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Obesity, thrombosis, venous disease, lymphatic disease, and lipedema: An obesity medicine association (OMA) clinical practice statement (CPS) 2023

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ABSTRACT

Background: This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) is intended to provide clinicians with an overview on obesity, thrombosis, venous disease, lymphatic disease, and lipedema.

Methods: The scientific support for this CPS is based upon published citations, clinical perspectives of OMA authors, and peer review by the Obesity Medicine Association leadership.

Results: Topics in this CPS include obesity, thrombosis, venous disease, lymphatic disease, and lipedema. Obesity increases the risk of thrombosis and cardiovascular disease via fat mass and adiposopathic mechanisms. Treatment of thrombosis or thrombotic risk includes healthful nutrition, physical activity, and the requisite knowledge of how body weight affects anti-thrombotic medications. In addition to obesity-related thrombotic considerations of acute coronary syndrome and ischemic non-hemorrhagic stroke, this Clinical Practice Statement briefly reviews the diagnosis and management of clinically relevant presentations of deep vein thromboses, pulmonary embolism, chronic venous stasis, varicose veins, superficial thrombophlebitis, lipodermatosclerosis, corona phlebectatica, chronic thromboembolic pulmonary hypertension, iliofemoral venous obstruction, pelvic venous disorder, post-thrombotic syndrome, as well as lymphedema and lipedema – which should be included in the differential diagnosis of other edematous or enlargement disorders of the lower extremities.

Conclusions: This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) on obesity, thrombosis, and venous/lymphatic disease is one of a series of OMA CPSs designed to assist clinicians in the care of patients with the disease of obesity.

1. Introduction

In addition to Obesity Medicine Association (OMA) Position Statements [1,2], the OMA has published a series of Clinical Practice Statements, reviews, and round-table discussions regarding obesity-related diagnostic and treatment consideration of cardiometabolic topics such as nutrition [3], physical activity [3], pediatrics [4–6], race/ethnicities [7–10], body composition [11,12], behavior modification [13], anti-obesity medications [14–16], concomitant medications [17], diabetes mellitus [18], hypertension [19], mental stress [20], sleep apnea [21], and bariatric surgery [22]. This OMA Clinical Practice Statement explores the relationship between obesity and thrombosis, venous disease, lymphatic disease, and lipedema.

2. Obesity and thrombosis: summary

Table 1, Fig. 1, and Fig. 2 summarize how obesity may increase the risk of thrombosis.

2.1. Obesity and thrombosis: stroke

Mendelian randomization analyses are sometimes inconsistent regarding the association of obesity with stroke, when measured by body mass index (BMI) alone [23,24]. However, anthropometric assessments may demonstrate a more consistent Mendelian randomization correlation (i.e., correlation between increased abdominal obesity and stroke [25]). Regarding clinical trial evidence, with few exceptions, clinical trials report increased adiposity to be significantly associated with increased risk for stroke [26].

Some clinical data suggest an "obesity stroke paradox" where a lower rate of mortality and better functional outcomes are observed after stroke in patients with overweight or obesity (compared with patients categorized as "normal" or underweight). However, as with other obesity paradoxes [27], such "paradoxical" findings are often limited by methodological concerns (e.g., absence of randomized trials, retrospective nature of most studies, assessment of obesity with BMI, non-linear relationship between BMI and outcome, short follow-up period, and differences in co-morbid conditions and stroke characteristics) [28]. Overall, it may be that overweight and obesity are associated with a greater incidence of ischemic stroke in both men and women, with underweight, overweight, and obesity all associated with a higher risk of hemorrhagic stroke in men [29].

Regarding increased bleeding risk, individuals with obesity are at increased risk for intracerebral hemorrhage and extracranial bleeding,

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Table 1
Ten takeaway messages regarding obesity, thrombosis, venous disease lymphatic disease, and lipedema.

1.	Obesity-related fat mass disease can contribute to vascular compression and venous stasis, which increases the risk of thrombosis
2.	Obesity contributes to obstructive sleep apnea, which can increase the risk of thrombosis due to hypoxemia, endothelial dysfunction, inflammation, and increased sympathetic nervous system activity. Sleep apnea may also contribute to cardiometabolic diseases that predispose to thrombosis (e.g., insulin resistance, type 2 diabetes mellitus, hypertension, and dyslipidemia).
3.	Obesity can lead to adiposopathic inflammation, hypercoagulability, increased platelet activation, and reduced fibrinolysis.
4.	Obesity can lead to adiposopathic hypoxia and endothelial dysfunction.
5.	Obesity may lead to adiposopathic insulin resistance, type 2 diabetes mellitus, hypertension, and dyslipidemia, which may all predispose to thrombosis.
6.	The dosing of several anti-thrombotic/anti-platelet drugs is influenced by, or based upon, body weight.
7.	Obesity management beyond weight reduction in patients with acute coronary syndrome, pulmonary embolus, and deep vein thrombosis may include interventions based upon the specific diagnosis and appropriate anti-thrombotic/anti-platelet drugs use.
8.	Obesity medicine clinicians might best have a working knowledge of the diagnosis and treatment of chronic venous stasis, varicose veins, superficial thrombophlebitis, lipodermatosclerosis, corona phlebectatica, chronic thromboembolic pulmonary hypertension, iliofemoral venous obstruction, pelvic venous disorder, and post-thrombotic syndrome.
9.	Lymphedema can be inherited/congenital, or secondary to several potential causes. Extreme obesity can cause lower extremity lymphedema, and is termed "obesity-induced lymphedema" (OIL).
10.	It is often recommended that patients with lipedema and overweight/obesity engage in weight reduction; however, such efforts often result in minimal benefits regarding lipedema. This may contribute to frustration, eating disorders, increased obesity risk, depression, and other psychological disorders. The point is that regarding many thrombotic, venous, lymphatic, and lipedemic disorders, while obesity management is frequently recommended, patients should not be given the impression that weight reduction is a universal "cure." Similarly, patients should not be "blamed"when weight reduction efforts fail to reverse or prevent recurrent thrombotic or venous diseases.

at least partially explained by increased risk of hypertension [30]. In addition, individuals with higher degrees of obesity undergoing procedures such as percutaneous coronary intervention may have increased periprocedural bleeding. This might prompt consideration of radial, rather than femoral venous access [30].

2.2. Obesity and thrombosis: deep vein thrombosis and pulmonary embolism

Mendelian randomization analyses support an association between obesity and deep vein thrombosis, with or without pulmonary embolism [31]. Along with older age, female sex [32], cigarette smoking, malignancy, and prolonged bed rest, increased adiposity is associated with an increase in venous thromboembolism [33,34]. Obesity alone is an independent risk factor for venous thromboembolism [35], and a risk factor for recurrent venous thromboembolism [36], although admittedly, studies of the risk of venous thromboembolic recurrence among patients with obesity report heterogenous findings [37]. That said, in addition to obesity alone, and in addition to fat mass disease, the adiposopathic complications of obesity (insulin resistance, impaired glucose homeostasis, hypertension, and dyslipidemia) clearly play a major role in increasing thrombotic events [38].

