in sources, or based on empirical experience. Conditions like diabetes, severe diabetic neuropathy with sensory loss, or microangiopathy posing a risk of skin necrosis are not contraindications or limitations for prescribing ISPC. In cases of severe limb ischemia, ISPC may provide relief for patients unsuitable for revascularization or amputation. ISPC is the sole form of compression therapy prescribed for severe peripheral arterial occlusion. ISPC can be used in infectious diseases if the condition is managed by pharmacotherapy. Recommendations have allowed prescribing ISPC for lower limb in COVID-19 patients. Further research is needed to explore the possibility of using ISPC for specific infections. Current recommendations state that ISPC can be used in patients with metastatic cancer. Additional research is necessary to specify a safe procedural methodology. There have been no documented cases of pulmonary embolism when ISPC was applied to patients with deep vein thrombosis. Dangerous complications of acute deep vein thrombosis occur less frequently during ISPC than when using heparin. ISPC is not recommended for patients with severe cases of stage IV NYHA heart failure. More contraindications are becoming limitations. The formulation should specify the conditions under which the described condition becomes a contraindication. Attention should be devoted to studying the systemic effects of ISPC. Trust in manufacturer recommendations should be fundamental, while further research on ISPC safety and monitoring new data regarding contraindications is necessary.

D.V. Zaitsev¹, and S.V. Vasylyuk-Zaitseva²

¹ Department of Occupational Medicine, Psycophysiology and Medical Ecology, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine. ORCID iD: 0000-0002-0841-1504

² IT Department, National University of Life and Environmental Sciences of Ukraine,

Kyiv, Ukraine. ORCID iD: 0000-0002-0875-462X



When exploring the contraindications for intermittent sequential pneumatic compression (ISPC), doctors should follow the manufacturer's recommendations for a specific pneumatic compression device model, while manufacturers tend to defer clinical decision-making to the doctor. Contraindications can be determined through expert assessments, leading to discrepancies in sources, or based on empirical experience. Conditions like diabetes, severe diabetic neuropathy with sensory loss, or microangiopathy posing a risk of skin necrosis are not contraindications or limitations for prescribing ISPC. In cases of severe limb ischemia, ISPC may provide relief for patients unsuitable for revascularization or amputation. ISPC is the sole form of compression therapy prescribed for severe peripheral arterial occlusion. ISPC can be used in infectious diseases if the condition is managed by pharmacotherapy. Recommendations have allowed prescribing ISPC for lower limb in COVID-19 patients. Further research is needed to explore the possibility of using ISPC for specific infections. Current recommendations state that ISPC can be used in patients with metastatic cancer. Additional research is necessary to specify a safe procedural methodology. There have been no documented cases of pulmonary embolism when ISPC was applied to patients with deep vein thrombosis. Dangerous complications of acute deep vein thrombosis occur less frequently during ISPC than when using heparin. ISPC is not recommended for patients with severe cases of stage IV NYHA heart failure. More contraindications are becoming limitations. The formulation should specify the conditions under which the described condition becomes a contraindication. Attention should be devoted to studying the systemic effects of ISPC. Trust in manufacturer recommendations should be fundamental, while further research on ISPC safety and monitoring new data regarding contraindications is necessary.

Common perception

Intermittent Sequential Pneumatic Compression (ISPC) is a therapeutic hardware technology based on the use of chambers with increased air pressure, specialized for local or systemic stimulation of blood circulation. It represents a group of treatment methods applied in various medical fields to prevent, correct, or compensate for pathological conditions, whose sanogenesis is determined by the ability of circulation, nervous regulation, and related processes.

When a healthcare professional encounters the new direction of ISPC, one of the stages in this process is studying the contraindications. Due to the lack of scientific publications that adequately focus on this issue, authoritative sources of information could be documents and websites of medical device manufacturers. An illustration of the information that can be gathered in this way is Table 1. One of the fundamental factors defining the spectrum of contraindications is the sphere of ISPC application. Although we are interested in perceptions regarding contraindications to ISPC in general, for understanding contradictions between sources, it is expedient to divide the general practice into six spheres, namely – the use of ISPC in cosmetic salons and health improvement offices, in sports medicine, in long-term and maintenance therapy for lymphedema, for thromboprophylaxis (especially in surgical hospitals), and in general medical rehabilitation.

This classification is based on the specifics of known pneumatic compression devices. From a physiological point of view, the division into local lymphatic drainage, local hemodynamic and general hemodynamic methods would be more systematic.



Table 1. Contraindications (1), limitations (2) for medical application of intermittent sequential pneumatic compression and its adverse effects and complications (3) according to the recommendations of product manufacturers as of November 2023.

ISPC in healthy people [1][2]	ISPC in sports [3]	ISPC for lymphedema [4][5]	ISPC for thrombosis prevention ^[6]	Portable ISPC for thrombosis prevention [7]	ISPC in general rehabilitation [8]
Pregnancy, lactation; blood disorders ¹ Pediatric and elderly age ²	Ossifying myositis ¹ Pregnancy ²	Conditions requiring medical device usage; risk of exacerbating normal well-being ¹ Pregnancy (possible/existing) ²	Thin/damaged skin ²		Emergency condition; acute surgical pathology (risk/existing); acute functional insufficiency ¹ General exhaustion; acute/unstable course of any disease ² Emergence of atypical complaints ³
Chronic heart diseases ²	Heart disease (acute/severe ¹ /other ²); decompensated chronic heart failure (CHF); edema due to congestive CHF; pulmonary edema ¹ Undesirable increase in venous/lymphatic return ³	Heart disease; decompensated CHF; edema due to congestive CHF; pulmonary edema ¹ Undesirable increase in venous/lymphatic return ³	Severe congestive heart failure ¹ Undesirable increase in venous return ³	Severe congestive heart failure; pulmonary edema ¹ Undesirable increase in venous return ³	Chronic CHF IV stage; pronounced pulmonary insufficiency ¹ Worsening of CHF; undesirable increase in venous return ³
	Acute/severe liver or kidney disease ¹	Liver failure ¹			Decompensated disease ¹ Organ cavity concrement; abdominal hernia; polyp; cyst ²
	Uncontrolled hypertension ¹ Controlled hypertension ²	Severe unstable hypertension ¹			Hypertensive crisis ²
Menstrual bleeding ¹	Blood clotting disorders ¹				Active bleeding; acute hemorrhage (moderate and above) ²
	Deep vein thrombosis (DVT, suspected/present); pulmonary embolism (PE, in history/present); active phlebitis ¹ Varicose veins ²	DVT (suspected/present); vein ligation; phlebitis; thrombophlebitis; thrombosis (suspected/present) ¹	DVT (suspected/acute); PE; thrombophlebitis ¹	DVT (suspected/acute/chronic); vein ligation; thrombophlebitis ¹	Phlebitis; thrombosis (unspecified; acute) ² Exacerbation of phlebitis ³



Obliterating atherosclerosis ¹ Chronic vascular diseases ²	Severe peripheral artery occlusion (atherosclerosis, other ischemic disease); severe arterial insufficiency; recent local vessel shunting ¹	Severe atherosclerosis; Buerger's disease; vascular ischemic diseases; gangrene ¹	Severe atherosclerosis; ischemic vascular diseases; gangrene ¹	Severe atherosclerosis; ischemic vascular diseases; gangrene ¹	
	Compartment syndrome ¹	Raynaud's disease; unspecified vascular diseases; compartment syndrome; lymphatic vessel occlusion ¹	Circulatory disorders ²	Deforming edema ¹	Arterial aneurysm; hemangioma ²
	Diabetes mellitus ²	Diabetic angiopathy ¹	Diabetes mellitus ²		
Epilepsy ¹ Nervous disorder; mental disorder ²	Absent/changed local sensitivity; severe migraines ¹ Abnormal local sensations; pressure hypersensitivity ² Appearance of discomfort, pain ³	Neuropathy; absent local sensitivity ¹ Reduced local pain sensitivity ² Appearance of tingling, numbness, pain ³	Unconsciousness; absent/reduced local sensitivity; reduced local mobility ² Appearance of tingling, numbness, pain ³	Neuropathy; absent local pain sensitivity ¹	Weakness growth against the background of myopathies/multiple sclerosis ³
Oncological process; benign neoplasms; malignant neoplasms ¹	Lymphangiosarcoma ¹	Cancer ¹			Metastasis ¹
Intoxication; fever; acute infectious diseases; tuberculosis ¹		Fever; active infectious diseases; tuberculosis ¹			Fever; infectious diseases ² Exacerbation of hyperthyroidism; exacerbation of autoimmune inflammations ³
Metal prostheses; pacemaker; defibrillator ¹	Any implanted equipment; pacemaker; defibrillator ¹				
Unhealed injury (dislocation, fracture) ¹	Bone fractures ¹ Osteopenia, osteoporosis; local bone protrusions; spinal deformity ²	Severe limb deformity ¹		Severe limb deformity ¹	Trauma (prior to anatomical integrity restoration) ²
	Skin rash; recent skin graft; open wound, blister, bruise; local wound infection; local inflammation; cellulitis (phlegmon) ¹ Recent trauma/surgery ²	Skin rash; dermatitis; recent skin graft; acute trauma of local soft tissues; local inflammation; acute erysipelas; cellulitis (phlegmon) ¹ Recent surgery/medical procedures ²	Dermatitis; recent skin graft; local wound infection ¹ Redness or skin damage due to the procedure ³	Dermatitis; recent skin graft; open wound, local wound infection ¹	Trauma (prior to anatomical integrity restoration) ²



Contraindications represent a state in which any intervention of ISPC will inevitably lead to deterioration; limitations indicate contraindications regarding specific settings of the procedure. However, in ISPC practice, the boundary between these concepts is not always straightforward and universally accepted, and the gradation of recommendations may involve prior consultation and/or periodic supervision by a physician or medical professional, adjustments in settings and/or procedure techniques, and so forth. Considering the individual approach, manufacturers often lean towards granting the final clinical decision-making authority to the physician. In turn, the physician should primarily focus on contraindications specified by the manufacturer for a specific model of pneumatic compression device.

How are contraindications formed?

The definition and documentary presentation of contraindications, warnings, necessary precautions, adverse effects, and other safety-related information, as well as benefit-risk assessments by the manufacturer, are governed by national and supranational regulations. Sources of such information for the manufacturer can include both clinical studies of their own products and literature data related specifically to analogous devices. An exceptional source of information, typically not disclosed publicly and available only to the manufacturer and regulatory bodies, comprises reports and complaints received during the device's market presence. The strength of the studies also depends on the manufacturer. From this, it's evident that the manufacturer is primarily concerned with contraindications specific to a particular device rather than the therapy in general. Simultaneously, one can conclude that the manufacturer's information regarding contraindications holds the most responsibility—not only due to formal responsibility to consumers but also because of access to undisclosed information.

There are two approaches to defining the list of conditions where the use of ISPC may lead to adverse effects.

- The expert assessment approach (in our context, conventionally referred to as traditional) involves the expert predicting
 potential adverse outcomes based on their understanding of the therapeutic mechanism and disease pathogenesis.
 The patient is safeguarded from harm to their health in this case.
- The evidence-based approach (in our context, hypothetically characterized as modern) involves isolating adverse
 conditions that actually occurred during therapy by analyzing scientific literature, especially if there was a confirmed
 cause-and-effect relationship between the therapy factor and documented deterioration. In this case, if justified, the
 patient can benefit from treatment since the danger is not proven.

As indicated, most of the history of ISPC contraindications was determined by experts. The evolution of recommendations from theory is one reason why contraindication lists differ across sources. Another significant factor is that medical equipment manufacturers inform users about restrictions specifically related to their products, down to specific models, while ISPC as a whole encompasses a wide range of devices (from portable single-chamber cuffs to compression suits) and methodologies (from a few minutes to round-the-clock, from single sessions to multi-month courses, from barely perceptible compression to almost painful compression). The literature analysis in recent years has brought about several



radical changes.

In a significant number of thromboprophylaxis recommendations, ISPC prevails over pharmacotherapeutic agents in patients at increased risk of bleeding. There's also a known practice of intraoperative ISPC application. This suggests that it's not bleeding itself but rather the degree of blood loss that might be considered a limitation.

ISPC is used with caution in pregnant women without worsening of the condition. In three studies (M. Reinhard & al., 2022; M.K. Jacobs & al., 1986; M.K. Jacobs & al., 1982) with a total power of 99 pregnant women, the episodic use of lower extremity ISPC did not have adverse effects on pregnancy. In these studies, ISPC was used to prevent thrombosis or to reduce edema, and at least 2/3 of the women involved were diagnosed with a normal pregnancy without complications. For the purpose of thromboprophylaxis, ISPC is routinely used during natural or caesarean childbirth ^[9] and in the postpartum period.

ISPC is routinely applied in patients with chronic kidney disease undergoing hemodialysis^[10].