2.3. Obesity and thrombosis: fat mass disease

Pregnancy is a well-known risk factor for thrombosis due to being a hypercoagulable state, as well as due to the gravid uterine compression of pelvic veins and inferior vena cava [39]. Similarly, the etiology of obesity-associated thrombosis is multifactorial, and includes “fat mass” pathogenic physical forces, clinically manifested by biomechanical and structural abnormalities that alter blood flow (See Fig. 1). Obesity may increase intraabdominal pressure with venous compression, which along with immobility or impaired gait, may result in blood stasis [40], and thus increase the risk of thrombosis [32]. A common clinical example of how immobility may partially contribute to thrombotic lesions (e.g., deep vein thrombosis) is the increased risk of thromboembolism during surgery among those with increasing BMI [41]. Common procedures to help prevent post-operative thromboembolic events are early ambulation/walking, sequential compression devices to the lower extremities, and if appropriate, anticoagulation [42].

2.4. Obesity and thrombosis: obstructive sleep apnea

Obesity is a major cause of obstructive sleep apnea [21]. Obstructive sleep apnea may increase the risk of venous thromboembolism due to creation of a pro-inflammatory state, intermittent hypoxia, blood hypercoagulability, venous stasis, sympathetic nervous stimulation, and endothelial dysfunction [43,44].

2.5. Obesity and thrombosis: adiposopathic inflammation, hypercoagulability, and platelet hyperreactivity

Obesity increases the risk of thrombotic complications (e.g., acute myocardial infarction, stent thrombosis after percutaneous interventions, ischemic stroke, and vein thrombosis), especially when the obesity is manifested by an adiposopathic body composition (i.e., central obesity) [45]. Among the mechanisms accounting for the increased risk of thrombosis with obesity are increased inflammation, increased systemic oxidative stress, altered blood flow, damage to the vascular endothelium (i.e., endothelial dysfunction), and reduced antithrombotic processes [45].

While the published data is not always consistent, reports suggest adiposopathic alterations in adipokines (e.g., increased leptin and decreased adiponectin) enhance platelet activation and aggregation [32,45], increase platelet counts [32], and promote coagulation through increased circulating levels of von Willebrand factor [46], tissue factor [47], factor VII [48] and VIII [46], and fibrinogen [49], all favoring a mild-to-moderate hypercoagulable state. Obesity is also associated with increased secretion of plasminogen activator inhibitor (PAI)-1 [50] and thrombin activatable fibrinolysis inhibitor (TAFI) [51], both that impair fibrinolysis [40,45]. Other adiposopathic inflammatory factors may also increase the risk of thrombosis, such as increased secretion of tumor necrosis factor (i.e., produced by both adipocytes and adipose tissue stroma) which may also upregulate tissue factor [52] – leading to formation of thrombin and is thus a primary initiator of blood coagulation [53]. Bariatric surgery may improve many of these hemostatic factors potentially leading to less potential for thrombosis, which may be as the result of weight reduction, improvement in adiposopathic metabolic diseases, or both [54].

2.6. Obesity and thrombosis: hypoxia

Three major risk factors for thrombus formation are described by Virchow’s triad, which includes venous stasis, endothelial injury, and increased coagulation [32,55]. Hypoxia is both a cause and an effect of thrombosis. Tissue hypoxia may occur when blood flow is reduced (e.g., immobility, disruptive trauma, or vessel obstruction such as due to compression from body fat mass leading to hypercoagulability and thrombosis). Conversely, impaired oxygenation may trigger molecular and cellular signaling pathways that contribute to thrombosis (e.g., inflammation, endothelial dysfunction, increased prothrombotic state, and increased platelet activation [55]). Hypoxia can also alter blood rheologic effects, increase hemoglobin/hematocrit concentration, increase blood viscosity, and impair blood flow [56], which also increases the risk of thrombosis. In short, hypoxia may be both a clinical consequence of vascular occlusion and a stimulus for thrombogenesis [55].

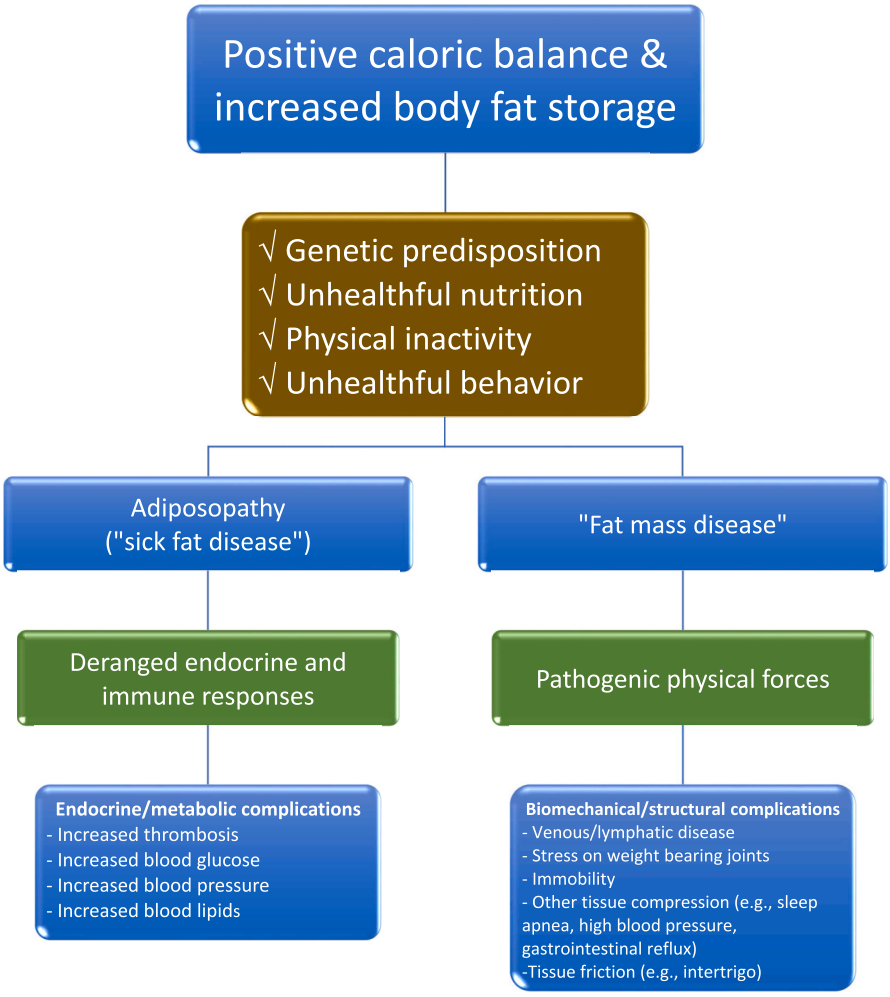

Fig. 1. Obesity, adiposopathy (sick fat disease), fat mass disease, and obesity complications. An increase in body fat can ultimately lead to endocrine/metabolic and biomechanical/structural abnormalities, potentially leading to complications such as increased risk of thrombosis and venous/lymphatic disease (Adapted from Ref. [19]).

2.7. Obesity and thrombosis: endothelial dysfunction

The vascular endothelium modulates vascular function and structure. Endothelial production of the vasodilatory nitric oxide protects the vasculature against atherosclerosis and thrombosis. Adiposopathic body composition (i.e., abdominal obesity) is associated with decreased nitric oxide availability secondary to insulin resistance and enhanced oxidative stress, resulting in endothelial dysfunction [18]. Adiposopathic perivascular adipose tissue may have an especially adverse effect on nitric oxide production [57]. Pro-inflammatory adipocytokines reduce nitric oxide availability, impairing the vasodilatory effects of perivascular adipose tissue (PVAT), resulting in endothelial dysfunction that predisposes to thrombosis [58]. Adiposopathic inflammation (e.g., release of pro-inflammatory cytokines, increased expression of adhesion molecules) may also disrupt coagulation/anticoagulation balances relative to procoagulant, anticoagulant, and fibrinolytic effects, potentially leading to a prothrombotic state. Shared mechanisms underlying pathogenic alterations in endothelial dysfunction may help explain why venous and arterial thrombosis may be linked [59].