ISPC is also used in the preoperative period for fractures^{[11][12]}.

Positive experiences with ISPC application have been recorded in the US^[13] and in Ukraine ^{[[14], p. 152]} in patients with epilepsy.

There are individual positive observations of ISPC usage in patients with arterial hypertension during crises^[15], which require further clarification.

There's positive experience with ISPC use in an infant in the first month of life 16].

The magnitude of some of these examples involves tens of thousands of patients, while in some cases, it's only dozens, and occasionally singular cases. It can be said that concerning many pathological processes, ISPC is in the Phase II of clinical trials, the outcomes of which will conclusively show whether the assessments of ISPC as contraindicated intervention were justified.

Diabetes as an indicator for medical equipment

It's somewhat surprising today to hear about diabetes being a contraindication for prescribing ISPC procedures. However, it wasn't always this way. In certain fields of ISPC (sports medicine, lymphedema therapy, and thromboprophylaxis), diabetes or its vascular or neurological complications might at least be considered reasons for caution. This could be linked to relatively high pressure levels (starting from 70 mm Hg), typical for devices in these fields, or due to the significantly prolonged duration of the procedure (up to round-the-clock sessions). In essence, it's about settings and methodologies often optimized for specific medical purposes, thus shaping restrictions for models, entire product lines, brands, and ultimately market niches.

An example of this phenomenon in our practice in the early 2010s was a semi-serious empirical criterion for differentiating



between pneumatic compression devices with different purposes. The question was raised: Can this device be recommended for someone with diabetes? If the answer was a firm "No, under no circumstances," the device was designed for cosmetic and beauty salons. If the response was "It's theoretically possible, but what's the point?"—the device was oriented toward surgical needs. But if the answer was "Absolutely and as soon as possible," the device was optimized for medical rehabilitation needs. Today, this criterion is no longer effective, indicating the exchange of expertise among different ISPC niches, equipment modernization, and methodologies.

The question of the feasibility of using ISPC to support patients with diabetes-related consequences can be considered debatable ^{[17][18]}. However, within our topic, diabetes itself is certainly not a contraindication; it may appear differently only concerning a specific model of pneumatic compression device.

Critical ischemia: from risk to possibility

It's understandable that concerns about negative effects related to diabetes were a distinct part of the overall vascular compression safety issue in ischemic conditions. Reviewing Table 1, it's noticeable that severe forms of limb ischemia are mostly considered a contraindication for local application of ISPC. This recommendation is traditional and specific to certain devices, but the situation for ISPC as a whole requires commentary.

In 2001, K. Delis & al. observed increased arterial blood flow when applying ISPC to patients with intermittent claudication or after revascularization ^[19]. The following year, the results of a three-year observation of 107 patients with critical limb ischemia or active ulcers were published. Researchers concluded that using ISPC in patients with critical limb ischemia and non-healing wounds at high risk of amputation could lead to complete wound healing and limb salvage ^[20]. In 2005, a report highlighted the benefits of ISPC in patients ineligible for surgical revascularization ^[21]. Later, S. Kavros & al. compared outcomes with and without ISPC in patients with chronic critical limb ischemia and non-healing amputation wounds. In the ISPC group, treatment ended in amputation for 10 out of 24 patients, while in the non-ISPC group, it was 20 out of 24 ^[22].

Ultimately, after a series of studies, it was established that for patients ineligible for revascularization or amputation, ISPC could alleviate symptoms and promote wound healing ^{[23][24][25]}. ISPC found its way into clinical recommendations as one of the promising means of conservative therapy for arterial diseases of the limbs ^[26]. This year's review ^[27] confirms the practice of using ISPC in patients with critical limb ischemia. However, like with diabetes, our concern is about the possibility, not the appropriateness, of therapy. While the mentioned studies are not the only ones, in our opinion, they suffice to illustrate the role ISPC can play in critical limb ischemia.

Did COVID-19 open doors to infectious diseases?

The next significant yet inconspicuous topic for discussion revolves around the interrelation of ISPC with infectious diseases. The main hindrances for applying ISPC in such patients can be deliberated as follows:



- The design of most devices poorly adapts to sterilization, antiseptic processing, or single-use. Conditions for device
 use, including staff competence, often do not meet the needs of working with individuals infected with infectious
 diseases.
- It is expected that ISPC might accelerate the hematogenous or lymphogenous spread of pathogens or toxins, necessitating, at least, the patient's informed consent, vigilant monitoring of their condition, and available resources for providing adequate assistance in case of deterioration. Additionally, ISPC might exacerbate disease progression (immune responses, fever, electrolyte imbalances, etc.), draining the patient and potentially undermining control over the situation.

The first point, as an organizational-technical matter, might be theoretically disregarded. The second point concerns risks to the patient, which, however, are observed only in cases of acute or active disease phases. Carrier and remission states pose no threat, except when ISPC mechanically irritates the infection site, which is usually a well-controlled risk.

Relying on the experience of countries with established good medical practice, we lack significant statistics on ISPC use in patients with poorly controlled infectious processes. Otherwise, we lack qualitatively executed studies. Therefore, there is limited and challenging-to-generalize evidence. There is experience in using ISPC in streptococcal skin infections with antibiotic therapy ^[28]. ISPC is widely used in treating chronic limb wounds^[29]. There are also no reservations regarding ISPC use in situations conducive to future infection development, such as during surgical interventions ^[30]. These and other works indicate that ISPC, in general, can be applied if the infectious process is controlled by pharmacotherapy and if it is localized with low spreading risk (even if localized in the procedure zone).

However, what should be done when the disease rapidly progresses with complications up to lethal consequences? Or if there's hematogenous pathogen spread? This was the challenge we faced at the beginning of the coronavirus disease pandemic. Moreover, COVID-19 affected lung tissue, a critical organ for the feasibility of ISPC.

After debates with colleagues in the absence of necessary information, we concluded that there is no stringent necessity to consider COVID-19 as an absolute contraindication for prescribing ISPC; however, thorough medical supervision and the availability of adequate medical care are necessary. We assumed that since ISPC might hasten the development of undesirable symptoms when used during an unstable state (rapidly deteriorating condition), the predictability of the patient's state for at least a day is a decisive factor in deciding the appropriateness of therapy. We also noted that ISPC can be performed on any pneumatic compression apparatus following instructions, operator experience, and expert consensus. The first message was put forward for public discussion on the Facebook social network on June 14, 2020.

Shortly after this conclusion, we came across similar views of foreign colleagues, with the first being the November recommendations from the Algerian Society of Transfusion and Hemobiology [31] and consensus-based recommendations from the International Society on Thrombosis and Hemostasis [32]. Both documents allowed the use of ISPC for lower limb thromboprophylaxis in COVID-19 patients without any reservations about the interaction of this intervention with the infectious agent.

Thus, for the first time at the clinical guideline level, ISPC application was permitted in infectious diseases with severe



systemic (especially circulatory and immune) manifestations, regardless of the infection process control quality. Most likely, infectious diseases, in general, can be regarded as a state indifferent to ISPC feasibility, requiring additional research and clarifications for specific pathogens and disease courses. Fever is considered a contraindication for ISPC, despite existing ISPC techniques with hypothermic effects (such as when compression chambers are filled with cold air). As ISPC can somewhat accelerate processes in the circulatory system, it would be interesting to clarify the prospects of ISPC in cases of toxic syndrome and supporting weak or compromised immune reactions.

When does ISPC become safe for oncological patients?

Lymphedema is a common complication of malignant neoplasm treatment, and ISPC has been a widely known method for lymphedema management for decades. ISPC often becomes part of the lives of oncology patients, but when does its application become safe? Benign neoplasms are mostly seen neutrally regarding ISPC prescription, and limitations are individualized based not so much on their nature and pathogenesis but rather on localization and size. Conversely, malignant neoplasms have a controversial assessment. On one hand, due to lymphatic drainage stimulation, ISPC may accelerate metastasis spread. Also, if ISPC promotes proliferative processes in general, it's expected to foster the growth of existing tumors. On the other hand, tissue oxygenation during ISPC might contribute to local free radical formation and the development of oxidative stress in tumor tissues with subsequent protective cytotoxic effects. However, several small studies, such as those on operated patients with ischemia-reperfusion [33] and athletes after workouts [34], generally showed that ISPC, on the contrary, reduces the likelihood of developing oxidative stress. An alternative perspective would be to involve ISPC as a mechanical hemodynamics stimulator in detoxification programs.

The practice of approaching the fundamental possibility of performing ISPC in patients with malignant neoplasm metastasis is reflected in few publications. It should be noted that in all cases, localized ISPC for thromboprophylaxis or lymphostasis therapy is meant.

In a study approved by Ohio University, 348 patients with musculoskeletal neoplasms received thromboprophylaxis, including ISPC, without negative consequences regarding metastasis. However, it's unknown whether sufficient attention was paid to this aspect and whether enough observation time was provided [35].

The current recommendations of the European Society of Anesthesiology^[36] note that among other measures, ISPC (class 2B) may be used in patients with high thrombotic risk, including those with metastatic thoracic cancer.

In the clinical guideline of the National Institute for Health and Care Excellence (2008), patients in bed suspected of spinal cord metastatic compression were offered ISPC procedures for thromboprophylaxis. In 2023, this guideline was replaced by a new one [37], where thromboprophylaxis in patients with metastases was conducted according to the sections "Elective Spinal Surgery," "Cranial Surgery," and "Spinal Trauma" of the NICE 2018-2019 thromboprophylaxis recommendations. ISPC is considered one of the recommended thromboprophylaxis methods in all these sections of the recommendations [38]. Summing up, both in 2008 and as of 2023, NICE has no objections to ISPC prescription for patients with metastases, at least in the specified cases.



Recently, it has been emphasized [39] that one of the factors of metastasis is neoangiogenesis induced by VEGF (the expression of which directly depends on ISPC). Additional research is necessary to specify the acceptable safe duration and number of ISPC procedures in patients with metastasis or its risk.

Thromboembolism: the silent revolution

One of the most common concerns among medical professionals regarding ISPC is the fear of dislodging a thrombus leading to subsequent PE. A survey conducted several years ago among Chinese physicians and nurses [40] revealed that 35% of respondents shared this fear. From our observations, this fear is classic and one of the first critical remarks expressed by Ukrainian medical workers when introduced to ISPC.

There are two scenarios to consider: when ISPC starts after the onset of thrombosis and when thrombosis occurs after the initiation of ISPC. The former scenario is more common in adverse conditions when adequate thrombosis diagnosis faces challenges. These could be cases involving silent clots, low scores on thrombotic risk scales, making planned ultrasound diagnostics impossible, or when part of the vascular bed is inaccessible to the sensor.

In 2015, one of the reports from the massive CLOTS-3 study, "Can intermittent pneumatic compression reduce the risk of post-stroke deep vein thrombosis?" provided the first answer to this scenario. During stroke, ISPC thromboprophylaxis commences post-factum when the thrombotic risk is already elevated. Although patients with existing thrombosis symptoms were excluded, the risk of forming a "silent" clot was not entirely low. Initial ultrasound was not performed, and on follow-up, veins were fully visualized in almost half of the patients. Commenting on this, the authors noted: "There was concern that applying ISPC to patients who may already have deep vein thrombosis might dislodge the clot and increase the risk of PE. However, this potential risk has not been documented in randomized controlled trials. We found no reports providing compelling evidence that this has occurred" [41].

The second scenario, where despite preventive efforts, thrombosis occurs against the backdrop of ongoing ISPC, is more typical. During 2017-2019, 10 clinical studies were published involving over 40,000 patients in total. The design allowed for comparing the frequency of pulmonary embolisms in patients receiving ISPC with those on pharmacotherapeutic prevention (mostly low molecular weight heparin). The summarized data are presented in Table 2.

Table 2. Frequency of symptomatic pulmonary embolism in patients receiving or not receiving ISPC therapy.



Patient Profile	Patients with ISPC		Patients without ISPC	
rationic	Total	Incl. PE	Total	Incl. PE
Neurosurgery, neurology [42][43]	3870	10 (0,26%)	3218	37 (1,15%)
Orthopedics, traumatology [44][45][46]	607	2 (0,33%)	1238	15 (1,21%)
Oncology [47][48][49]	688	5 (0,73%)	370	7 (1,9%)
Other [50][51]	20324	6 (0,03%)	10819	6 (0,06%)
Total	25489	23 (0,09%)	15645	65 (0,42%)

Most cases of PE are not only non-lethal but often proceed without significant clinical symptoms and thus typically remain undiagnosed. The studies presented in the table showed that thrombus formation is more common in patients receiving ISPC prophylaxis rather than heparin [42][43][46][50]. Therefore, concerning thrombus formation itself, ISPC might not be the optimal choice. However, it has also been found that dangerous complications of acute deep vein thrombosis, such as clinical or lethal PE, occur slightly less frequently in the context of ISPC than with heparin treatment. One possible reason for this phenomenon could be that ISPC mimics physical activity. A thrombus growing during ISPC procedures is inherently adapted to movement, whereas the anatomical structure of a thrombus formed under pharmacotherapy conditions might be unstable against sudden hemodynamic forces. Another reason could be that during ISPC, the thrombus mainly progresses in those vessels where external mechanical pressure and hemodynamic stimuli scarcely reach. Therefore, ISPC therapy simply leaves the thrombus intact and does not fragment it.