2.8. Obesity and thrombosis: insulin resistance and diabetes mellitus

Insulin resistance and type 2 diabetes mellitus are common adiposopathic complications of obesity [18]. Some suggest that diabetes mellitus is not an independent risk factor when corrected for BMI [60]. That said, patients with insulin resistance and type 2 diabetes mellitus may be at increased risk for vascular ischemia due to predisposition to more extensive atherosclerotic disease and an enhanced thrombotic environment due to increased platelet activation, increased procoagulant protein activity, and compromised fibrinolytic system [61]. Obesity-mediated hyperglycemia and insulin resistance [18] increase the risk of atherosclerosis, adversely affect endothelial function, increase inflammation, increase platelet number and activation (i.e., prothrombotic state), as well as modify coagulation and fibrinolytic factors, resulting in an increased risk of fibrinolysis-resistant clots among patients with diabetes mellitus [62]. Overall, in patients with diabetes, enhanced thrombosis in combination with enhanced atherosclerosis necessitate preventive measures to reduce vascular disease risk, with therapeutic interventions that include weight reduction in patients with diabetes and obesity [63].

2.9. Obesity and thrombosis: hypertension

Hypertension is a common adiposopathic complication of obesity [19]. Some suggest that hypertension is not an independent risk factor for thrombosis when corrected for BMI [60]. That said, patients with hypertension are at increased risk for deep vein thrombosis, such as after orthopedic surgery [64]. Increased blood pressure contributes to endothelial dysfunction (i.e., vasoconstriction, cell proliferation, and proinflammatory and prothrombotic state) [65], altered blood flow due to

Fig. 2. Mechanisms linking obesity to increased risk of thrombosis.

shear stress, increased arterial stiffness, and platelet activation [66]. Patients with obesity and hypertension [19] often have increased activation of the renin-angiotensin system (e.g., potentially leading to increased reactive oxygen species, inflammation, and increased thrombin generation) [67,68] and increased sympathetic nervous system activation [19] (e.g., potentially leading to cardiac dysrhythmias such as atrial fibrillation, vasoconstriction, altered blood flow, inflammation, and platelet activation) which have pro-thrombotic effects as well. Of interest is that the interactions between renin-angiotensin and autonomic nervous system are bidirectional [69].

2.10. Obesity and thrombosis: dyslipidemia

Dyslipidemia is a common adiposopathic complication of obesity [70]. Some suggest that dyslipidemia is not an independent risk factor for thrombosis when corrected for BMI [60]. Increased atherogenic lipoproteins can contribute to endothelial dysfunction (e.g., inflammation and oxidative stress), potentially leading to increased prothrombotic processes and reduced antithrombotic processes. Dyslipidemia mediated atherosclerosis can increase the risk of thrombosis via disruptive rheologic effects upon blood flow and obstruction resulting in hypoxia. Dyslipidemia-associated atherosclerotic inflammation can lead to chronic platelet activation [71] and endothelial dysfunction. Atheromatous plaque rupture can acutely activate platelets and cause thrombosis, leading to acute myocardial infarction or acute stroke [72].

2.11. Obesity and thrombosis: unhealthful nutrition and physical inactivity

Nutrition factors most associated with increased risk of thrombosis include high saturated fat intake and excessive salt intake, which are dietary components often found in ultra-processed foods [73]. Limited intake of saturated fats [74] and sodium are mainstay nutritional recommendations to reduce cardiovascular disease risk [3,75]. It is perhaps unsurprising that the components of the dietary patterns most associated with a decreased risk of thrombosis are the ones with the greatest evidence of reduced cardiovascular disease risk (e.g., Mediterranean Diet or some plant-based diets) [3,76,77].

Among physically inactive individuals, acute physical exertion can promote shear stress, atherosclerotic plaque rupture, thrombosis, and an acute coronary syndrome [78,79]. Otherwise, chronic physical inactivity can also increase the risk of thrombosis due to reduced blood flow, reduced blood pumping, venous stasis, increased platelet activation [79], and increased risk of pro-thrombotic diseases such as obesity, diabetes mellitus, hypertension, dyslipidemia, and sleep apnea.

2.12. Obesity and thrombosis: contraception and pregnancy

Obesity and estrogen-containing contraceptives may increase the risk of thromboembolism leading to cardiovascular events [80]. Progestin-only contraceptives may be a safer alternative to estrogen-containing oral contraceptive therapies [80]. Most evidence suggests progestins contribute little to no increased risk of venous or arterial events, with the same conclusion applicable to progestin injectable/subdermal implant contraception [81,82]. Similarly, progestin-containing (and copper containing) intrauterine devices are not thought to increase thromboembolic risk [82,83]. General principles applicable to contraceptive use and thromboembolic risk include [84]: (a) higher doses of estrogens (such as the historic 150 μg of estrogen used in early formulations [82]) increase the risk of venous thromboembolism, with doses less than 35 to 50 helping to minimize venous thrombotic risk; (b) insufficient evidence supports contraceptive patches or vaginal rings have differing risks of venous thromboembolism compared with combined oral contraceptives; and (c) irrespective of the type of contraception used, the risk of venous thromboembolism is increased with the presence of risk factors such as obesity, smoking, and hereditary/genetic predisposition.

Regarding pregnancy, deep venous thrombosis is associated with high mortality, morbidity, and cost. Pulmonary embolism is a leading cause of maternal death in the developed world. Women are up to 5 times more likely to develop deep vein thrombosis when pregnant [85] Pregnancy may represent a pro-thrombotic state, in that pregnancy has all components of Virchow's triad (See section 2.6). [85]. An enlarging uterus contributes to venous stasis. Venous stasis can contribute to endothelial damage. The physiologic preparation for the hemostatic challenge of delivery can be manifest by hypercoagulation due to alterations in blood factors leading to thrombosis [85]. Approximately 80 % of venous thromboembolic events during pregnancy are deep vein thrombosis while 20 % are pulmonary emboli; approximately one third of pregnancy-related DVT and half of pregnancy-related pulmonary emboli occur after delivery [86]. Post-pregnancy long-term risk of venous thromboembolism is high among women with high normal body mass index compared with lean women; women with pregnancy and severe obesity have a markedly high risk for venous thromboembolism [87].

3. Obesity and thrombosis: other risk factors for thrombosis

When patients with obesity experience a thromboembolic event, it is prudent to not assume all cases are due to the obesity. Other risk factors may be present that may need to be diagnosed and managed. Beyond obesity, risk factors for thrombosis include older age, race (e.g., African Americans), smoking, surgery, trauma, immobilization, malignancy, pregnancy (see Section 2.12), antiphospholipid syndrome, concomitant medical conditions (e.g., heart disease, diabetes mellitus, hypertension, dyslipidemia, sleep apnea, asthma, renal disease, hematologic diseases, rheumatologic diseases, inflammatory bowel disease, sepsis, coronavirus disease, polycystic ovary syndrome), medications (e.g., systemic glucocorticoids, estrogens, tamoxifen, testosterone, and some antidepressants) and prior history of thromboembolism, which may reflect a persistent acquired risk factor or an inherited hypercoagulable genetic disorder (e.g., factor V Leiden mutation [88], prothrombin gene mutation, protein C deficiency, protein S deficiency, antithrombin deficiency, dysfibrinogenemia, Factor XII deficiency, hyperhomocyteinemia, non-O

blood group).