International consensus: is the case closed?

In 2020, a document was published as an international consensus^[52], outlining the risks and contraindications for the application of medical compression. Within this document, ISPC is implicitly considered, noting that its side effects and contraindications are highlighted only in cases where they differ from other forms of compression therapy.

To illustrate the evolving perspectives, the theses of the 2020 consensus can be compared with those of another document developed under the guidance of the German Society of Phlebology and updated two years earlier ^[53]. Both documents focus on therapies rather than pathologies.

- The consensus emphasizes the need to prevent the use of allergenic materials during procedures, check and select
 compression devices, pre-screen patients for conditions that increase the risk of complications, and care for the skin
 during and after procedures. It emphasizes the necessity of equipment functionality checks, proper procedure
 execution, application of low pressure, and initial therapy stages control for patients with polyneuropathy and weakened
 skin.
- It underscores that peripheral nerve damage resulting in numbness or paralysis is a common complication of
 compression devices, particularly ISPC (especially during surgeries). It's recommended to avoid high pressure at
 points where nerves are least protected from external compression and to exercise particular caution in patients with
 diabetes and neuropathy. Patients with diabetes are recommended for light compression. Severe diabetic neuropathy



with sensory loss or microangiopathy with a risk of skin necrosis are contraindications for some types of compression but not for ISPC.

- In the 2018 guidelines, peripheral neuropathy was noted as a relative contraindication to ISPC, and damage to the sural nerve was cited as a possible complication in individuals with cachexia.
- It is noted that the risk of genital lymphedema due to ISPC of the lower limbs is not confirmed by current experience, possibly due to technological advancements. At the same time, more individualized work with lymphedema of atypical localization is recommended.
 - In the 2018 guidelines, there was a warning about the possibility of genital lymphedema, last described in 1998.
 Occlusive processes in the lymphatic drainage area were mentioned as an absolute contraindication to ISPC.
- The documented experience of developing skin folliculitis associated with ISPC is highlighted. Simultaneously, in the case of dermatosis, ISPC has advantages over compression bandages. Parallel to ISPC, patients with local infection are recommended antiseptic treatment or local antibiotics, while patients with fever, lymphadenitis, erysipelas, or cellulitis receive systemic treatment. In other cases of systemic and severe local infections, the decision on compression therapy is made individually. In infectious inflammations, compression therapy is recommended only in combination with antibacterial treatment.
 - In the 2018 guidelines, acute erysipelas and acute cellulitis were noted as absolute contraindications to ISPC, and
 vesicular dermatoses were considered relative contraindications requiring control. In severe stasis dermatosis, skinlymphatic fistula, and similar unstable skin conditions, ISPC was allowed only with antibiotic therapy.
- Severe peripheral arterial occlusion (systolic pressure on the ankle <60 mmHg, pressure on the foot <30 mmHg) is a contraindication for any compression devices except ISPC, which can be prescribed. After shunting, compression is arranged in such a way as to exclude direct mechanical impact on the shunt (possible with its superficial placement).
- Venous thromboembolic conditions are not a contraindication for any compression therapy. Since there is no factual
 data to support whether compressing thrombosed veins can lead to an increased risk of PE or post-thrombotic
 syndrome, acute deep vein thrombosis is not a contraindication for compression therapy, although its application
 requires an individual decision with a balance of benefits and risks, clinical monitoring, and appropriate personnel
 competencies.
 - In the 2018 guidelines, widespread thrombophlebitis, thrombosis, or suspicion of thrombosis were stated as absolute contraindications to ISPC, and pulmonary artery embolism was considered a possible complication.
- It's indicated that decompensated heart failure is a contraindication for compression therapy based on national and
 international recommendations. Literature review suggests that only existing pulmonary edema should be considered a
 contraindication. Peripheral cardiac edemas may be an indication for prescribing compression therapy. Cautionary
 (gradual, starting distally and weakly) use of compression devices is recommended in patients with stage III NYHA
 heart failure in the presence of strict indications, hemodynamic and clinical monitoring. Compression therapy is not



recommended for patients with severe cases of stage IV NYHA heart failure.

- In the 2018 guidelines, congestive heart failure was noted as an absolute contraindication to ISPC.
- It's noted that there is no data to evaluate refractory or unstable arterial hypertension as a contraindication, but models predict that compression therapy under this condition may contribute to pulmonary edema.
 - In the 2018 guidelines, severe or uncontrolled hypertension was stated as an absolute contraindication to ISPC.
 - Additionally, compartment syndrome was noted as an absolute contraindication, and significant or open soft tissue injury of the limbs was considered a relative contraindication.

Summary and Perspectives

Drawing on experience and the expectations of medical equipment manufacturers, approximately 60 conditions are generally considered contraindications for ISPC. However, evidence-based consensus among medical experts identifies fewer than ten such conditions. These include chronic heart failure at stage IV, pulmonary edema, uncontrolled urgent conditions (particularly acute functional insufficiency), uncontrolled active infectious processes, compartment syndrome, and fractures at risk of displacement. More pathological conditions out of contraindications are becoming limitations. However, the primary goal should not be reducing the number of contraindications but rather refining their qualitative specifics. In the future, formulating contraindications should involve specifying circumstances and conditions under which a particular condition becomes a contraindication.

It's easy to vary the strength, duration, and other parameters of the procedure, but one parameter is challenging to alter: it heavily depends on localization. Consequently, developing alternative localizations should focus on studying the systemic effects of ISPC. In practical work, trust in contraindications recommended by the manufacturer regarding a specific device model, procedural methodology, or working conditions should be fundamental. Simultaneously, ongoing research on ISPC safety aspects and continuous monitoring of new contraindication data are necessary.

References

- 1. ^Zemits. (2022). Апарати пресотерапії Zemits [Pressotherapy devices Zemits]. Retrieved November 19, 2023, from https://zemits.com.ua/ua/category/body/apparaty-dlya-pressoterapii
- 2. ^Alvi Prague. (2021). Апарат пресотерапії PR-2000 купити в Києві з доставкою по Україні | Інтернет-магазин Alvi Prague [Pressotherapy device PR-2000 buy in Kyiv with delivery across Ukraine | Online store Alvi Prague]. Retrieved November 19, 2023, from https://alvi-prague.ua/uk/aparat-pressoterapii-pr-2000
- 3. ^Therabody, Inc. (2023). Therabody | Precautions and Contraindications. Retrieved November 19, 2023, from https://www.therabody.com/us/en-us/precautions-and-contraindications.html
- 4. ^BÖSL Medizintechnik GmbH. (n.d.). lympha-mat® GRADIENT 12. Retrieved from https://www.boesl-med.de/download/BOESL_lymphamat_E.pdf



- 5. ^Mego Afek AC LTD. (2023). Indications and contraindications Mego Afek AC Ltd. | Pneumatic compression therapy for circulatory enhancement. Retrieved November 19, 2023, from https://www.megoafek.com/index.php/indications-and-contraindications
- Arjo. (2022). Flowtron ACS900. Instructions for use. Retrieved from https://qbank.arjo.com/productdocumentation/526933EN%20Rev%2013.pdf
- 7. ^Ortho8 Inc. (2021). VENAPRO®. Retrieved from https://r3n9i3w6.rocketcdn.me/wp-content/uploads/2022/01/VenaPro-IFU.pdf
- 8. ^Kalnish, V. V., Zaytsev, D. V., Klimov, S. V., & Pishnov, G. Yu. (2017). Об'ємний пневмопресинг у лікарській прак тиці: Ме тодичні рекомендації [Volumetric pneumopressing in medical practice: Methodical recommendations]. Retrieved from http://ir.nmapo.edu.ua:8080/jspui/bitstream/lib/5165/1/MP_Пишнов_2017.pdf
- 9. ^Donnelly, J. C., Raglan, G. B., Bonanno, C., Schulkin, J., & D'Alton, M. E. (2014). Practice patterns and preferences of obstetricians and gynecologists regarding thromboprophylaxis at the time of Cesarean section. The Journal of Maternal-Fetal & Neonatal Medicine, 27(18), 1870–1873. https://doi.org/10.3109/14767058.2014.898057
- 10. ^Ramanarayanan, S., Sharma, S., Swift, O., Laws, K. R., Umar, H., & Farrington, K. (2023). Systematic review and meta-analysis of preoperative interventions to support the maturation of arteriovenous fistulae in patients with advanced kidney disease. Nephrology, Dialysis, Transplantation, 38(10), 2330–2339. https://doi.org/10.1093/ndt/gfad040
- 11. ^Schnetzke, M., El Barbari, J., Schüler, S., Swartman, B., Keil, H., Vetter, S., Grützner, P. A., & Franke, J. (2021).

 Vascular impulse technology versus elevation for the reduction of swelling of lower extremity joint fractures: Results of a prospective randomized controlled study. The Bone & Joint Journal, 103-B (4), 746–754.

 https://doi.org/10.1302/0301-620X.103B4.BJJ-2020-1260.R1
- 12. ^Clarkson, R., Mahmoud, S. S. S., Rangan, A., Eardley, W., & Baker, P. (2017). The use of foot pumps compression devices in the perioperative management of ankle fractures: Systematic review of the current literature. Foot (Edinburgh, Scotland), 31, 61–66. https://doi.org/10.1016/j.foot.2017.03.002
- 13. ^Cysyk, B. J., & Wruble, E. R. (1996). A deep vein thrombosis prevention program for patients undergoing long-term invasive epilepsy monitoring. The Journal of Neuroscience Nursing, 28(5), 298–304. https://doi.org/10.1097/01376517-199610000-00003
- 14. ^Tarshinova, L., Elchits, T., & Zaitsev, D. (2015). Teoriya i praktika obyemnogo pnevmopressinga [Theory and practice of volumetric pneumopressing]. LAP Lambert Academic Publishing.
- 15. ^Zaitsev, D. V. (2015). Primenenie obyemnogo pnevmopressinga v sochetanii s farmakoterapiey pri arterial'noy gipertenzii [Application of volumetric pneumopressing in combination with pharmacotherapy at arterial hypertension]. Ukrains'kyi Zhurnal Biologii, Medytsyny ta Sportu [Ukrainian Journal of Biology, Medicine and Sport], 2(2), 75–78.
- 16. ^Currie, B. G., Schell, D., & Bowring, A. C. (1991). Giant hemangioma of the arm associated with cardiac failure and the Kasabach-Merritt syndrome in a neonate. Journal of Pediatric Surgery, 26(6), 734–737. https://doi.org/10.1016/0022-3468(91)90022-I
- 17. ^Ruemenapf, G., Morbach, S., & Sigl, M. (2022). Therapeutic alternatives in diabetic foot patients without an option for revascularization: A narrative review. Journal of Clinical Medicine, 11(8), 2155. https://doi.org/10.3390/jcm11082155



- 18. ^Vas, P., Rayman, G., Dhatariya, K., Driver, V., Hartemann, A., Londahl, M., Piaggesi, A., Apelqvist, J., Attinger, C., & Game, F. (2020). Effectiveness of interventions to enhance healing of chronic foot ulcers in diabetes: A systematic review. Diabetes/Metabolism Research and Reviews, 36 Suppl 1, e3284. https://doi.org/10.1002/dmrr.3284
- 19. ^Delis, K. T., Husmann, M. J., Cheshire, N. J., & Nicolaides, A. N. (2001). Effects of intermittent pneumatic compression of the calf and thigh on arterial calf inflow: A study of normals, claudicants, and grafted arteriopaths. Surgery, 129(2), 188–195. https://doi.org/10.1067/msy.2001.110023
- 20. ^Montori, V. M., Kavros, S. J., Walsh, E. E., & Rooke, T. W. (2002). Intermittent compression pump for nonhealing wounds in patients with limb ischemia: The Mayo Clinic experience (1998-2000). International Angiology, 21(4), 360–366.
- 21. ^Labropoulos, N., Leon, L. R., Jr., Bhatti, A., Melton, S., Kang, S. S., Mansour, A. M., & Borge, M. (2005).

 Hemodynamic effects of intermittent pneumatic compression in patients with critical limb ischemia. Journal of Vascular Surgery, 42(4), 710–716. https://doi.org/10.1016/j.jvs.2005.05.051
- 22. ^Kavros, S. J., Delis, K. T., Turner, N. S., Voll, A. E., Liedl, D. A., Gloviczki, P., & Rooke, T. W. (2008). Improving limb salvage in critical ischemia with intermittent pneumatic compression: A controlled study with 18-month follow-up.