4. Obesity and thrombosis: treatment

4.1. Obesity and thrombosis treatment: nutrition

A definitive conclusion regarding which foods have the best potential to reduce thrombotic risk is challenging. The objective evidence supporting a reduction in thrombosis with certain foods is often sparce and inconsistent [76]. The greatest evidence supporting potential benefits of specific foods is from smaller experimental studies or from studies regarding cardiovascular disease events. Large-scale, prospective, randomized human studies specifically evaluating thrombosis are relatively lacking. With these caveats aside, experimental studies support that foods most likely to reduce thrombogenic processes include vegetables, fruits, marine fish, olive oil, nuts, cocoa, and red wine [76].

4.2. Obesity and thrombosis treatment: physical activity

Regular physical activity is associated with a lower incidence of venous thromboembolism [89].

4.3. Obesity and thrombosis treatment: anti-obesity medications

Definitive studies are scarce regarding the effects of anti-obesity medications on thrombotic events. Detailed analysis of published and forthcoming cardiovascular outcome studies are pending [14]. Nonetheless, the general sense is that a reduction in body weight with anti-obesity medications may lower inflammatory and prothrombotic markers [90].

4.4. Obesity and thrombosis treatment: bariatric surgery

Thromboembolism is an important acute perioperative complication of bariatric surgery [91,92]. On a more chronic postoperative basis in patients treated for obesity, weight reduction via bariatric surgery reduces venous thromboembolic risk, mainly due to a reduction in deep vein thrombosis [93]. In addition to other health benefits [22], bariatric surgery improves many of the risk factors for thrombosis as described in Section 2. Among the more important effects of bariatric surgery are a less vascular compression and venous stasis due to a reduction in fat mass impairment of blood flow (see Figs. 1 and 2), reduced inflammation, reduced hypercoagulability, reduced platelet activation [54], improvements in sleep apnea and hypoxia [94], as well as improvement in metabolic abnormalities that may predispose to thrombosis (e.g., enhanced insulin sensitivity, reduced blood glucose, reduced blood pressure, and reduced blood lipids) [95]. Finally, bariatric surgery may allow for increased physical activity and enhanced mobility [96].

4.5. Obesity and thrombosis treatment: anti-thrombotic medications

The adiposopathy that often accompanies obesity may be characterized by adipocyte hypertrophy, hypoxia, and cellular and organ dysfunction, resulting in a pro-inflammatory response via the release of pro-inflammatory cytokines (e.g., tumor necrosis factor and interleukins) and chemokines (e.g., ICAM or intercellular adhesion molecule and MCP-1 or monocyte chemoattractant protein-1) that attract pro-inflammatory cells such as neutrophils, CD8 T cells, B cells, mast cells, and interferon [18,30]. In addition, macrophages polarize towards a pro-inflammatory M1 phenotype, remove the dead adipocytes, and release tissue factor which helps trigger coagulation. Adiposopathic adipocytes and associated stromal cells also release plasminogen activator inhibitor-1 (especially in visceral adipose tissue) which has anti-fibrinolytic and pro-thrombotic activities, and potentially helps mediate venous thromboembolism that occurs in patients with obesity [30,97]. Finally, in addition to endocrinopathies (e.g., increased leptin and decreased adiponectin) and the immunopathies described before, the adiposopathy of obesity also results in a net release of free fatty acids, which contribute to lipotoxicity, insulin resistance, macrophage polarization, reactive oxygen species, and platelet activation [18,30]. Table 2 summarizes the consensus of "Antithrombotic therapy and body mass: an expert position paper of the European Society of Cardiology Working Group on Thrombosis" [30].

5. Obesity and venous thrombosis

5.1. Classification

Table 3 provides a summary of arteriovenous thromboembolic diseases that may be associated with obesity. Chronic venous disease can be classified based on CEAP (clinical, etiologic, anatomic, and pathophysiologic) criteria [162].

- C0: No visible or palpable signs of venous disease
- C1: Telangiectasia or reticular veins
- C2: Varicose veins
  - o C2r: Recurrent varicose veins
- C3: Edema
- C4: Changes in skin and subcutaneous tissue secondary to chronic venous disease
  - o C4a: Pigmentation or eczema
  - o C4b: Lipodermatosclerosis or atrophie blanche
  - o C4c: Corona phlebectatica
- C5: Healed venous ulcers
- C6: Active venous ulcers
  - o C6r: Recurrent active venous ulcer

5.2. General principles of venous thrombosis management in patients with obesity [88,163]

- Risk factors for thrombosis beyond obesity
  - o Personal or family history of thrombotic disease
  - o Inherited coagulation or platelet disorders
  - o Older age
  - o Female sex
  - o Pregnancy
  - o Antiphospholipid antibody syndrome
  - o Smoking
  - o Immobilization
  - o Malignancy
  - o Pathogenic medical conditions involving the following body systems: cardiovascular, renal, hematologic, rheumatologic, gastrointestinal, infectious, respiratory, and endocrine (e.g., polycystic ovary syndrome and diabetes mellitus)
  - o Trauma or surgery (especially major orthopedic and neurovascular surgery)
  - o Medications (e.g., estrogens, systemic glucocorticoids, tamoxifen, testosterone, and some antidepressants [164])
  - o Inflammatory disorders
- Diagnosis of venous thrombosis
  - o D-dimer testing
  - o Venous ultrasonography
  - o CT pulmonary angiography and ventilation-perfusion scan for possible pulmonary emboli
  - o Venography (i.e., contrast dye and imaging via X-ray, computed tomography, or magnetic resonance imaging)
- Challenges with imaging techniques among patients with obesity suspected of deep venous thrombosis and/pulmonary embolism [132].
  - o Imaging table sizes and gantry diameter may not accommodate patients with severe obesity
  - o Obesity may compromise image quality

Table 2
Summary of anti-thrombotic/anti-platelet medication treatment of patients with obesity based upon the 2018 European Society of Cardiology Working Group [30]. Obesity can affect drug pharmacodynamics and pharmacokinetics [14]. Shown are some dosing and usage considerations of anti-thrombotic/anti-platelet medication treatment of patients with obesity. See Tables 3 and 4 in Ref. [30]. Dual antiplatelet therapy (DAPT) is the use of two antiplatelet therapies for a variable length of time after acute coronary syndrome (i.e., myocardial infarction or unstable angina) or stroke - often being aspirin and a P2Y12 inhibitor. Because obesity may result in reduced sensitivity to antiplatelet therapy, such as with either aspirin or clopidogrel, then such patients may benefit from treatment with more potent platelet inhibitors [106].

Category of anti-thrombotic/anti-platelet medication	Discussion
Aspirin	If aspirin is to be used for anti-thrombotic intent (e.g., reduce risk of myocardial infarction or stroke), then unless otherwise clinically indicated due to gastrointestinal safety, plain (rather than enteric coated) low dose aspirin may be preferred in some patients with obesity. Also, dose or frequency of administration may need to be increased in patients with very high body mass index (BMI).
Thienopyridines (P2Y12 inhibitors)	Although dosing adjustment is not typically weight based, severe obesity may reduce active metabolite generation for clopidogrel; thus, treatment with prasugrel and ticagrelor may be preferable to clopidogrel for patients experiencing acute coronary syndrome.
Glycoprotein IIb-IIIa inhibitors (e.g., abciximab, eptifibatide, and tirofiban)	These inhibitors of platelet aggregation used in patients with acute coronary syndrome should be adjusted based upon body weight (i.e., kg) [98].
Vitamin K antagonist (e.g., warfarin)	Warfarin is used for prophylaxis and treatment of venous thrombosis and pulmonary embolisms. The effect of BMI on warfarin is limited; however, closer surveillance of international normalized ratio (INR) may be warranted.
Direct FXa and FIIa inhibitors (e.g., rivaroxaban, edoxaban, apixaban, dabigatran)	Direct oral anticoagulants (DOAC) may be used for stroke prevention among patients with atrial fibrillation or venous thromboembolism. The effects of BMI on DOAC are limited. Thus, they may be considered generally safe and effective across weight classes [99]. A systematic review and meta-analysis suggests that DOAC has similar efficacy and safety in preventing recurrent thromboembolic events in patients with severe obesity [100].
Heparin	Unfractionated heparin (UFH) is administered intravenously or via multiple subcutaneous injection, and commonly used for unstable angina or non-ST segment elevation myocardial infarction during cardiac procedures such as percutaneous coronary interventions. Due to a lower half-life more amenable to reversal, UFH may be preferred for patients more likely to have bleeding complications; however, UFH does require frequent monitoring of aPTT and potential heparin dose adjustment. Dosing is weight-based, with patients having higher classes of obesity perhaps requiring less body weight adjusted UFH. Lower molecular weight heparin (LMWH) is administered by subcutaneous injection, does not require routine monitoring of activated partial thromboplastin time (aPTT), and is commonly used to treat and prevent deep vein thrombosis and venous thromboembolism. While dosing is weight based, it is uncertain that the dose of LMWH should be capped at higher ranges BMI; instead, dosing might better be determined by measuring anti-Xa activity, which is the primary measure of LMWH anticoagulant effect [101] Fondaparinux is a synthetic LMWH administered subcutaneously once daily and has weight-based dosing.
Bivalirudin	Bivalirudin is a short-acting direct thrombin inhibitor indicated for intravenous anticoagulation in patients with acute myocardial infarction, unstable angina, percutaneous coronary intervention, and thrombosis in patients with a history of heparin-induced thrombocytopenia (HIT) [102]. Bivalirudin dosing is weight based.
Fibrinolytic drugs (e.g., streptokinase and fibrin-specific plasminogen activators such as alteplase and tenecteplase)	Fibrinolytic drugs are used in acute ST-segment elevation myocardial infarction (STEMI), acute ischemic stroke, pulmonary embolism, or mechanical heart valve thrombosis. Streptokinase dosing is not weight based [103]. Alteplase [104] and tenecteplase [105] dosing are weight based.

o Patients with obesity may present difficulties in locating anatomical landmarks, which can impair proper technique and positioning
o Patients with obesity may require higher radiation doses and prolonged CT imaging time, increasing radiation exposure
o CT pulmonary angiography is the most common imaging study to assess for potential pulmonary embolism. While the accuracy of CT pulmonary angiography is generally good, obesity may contribute to increased risk of worsening diagnostic yield with indeterminate results. Also, because obesity is associated with higher blood volume, increased contrast medium or more concentrated contrast medium may be required. Finally patients with obesity have increased soft tissue thickness, which may contribute to difficulty with intravenous access, which may require ultrasound guidance to locate veins.
o CT venography is rarely used alone, but sometimes used to evaluate veins of the calves, iliac veins, inferior vena cava and profunda femora veins – which may be applicable among patients with obesity having deep vein disorders (See Table 3).
o Dual-energy CT (DECT) may have some advantages over single-source CT in the diagnosis of pulmonary embolism; however, DECT scanners may have limitations in patients with obesity due to smaller field of view (FOV) – although this may be less of a challenge with newer DECT machines.
o Peripheral vein ultrasound is the imaging examination of choice for suspected deep vein thrombosis; however, ultrasonography has a substantial likelihood of impaired image visualization among patients with obesity
o Lung ventilation perfusion scan (VQ Scan) may still be used to help diagnose pulmonary embolism, especially in patients who do not tolerate the intravenous contrast, at risk with the radiation exposure from definitive diagnostic test (i.e., CT pulmonary angiography), have severe renal insufficiency, or severe allergic reaction to contrast material [165]. Obesity complicates VQscans due to exam table weight limits and degradation of image quality.
o Conventional lower extremity venography and pulmonary angiography are as routine due to CT pulmonary arteriography. Additionally, regarding patients with obesity, fluoroscopy tables

Table 3
Summary of arteriovenous thromboembolic diseases that may be associated with obesity.

Arteriovenous thromboembolic disease	Description	Diagnostic considerations with obesity	Treatment considerations with obesity
Acute coronary syndrome [e.g., unstable angina, non-ST Segment Myocardial Infarction (NSTEMI) and ST-Segment Elevation Myocardial Infarction (STEMI)]	An important aspect of acute coronary syndrome (ACS) involves plaque rupture, with fatty core activating platelets and promoting thrombus formation. In patients with STEMI, those with mild to moderate obesity may have lower odds of mortality while those with severe obesity may have higher odds of mortality compared to those without obesity [107].	Regarding diagnosis of potential ischemia or infarction, patients with obesity often have electrocardiogram abnormalities [108]. Obesity may also be associated with baseline elevated high sensitivity troponin measures [109]. Echocardiography and nuclear cardiology may have technical limitations in patients with obesity [110]. In patients with mild to moderate obesity, coronary computed tomography (CCTA) can effectively be performed in patients with obesity via later generation CCTA machines [111]. Obesity may present challenges with cardiac catheterization due to technical challenges, such as detection of hematomas at catheter injection site, vessel injury, increased radiation exposure, poor wound healing, and diminished postoperative mobility and respiratory recovery.	Reports vary regarding outcomes after coronary artery bypass grafting (CABG) among patients with overweight and mild to moderate obesity [112–116]. However, severe obesity increases risk of early CABG complications and extends length of hospital stay [117]. Similarly, while patients with mild to moderate obesity compare favorably to those without obesity, regarding percutaneous coronary intervention (PCI), long-term mortality increases among patients with severe obesity (BMI > 40 kg/m^2) [118]. Dose of antithrombotic and anti-platelet therapies may need to be adjusted (see Table 2). Cardiovascular disease events are reduced by treatment with anti-obesity medications such as semaglutide [119], as well as bariatric surgery [120].
Ischemic (non-hemorrhagic) stroke	Obesity increases the risk of ischemic thrombotic stroke, especially in patients with adiposopathic complications such as hypertension, diabetes mellitus, dyslipidemia, atherosclerosis, atrial fibrillation, and obstructive sleep apnea [26,121].	Clinical diagnosis of stroke includes sudden numbness, weakness of the face, arm, or leg (especially on one side of the body), confusion, trouble speaking, difficulty understanding speech, headache, dizziness, and ataxia. Computed tomography (CT) scan is often the initial imaging study. Magnetic resonance Imaging (MRI) may provide greater detail. In some cases, echocardiography is used to evaluate for possible cardioembolic stroke. Echocardiography may have technical limitations in patients with obesity [110], and CT scan and MRI machines may have weight limitations [122,123] When necessary and when applicable machines are available, patients with obesity should undergo image testing via machines with high table load limits, wide gantry apertures, larger scan fields of view, and more powerful generators [124].	Treatment options for ischemic thrombotic stroke include anticoagulation and possibly thrombolytic therapy (see Table 2) or mechanical thrombectomy. Achieving a healthy body weight is a more long-term goal, as is stopping secondary causes (e.g., smoking, medications), healthful nutrition and routine physical activity, as well as optimal management of blood sugar, blood pressure, and blood lipids. This often requires combination cardiovascular drug treatment [125]. Rehabilitation improvement in functional parameters may be impaired among patients with obesity [126]. Glucagon-like peptide −1 receptor agonists (often used as anti-diabetes and anti-obesity medications) can reduce the risk of stroke [127]. Bariatric surgery in patients with obesity may also reduce the risk of stroke [128].
Deep vein thrombosis (DVT)	DVT is characterized by thrombus formation in a deep vein (e.g., legs). If a section of the DVT breaks off and circulates to the lung, then this may result in a life-threatening pulmonary embolism. Phlegmasia cerulea dolens is a severe manifestation of DVT which results in pain and cyanosis of the extremity, which may lead to compartment syndrome, arterial ischemia, gangrene, amputation, and death [129]	Risk factors for DVT include age > 65 years, inherited or acquired coagulation or platelet disorders, family history, female sex, pregnancy, inactivity, immobility, surgery, sedentary occupations, smoking, malignancy, medications (e.g., estrogens), atrial fibrillation, heart failure, obstructive sleep apnea, and obesity. Symptoms include usually unilateral swelling and pain to the calf or thigh, with warmth, redness, and visible veins [130]. Severe obesity (i.e., ≥ 40 kg/m^2) may limit the accuracy of duplex ultrasound studies [131]. Patients with obesity may have weights that exceed imaging table weight limits (i.e., computed tomography or CT) [132]	Table 2 lists various treatments for thrombosis, including several medications whose dose is adjusted based upon body weight. Historically, treatment for DVT included acute heparin for about a week, followed by longer term warfarin [133]. For patients with uncomplicated DVT, direct oral anticoagulants (DOAC) may be used as first line therapy, with less risk for bleeding [134,135] (see Table 2). Thrombolytic therapy may be considered for patients with limb threatening DVT (e.g., phlegmasia cerulea dolens) [135].
Pulmonary embolus (PE)	A PE occurs when a blood clot breaks (i.e., from a DVT) and circulates to become lodged into a pulmonary artery, leading to potentially life-threatening hypoxia.	The symptoms of a PE include sudden onset of chest pain, shortness of breath, and feeling of impending doom. Diagnostic techniques include CT pulmonary angiography (CTPA), ventilation-perfusion scan (V/Q scan), or Doppler ultrasound for DVT detection. As previously noted, diagnosis of both DVT and PE may be	As with DVT, treatment of PE has historically included acute heparin followed by longer term warfarin. Treatment approaches are now increasingly being based on severity of the clinical presentation (i.e., Pulmonary Embolism Severity Index). For example, with otherwise uncomplicated PE (or DVT), DOAC can be first-line treatment.