 Journal of Vascular Surgery, 47(3), 543–549. https://doi.org/10.1016/j.jvs.2007.11.043
- 23. Slovut, D. P., & Sullivan, T. M. (2008). Critical limb ischemia: Medical and surgical management. Vascular Medicine (London, England), 13(3), 281–291. https://doi.org/10.1177/1358863X08091485
- 24. ^Mangiafico, R. A., & Mangiafico, M. (2011). Medical treatment of critical limb ischemia: Current state and future directions. Current Vascular Pharmacology, 9(6), 658–676. https://doi.org/10.2174/157016111797484107
- 25. ^Tawfick, W. A., Hamada, N., Soylu, E., Fahy, A., Hynes, N., & Sultan, S. (2013). Sequential compression biomechanical device versus primary amputation in patients with critical limb ischemia. Vascular and Endovascular Surgery, 47(7), 532–539. https://doi.org/10.1177/1538574413499413
- 26. ^European Stroke Organisation, Tendera, M., Aboyans, V., Bartelink, M. L., Baumgartner, I., Clément, D., Collet, J. P., Cremonesi, A., De Carlo, M., Erbel, R., Fowkes, F. G., Heras, M., Kownator, S., Minar, E., Ostergren, J., Poldermans, D., Riambau, V., Roffi, M., Röther, J., Sievert, H.,... ESC Committee for Practice Guidelines. (2011). ESC Guidelines on the diagnosis and treatment of peripheral artery diseases: Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: The Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). European Heart Journal, 32(22), 2851–2906. https://doi.org/10.1093/eurheartj/ehr211
- 27. ^Nickles, M. A., Ennis, W. J., O'Donnell, T. F., Jr., & Altman, I. A. (2023). Compression therapy in peripheral artery disease: A literature review. Journal of Wound Care, 32(Sup5), S25–S30. https://doi.org/10.12968/jowc.2023.32.Sup5.S25
- 28. ^Vaillant, L., Müller, C., & Goussé, P. (2010). Traitement des lymphædèmes des membres [Treatment of limbs lymphedema]. Presse Médicale (Paris, France: 1983), 39(12), 1315–1323. https://doi.org/10.1016/j.lpm.2009.12.011
- 29. ^James, C., Park, S. Y., Chan, M., Khajoueinejad, N., Alabi, D., Lee, J., & Lantis, J. C., II. (2021). The role of intermittent pneumatic compression in the treatment of lower extremity chronic wounds. Surgical Technology International, 38, 79–86. https://doi.org/10.52198/21.STI.38.WH1417



- 30. ^Swierstra, B. A., Bijlsma, J. W., de Beer, J. J., Kuijpers, T., & Dutch Medical Association. (2009). Richtlijn 'Diagnostiek en behandeling van heup- en knieartrose' [Guideline 'Diagnostics and treatment of osteoarthrosis of the hip and knee']. Nederlands Tijdschrift voor Geneeskunde, 153, B39.
- 31. ^Chekkal, M., Deba, T., Hadjali, S., Lamara, H., Oulaa, H., Zouai, K., & Hariti, G. (2020). Prevention and treatment of COVID-19-associated hypercoagulability: Recommendations of the Algerian society of transfusion and hemobiology. Transfusion Clinique et Biologique, 27(4), 203–206. https://doi.org/10.1016/j.tracli.2020.09.004
- 32. ^Goldenberg, N. A., Sochet, A., Albisetti, M., Biss, T., Bonduel, M., Jaffray, J., MacLaren, G., Monagle, P., O'Brien, S., Raffini, L., Revel-Vilk, S., Sirachainan, N., Williams, S., Zia, A., Male, C., & Pediatric/Neonatal Hemostasis and Thrombosis Subcommittee of the ISTH SSC. (2020). Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalized for COVID-19-related illness. Journal of Thrombosis and Haemostasis, 18(11), 3099–3105. https://doi.org/10.1111/jth.15073
- 33. **Bickel, A., Drobot, A., Aviram, M., & Eitan, A. (2007). Validation and reduction of the oxidative stress following laparoscopic operations: A prospective randomized controlled study. Annals of Surgery, 246(1), 31–35. https://doi.org/10.1097/01.sla.0000262784.44278.b5
- 34. ^Haun, C. T., Roberts, M. D., Romero, M. A., Osburn, S. C., Mobley, C. B., Anderson, R. G., Goodlett, M. D., Pascoe, D. D., & Martin, J. S. (2017). Does external pneumatic compression treatment between bouts of overreaching resistance training sessions exert differential effects on molecular signaling and performance-related variables compared to passive recovery? An exploratory study. PLoS ONE, 12(6), e0180429. https://doi.org/10.1371/journal.pone.0180429
- 35. ^Patel, A. R., Crist, M. K., Nemitz, J., & Mayerson, J. L. (2010). Aspirin and compression devices versus low-molecular-weight heparin and PCD for VTE prophylaxis in orthopedic oncology patients. Journal of Surgical Oncology, 102(3), 276–281. https://doi.org/10.1002/jso.21603
- 36. ^Ahmed, A. B., Koster, A., Lance, M., Faraoni, D., & ESA VTE Guidelines Task Force. (2018). European guidelines on perioperative venous thromboembolism prophylaxis: Cardiovascular and thoracic surgery. European Journal of Anaesthesiology, 35(2), 84–89. https://doi.org/10.1097/EJA.00000000000000000
- 37. ^National Institute for Health and Care Excellence (NICE). (2023). Spinal metastases and metastatic spinal cord compression.
- 38. ^National Guideline Centre (UK). (2018). Venous thromboembolism in over 16s: Reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. National Institute for Health and Care Excellence (NICE).
- 39. ^Yang, Y., & Cao, Y. (2022). The impact of VEGF on cancer metastasis and systemic disease. Seminars in Cancer Biology, 86(Pt 3), 251–261. https://doi.org/10.1016/j.semcancer.2022.03.011
- 40. ^Sun, B., Tang, X., Liang, L., & Tong, Z. (2018). A survey of knowledge and application of mechanical thromboprophylaxis among the medical staff of intensive care units in North China. The Clinical Respiratory Journal, 12(4), 1591–1597. https://doi.org/10.1111/crj.12715
- 41. ^Dennis, M., Sandercock, P., Graham, C., Forbes, J., CLOTS (Clots in Legs Or sTockings after Stroke) Trials