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Table 3 (*continued*)

Arteriovenous thromboembolic disease	Description	Diagnostic considerations with obesity	Treatment considerations with obesity
		challenging in patients with high BMI because: (1) patients with obesity may have baseline dyspnea, tachypnea, tachycardia, hypoxemia, leg edema/skin changes and cellulitis, which are not necessarily related to pulmonary venous thromboembolism, (2) because d-dimer (i.e., global biomarker for activation of coagulation and fibrinolysis) levels are higher in patients with obesity at baseline [136], and (3) because of challenges with imaging studies when evaluating patients at very high BMI [132,137,138].	Conversely, for patients with severe complications, more aggressive therapies such as thrombolysis and surgical interventions may be considered [135]. Table 2 describes medication dosing of PE and DVT treatments, respective to patient body weight.
Chronic venous stasis (chronic venous insufficiency) and venous ulcers	Chronic venous stasis involves venous vasculopathies and venous valvular dysfunction impairing efficient blood flow from the lower extremities back to the heart. Obesity (especially the compressive effects of abdominal obesity) may result in structural and hemodynamic venous changes that contribute to chronic venous stasis [139].	Pooling of blood with chronic venous stasis can cause lower extremity edema, pain, cramps, and/or pruritis. The skin may become erythematous and discolored with development of varicose veins. Impaired blood flow can contribute to venous ulcers. Patients with obesity are at increased risk for other potentially confounding diagnoses, such as obesity-related edema, congestive cardiomyopathy, DVT, lymphedema, lipedema, peripheral artery disease, cellulitis, peripheral neuropathy, and arthritic and joint disorders. Diagnosis sometimes requires duplex ultrasound, CT scans, or venography – with imaging studies sometimes challenging when evaluating patients at very high BMI [132,137,138].	Treatment of chronic venous stasis includes increased mobility, elevation of the lower extremities at rest, compression stockings or bandages, pain medications, and sometimes surgical procedures. Venous ulcers require wound care [140]. Treatment outcomes for chronic venous stasis are poor for patients with severe obesity, suggesting aggressive weight reduction management should be considered first line therapy [141]. For example, surgically-induced weight reduction may effectively help correct chronic venous stasis found in patients with obesity [142].
Varicose veins	Similar to the pathogenic findings of obstruction of deeper veins, superficial varicose veins may occur due to dysfunctional venous valves, resulting in pooling of blood and enlarged, twisted, and swollen veins – typically within the skin of the lower extremities.	Increased body fat (especially central obesity) may compress abdominal veins, impairing venous return from the lower extremities. Other than central obesity, risk factors for varicose veins include family history of venous disease, female sex, older age, prolonged standing, and chronically increased intra-abdominal pressure due to pregnancy, chronic constipation, and abdominal tumor [143]. Depending on the quality of the equipment, expertise of the technician, and proper interpretation by the reader, duplex ultrasound may be useful to evaluate for venous reflux [144].	Treatment of varicose veins include weight reduction among those with obesity, routine physical activity, external compression, avoidance of prolonged standing and straining, wearing nonrestrictive clothing, and leg elevation [143]. More interventional treatments include external laser thermal ablation, endovenous thermal ablation, endovenous sclerotherapy, as well as ligation and phlebectomy (i.e., vein stripping) [143,144]. Some reports suggest that foods high in anti-oxidants may improve vascular function and reduce risk of thrombotic events [145].
Superficial thrombophlebitis	Superficial thrombophlebitis is the inflammation of a superficial vein of an extremity, accompanied by thrombus formation.	Beyond obesity, other risk factors for superficial thrombophlebitis include older age, exogenous estrogens, autoimmune or infectious diseases, recent trauma or surgery, active malignancy, history of venous thromboembolic disease, and respiratory or cardiac failure, and especially a history of varicose veins [146]. Symptoms of superficial thrombophlebitis include localized pain, redness, warmth, and swelling at the site of the affected vein. It can also be associated with certain medical conditions like clotting disorders.	Superficial thrombophlebitis is often caused by injury to the vein, intravenous catheters, presence of varicose veins, or underlying coagulation or platelet disorders. Among individuals at low risk for DVT, treatment includes local heat and nonsteroidal anti-inflammatory agents. For more severe cases, anticoagulants may also be recommended [146] (see Table 2).
Lipodermatosclerosis	Lipodermatosclerosis is associated with venous insufficiency and primarily affects the skin and underlying tissue of the lower legs. The skin is often discolored with darkened pigmentation, swollen [147], and can sometimes give a shiny appearance. Differential diagnosis may include cellulitis, erythema nodosum, trauma-induced fat necrosis and other panniculitides, granuloma annulare,	Obesity is a risk factor for chronic venous insufficiency, thus increasing the risk of lipodermatosclerosis. Other risk factors include older age, a prior history of deep venous thrombosis, family history of venous insufficiency, and tobacco use [148]. Diagnosis is	Treating lipodermatosclerosis often involves weight reduction among patients with obesity, as well as compression therapy (i.e., compression stockings or bandages), leg elevation, anti-inflammatory medications to manage pain and inflammation, topical corticosteroids to improve inflammatory symptoms,

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Table 3 (*continued*)

Arteriovenous thromboembolic disease	Description	Diagnostic considerations with obesity	Treatment considerations with obesity
	necrobiotic xanthogranuloma, sarcoidosis, morphea, diabetic dermopathy, necrobiosis lipoidica, and nephrogenic systemic fibrosis [148].	usually clinical; however, biopsy may be required in some cases [148].	anabolic steroids, capsaicin cream, ultrasound treatment, and surgical interventions to improve venous blood flow [148].
Corona phlebectatica	Corona phlebectatica refers to when chronic venous insufficiency results in dilated and twisted superficial cutaneous veins that surround the ankle and lower calf area [149].	Corona phlebectatica often manifests with a bluish or reddish color and can be painful or uncomfortable. The classic four components include four components: "venous cups," blue and red telangiectasias, and capillary "stasis spots" [149]. The risk of chronic skin ulceration is increased with the increased severity of venous disease and BMI, with other risk factors including prior history of DVT, smoking, deep vein incompetence, and skin changes such as corona phlebectatica and lipodermatosclerosis [150].	Systemic treatment is similar to the treatment described for generalized chronic venous stasis above, and includes weight reduction among patients with obesity, and routine physical activity. More localized treatment includes compression stockings and/or surgical procedures such as sclerotherapy and topical laser therapy.
Chronic thromboembolic pulmonary hypertension (CTEPH)	CTEPH is characterized by high blood pressure in the pulmonary arteries due to chronic thromboemboli lodged in the pulmonary arteries. Blockage of the pulmonary artery increases pulmonary artery pressure and may lead to right sided heart failure.	Symptoms of CTEPH include exertional shortness of breath, fatigue, chest pain, and a decline in exercise tolerance. Diagnostic testing includes echocardiography, Ventilation/perfusion scan (V/Q) scan, CT pulmonary angiography, and other potential testing [151,152]. Imaging tests often present challenges in patients with severe obesity [132,153].	CTEPH treatment includes anticoagulation (See Table 2) and pulmonary thromboendarterectomy [152]. Pulmonary hypertension-specific drugs may also be beneficial [151,154]. Bariatric surgery may improve body weight, mitigate the adiposopathic factors that potentially contribute to pulmonary artery hypertension, improve heart function, and reduce the risk of thromboembolism, all collectively potentially improving CTEPH [155].
Iliofemoral venous obstruction	Ilio-femoral venous obstruction often involves compression of the iliac vein, increasing the risk of thrombosis. Increased body weight, especially due to central obesity, increases intra-abdominal pressure and pressure on the iliofemoral vein [139]. May-Thurner Syndrome is the specific compression of the left common iliac vein due to an overriding right common iliac artery [156].	Risk factors for iliofemoral venous obstruction include a family history, prolonged sitting or immobility, and a personal history of deep vein thrombosis. Symptoms include swelling, pain, discoloration, visible dilated veins (varicose veins). chronic venous insufficiency and potentially leg ulcers. Diagnosis may include doppler ultrasound, and venography, with imaging tests often presenting challenges in patients with severe obesity [132,153]	Treatment includes relief of the obstruction, anticoagulation, as well as thrombolysis, venous stenting, and venous bypass if indicated; prevention measures include maintaining a healthy body weight, routine physical activity, and avoiding prolonged periods of immobility [157,158].
Pelvic venous disorder (PeVD) (i.e., pelvic congestion syndrome)	PeVD is a venous insufficiency disorder that primarily affects women, with dilation and dysfunction of ovarian or internal iliac veins resulting in slow blood flow and reflux [159]. PeVD can be described by the Symptoms-Varices-Pathophysiology (SVP) classification [160].	PeVD is often undiagnosed due to nonspecific symptoms of pelvic pain after prolonged periods of sitting/standing, after intercourse, and after first days of menstruation [159]. Diagnosing PeVD can be challenging due to symptoms that overlap with gastroenterologic, gynecologic, musculoskeletal, neurologic, psychiatric, and urologic disorders [159]. Diagnostic procedures include pelvic ultrasound, CT, MRI, or venography [159]. Imaging procedures can present challenges among patients with obesity [132,153].	Treatment options for pelvic venous disorder may include hormonal therapy, nonsteroidal anti-inflammatory drugs, and micronized purified flavonoid fraction [159]. Elevation of the legs, compression stockings, and avoiding prolonged sitting or standing may help alleviate symptoms. Other treatments include endovascular embolization to block or close off the affected veins [159].
Post-thrombotic syndrome	Post-thrombotic syndrome (PTS) is a chronic disorder due to long-term effects of inflammation, scarring, and other damage to veins/valves in patients experiencing one or more deep vein thromboses (DVT) [161]. PTS can be described by the Villalta scale, as well as the Ginsberg measure and CEAP classification [161] (see section 5.1 below).	Symptoms include edema, pain or heaviness of the affected leg. The skin may become thickened or discolored. Imaging may include Doppler ultrasound. Another imaging procedure includes intravascular ultrasound (IVUS) and venography [161], with imaging studies sometimes presenting challenges among patients with obesity [132,153].	Noninterventional treatment of PTS focuses on relieving symptoms and preventing further complications via elevating legs, compression stockings, intermittent pneumatic compression sleeve units, venoactive drugs, anticoagulants (see Table 2), healthful nutrition, routine physical activity, and attaining a healthy body weight [161]. Interventional treatments include vein angioplasty or stent placement [161].

may have variable weight limits. Additionally, patients with obesity may present challenges with venous access and increased major bloods from angiography.

- Treatment
  - o Weight reduction to attain healthy body weight
  - o Routine physical activity
  - o Avoid prolonged periods of immobility
  - o Bariatric surgery
  - o Anticoagulation
  - o Thrombolytic therapy
  - o Thrombectomy
  - o Stenting
  - o Venous bypass

6. Lymphedema

6.1. Description

Lymphedema is a chronic medical condition resulting from impaired lymphatic drainage, manifest by swelling in one or more limbs. Primary lymphedema is frequently due to inherited/congenital abnormalities of the lymphatic system; secondary lymphedema is more common and may be due to surgery (i.e., removal of lymph nodes), radiation therapy, infection (i.e., filariasis), or trauma [166]. Extreme obesity can cause lower extremity lymphedema, and is termed "obesity-induced lymphedema (OIL)" [167]. Obesity can affect the structure and function of the lymphatic system, such as the accumulation of inflammatory cells around lymphatic vessels. Lymphatic stasis can impair transport of lipids and proteins from the interstitial space and impair transport of immune complexes (T cells or Langerhan cells) [168]. The adiposopathic immune and endocrine dysfunction the often accompanies obesity may influence both pro- and anti-symphandiogenic factors, increase permeability of lymphatic vessels, increase volume of interstitial fluid, and impair the contractility of the lymphatic vessel muscles, which sometimes prompts the therapeutic need for manual lymphatic drainage (i.e., lymphatic and venous massage) to increase blood flow in patients with lymphedema, venous edema, and lipoedema [168]. In addition to obesity contributing to lymphatic dysfunction, lymphatic system dysfunction may also contribute to the pathogenesis of obesity, attributable to activation and accumulation of adipocytes [168].