 Collaboration, & Smith, J. (2015). The Clots in Legs Or sTockings after Stroke (CLOTS) 3 trial: A randomised

 controlled trial to determine whether or not intermittent pneumatic compression reduces the risk of post-stroke deep



- vein thrombosis and to estimate its cost-effectiveness. Health Technology Assessment (Winchester, England), 19(76), 1–90. https://doi.org/10.3310/hta19760
- 42. a, bStulin, I. D., Podgornaya, O. A., Seleznev, F. A., Trukhanov, S. A., Solonskiy, D. S., Shamalov, N. A., Prikazchikov, S. V., Tagirov, I. S., Kudryakov, O. N., Seleznyova, M. G., Baranov, G. A., Dobrovolskaya, L. E., Dobryakov, A. V., Sklyar, I. A., & Sorokina, N. D. (2018). Profilaktika trombozov ven nizhnikh konechnostey i tromboembolii legochnoy arterii u nevrologicheskikh bolnykh v usloviyakh reanimatsionnogo otdeleniya s ispolzovaniem preryvistoy pnevmokompressii [Prevention of venous thrombosis of the lower extremities and pulmonary embolism in neurological patients in the intensive care unit using intermittent pneumatic compression]. Zhurnal Nevrologii i Psikhiatrii Imeni S.S. Korsakova[Journal of Neurology and Psychiatry Named After S.S. Korsakov], 118(10), 25–29. https://doi.org/10.17116/jnevro201811810125
- 43. ^{a, b}Chibbaro, S., Cebula, H., Todeschi, J., Fricia, M., Vigouroux, D., Abid, H., Kourbanhoussen, H., Pop, R., Nannavecchia, B., Gubian, A., Prisco, L., Ligarotti, G. K. I., Proust, F., & Ganau, M. (2018). Evolution of prophylaxis protocols for venous thromboembolism in neurosurgery: Results from a prospective comparative study on low-molecular-weight heparin, elastic stockings, and intermittent pneumatic compression devices. World Neurosurgery, 109, e510–e516. https://doi.org/10.1016/j.wneu.2017.10.012
- 44. ^Kim, K. I., Kim, D. K., Song, S. J., Hong, S. J., & Bae, D. K. (2019). Pneumatic compression device does not show effective thromboprophylaxis following total knee arthroplasty in a low incidence population. Orthopaedics & Traumatology, Surgery & Research, 105(1), 71–75. https://doi.org/10.1016/j.otsr.2018.11.010
- 45. ^Tyagi, V., Tomaszewski, P., Lukasiewicz, A., Theriault, S., & Pelker, R. (2018). The role of intraoperative intermittent pneumatic compression devices in venous thromboembolism prophylaxis in total hip and total knee arthroplasty.

 Orthopedics, 41(1), e98–e103. https://doi.org/10.3928/01477447-20171114-06
- 46. ^{a, b}Nam, J. H., Kim, D. H., Yoo, J. H., Hwang, J. H., & Chang, J. D. (2017). Does preoperative mechanical prophylaxis have additional effectiveness in preventing postoperative venous thromboembolism in elderly patients with hip fracture?—A retrospective case-control study. PLOS ONE, 12(11), e0187337. https://doi.org/10.1371/journal.pone.0187337
- 47. ^Hata, T., Yasui, M., Ikeda, M., Miyake, M., Ide, Y., Okuyama, M., Ikenaga, M., Kitani, K., Morita, S., Matsuda, C., Mizushima, T., Yamamoto, H., Murata, K., Sekimoto, M., Nezu, R., Mori, M., Doki, Y., & for the Clinical Study Group of Osaka University, Colorectal Group (CSGOCG) Investigators. (2019). Efficacy and safety of anticoagulant prophylaxis for prevention of postoperative venous thromboembolism in Japanese patients undergoing laparoscopic colorectal cancer surgery. Annals of Gastroenterological Surgery, 3(5), 568–575. https://doi.org/10.1002/ags3.12279
- 48. ^Jung, Y. J., Seo, H. S., Park, C. H., Jeon, H. M., Kim, J. I., Yim, H. W., & Song, K. Y. (2018). Venous thromboembolism incidence and prophylaxis use after gastrectomy among Korean patients with gastric adenocarcinoma: The PROTECTOR randomized clinical trial. JAMA Surgery, 153(10), 939–946. https://doi.org/10.1001/jamasurg.2018.2081
- 49. ^Dong, J., Wang, J., Feng, Y., Qi, L. P., Fang, H., Wang, G. D., Wu, Z. Q., Wang, H. Z., Yang, Y., & Li, Q. (2018). Effect of low molecular weight heparin on venous thromboembolism disease in thoracotomy patients with cancer. Journal of Thoracic Disease, 10(3), 1850–1856. https://doi.org/10.21037/jtd.2018.03.13



- 50. a, b Dhakal, P., Wang, L., Gardiner, J., Shrotriya, S., Sharma, M., & Rayamajhi, S. (2019). Effectiveness of sequential compression devices in prevention of venous thromboembolism in medically ill hospitalized patients: A retrospective cohort study. Turkish Journal of Haematology, 36(3), 193–198. https://doi.org/10.4274/tjh.galenos.2019.2018.0413
- 51. ^Kamei, H., Onishi, Y., Kurata, N., Ishigami, M., & Ogura, Y. (2017). Donor selection and prophylactic strategy for venous thromboembolic events in living donors of liver transplantation based on results of thrombophilia screening tests. Annals of Transplantation, 22, 409–416. https://doi.org/10.12659/aot.902791
- 52. ^Rabe, E., Partsch, H., Morrison, N., Meissner, M. H., Mosti, G., Lattimer, C. R., Carpentier, P. H., Gaillard, S., Jünger, M., Urbanek, T., Hafner, J., Patel, M., Wu, S., Caprini, J., Lurie, F., & Hirsch, T. (2020). Risks and contraindications of medical compression treatment A critical reappraisal. An international consensus statement. Phlebology, 35(7), 447–460. https://doi.org/10.1177/0268355520909066
- 53. *Schwahn-Schreiber, C., Breu, F. X., Rabe, E., Buschmann, I., Döller, W., Lulay, G. R., Miller, A., Valesky, E., & Reich-Schupke, S. (2018). S1-Leitlinie Intermittierende Pneumatische Kompression (IPK, AIK) [S1 guideline on intermittent pneumatic compression (IPC)]. Der Hautarzt; Zeitschrift für Dermatologie, Venerologie, und verwandte Gebiete [The Dermatologist; Journal for Dermatology, Venereology, and related areas], 69(8), 662–673. https://doi.org/10.1007/s00105-018-4219-1