6.2. Symptoms

Symptoms include swelling, discomfort, reduced flexibility, and feeling of heaviness or tightness in the affected limb. Histopathology includes dermal edema, hyperkeratosis, epidermal papillomatosis and hyperplasia, telangiectasia, and thickened upper dermis [166].

6.3. Diagnosis

Diagnosis is most often clinical, with imaging studies that may include lymphoscintigraphy and 3-dimensional magnetic resonance imaging (MRI), computerized tomography (CT), ultrasound, and bioelectrical impedance analysis [166]. Differential diagnosis includes congestive heart failure, glomerulonephritis, nephrotic syndrome, hypoproteinemia, drug reactions, cirrhosis of the liver, pretibial myxedema, constrictive pericarditis, lower limb dependency syndrome, bilateral chronic venous insufficiency, malignancy, deep vein thrombosis, cellulitis, Baker cyst, cyclical and idiopathic edema, and arthritic conditions associated with lower limb swelling, and lipedema [166].

6.4. Treatment

Decongestive lymphedema therapy can help mobilize lymph and dissipate fibrosclerotic tissue. Other treatments include manual lymphatic drainage (i.e., light lymph massage), compression therapy, skin care, routine physical activity, and sometimes surgery (e.g., microsurgical techniques such as vascularized lymph node transfer, lymphaticovenous anastomoses, and suction-assisted protein lipectomy) [166]. Achieving a more healthy body weight is a fundamental treatment for patients with OIL [167].

6.5. Emotional and logistical support

Lymphedema can adversely affect quality of life and self-esteem due to limitations in mobility, discomfort, and matters of body image, especially when accompanied by cancer surgery (i.e., breast cancer surgery) [169]. Support groups and counseling can be valuable for coping with the emotional aspects of the condition. Effective management of lymphedema often requires a multidisciplinary team approach involving healthcare professionals such as lymphedema therapists, physical therapists, physicians, and dermatologists.

7. Lipedema

7.1. Description

Lipedema is a genetic (possibly autosomal dominant with incomplete penetrance or X-linked dominant) [170] disorder that occurs almost exclusively in women, and which is clinically manifested by redistribution of fatty tissue to the extremities. Patients with lipedema can develop extremity enlargement even without overweight or obesity. However, obesity can be an aggravating factor, as the prevalence of lipedema increases progressively with the increase in body weight [171].

7.2. Symptoms

Lipedema is the symmetrical enlargement of the legs due to increased subcutaneous fat deposits, that may cause pain and bruising to the lower extremities, and may ultimately cause lymphedema [172].

7.3. Diagnosis

The diagnosis is mainly clinical [173], with a differential diagnosis that is not unlike lymphedema (see Section 6.0). In fact, some suggest that most cases of lipedema are misdiagnosed as lymphedema or obesity [174]. Diagnostic testing is largely performed to rule out competing diagnoses (see Section 6.3), and may include blood testing for causes of edema, as well as ultrasound, CT, or MRI of the extremity skin. Other testing might include structural and functional evaluation of the lymphatic system with tests such as indirect lymphography, fluorescence microlymphography, functional lymphatic scintigraphy, and magnetic resonance lymphangiography [173]. Dual-energy X-ray absorptiometry (DEXA) or bio-impedance analysis might better evaluate body composition. Some have proposed an algorithmic approach to the patient with painful, disproportionate increase in limb size [173].

7.4. Treatment

Treatment of lipedema includes nutrition, physical activity (especially in patients with generalized overweight or obesity). While such approaches are often recommended, weight reduction measures often result in minimal benefits on abnormal body fat distribution, potentially contributing to frustration, eating disorders, increased obesity risk, depression, and other psychological disorders [175]. Other potential treatments include manual lymphatic drainage (i.e., massages), and compression stretch bandages/hoses. Surgical treatment may include lipedema reduction procedures, lymph-sparing liposuction or debulking (dermato-fibro-lipectomy) [173].

7.5. Emotional and logistical support

Lipedema may present similar quality of life and self-esteem challenges as described with lymphedema (Section 6.5). As such, additional treatment considerations include psychosocial therapy and patient education on self-management [173,174].

8. Conclusion

This Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) describes how both obesity-related fat mass disease and adiposopathic coagulation and thrombotic mechanisms can contribute to thrombosis. Additional considerations are the increased thrombotic risks due to obesity-promoted sleep apnea, insulin resistance, type 2 diabetes mellitus, hypertension, and dyslipidemia. Additional mechanisms helping to explain increased risk of thrombotic disorders with obesity include adiposopathic inflammation, hypercoagulability, increased platelet activation, reduced fibrinolysis, hypoxia, and endothelial dysfunction. Once a thrombotic event has occurred, obesity medicine clinicians might best have a working knowledge of how the dosing of several anti-thrombotic/anti-platelet drugs is influenced by, or based upon, body weight. Beyond weight reduction in patients with obesity having acute coronary syndrome, pulmonary embolus, and/or deep vein thrombosis, obesity medicine clinician might best have a working knowledge of the diagnosis and knowledge of chronic venous stasis, varicose veins, superficial thrombophlebitis, lipodermatosclerosis, corona phlebectatica, chronic thromboembolic pulmonary hypertension, iliofemoral venous obstruction, pelvic venous disorder, and post-thrombotic syndrome, as well as lymphedema and lipedema. A final point is that while weight reduction is frequently recommended, patients with obesity should not be given the impression that weight reduction is a universal "cure," nor should patients be blamed when weight reduction efforts fail to reverse or prevent recurrent thrombotic or venous diseases.

Transparency and group composition [176]

Since 2022, the Obesity Medicine Association Clinical Practice Statements have represented a diverse range of clinicians, allied health professionals, clinical researchers, and academicians. The authors reflect a multidisciplinary and balanced group of experts in obesity science, patient evaluation, and clinical treatment.

Author contributions

All authors reviewed and edited this submission. HEB served as the main medical writer.

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Ethics review

This OMA Clinical Practice Statement manuscript was peer-reviewed and approved by the OMA Board of Trustee members prior to publication. Edits were made in response to reviewer comments and the final revised manuscript was approved by all the authors prior to publication. This submission did not involve human test subjects or volunteers.

Conclusions and recommendations

This Clinical Practice Statement is intended to be an educational tool that incorporates the current medical science and the clinical experiences of obesity specialists. The intent is to better facilitate and improve the clinical care and management of patients with pre-obesity and obesity. This Clinical Practice Statement should not be interpreted as "rules" and/or directives regarding the medical care of an individual patient. The decision regarding the optimal care of the patient with pre-obesity and/or obesity is best reliant upon a patient-centered approach, managed by the clinician tasked with directing an individual treatment plan that is in the best interest of the individual patient.

Updating

It is anticipated that sections of this Clinical Practice Statement may require future updates. The timing of such an update will depend on decisions made by Obesity Pillars Editorial team, with input from the OMA members and OMA Board of Trustees.

Disclaimer and limitations

In areas regarding inconclusive or insufficient scientific evidence, the authors used their professional judgment. This Clinical Practice Statement is intended to represent the state of obesity medicine at the time of publication. Thus, this Clinical Practice Statement is not a substitute for maintaining awareness of emerging new science. Finally, decisions by practitioners to apply the principles in this Clinical Practice Statement are best made by considering local resources, individual patient circumstances, patient agreement, and knowledge of federal, state, and local laws and guidance.

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used Chat GPT to help list and categorize topics, where afterwards, the author(s) crafted the text and took full responsibility for the content of the publication.

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