Difficulties in the Management of Obese Patients with Pulmonary Embolism

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EDITORIAL

Over the recent decades, the prevalence of obesity has increased dramatically, leading to a high rate of cardiovascular complications and mortality. On the other hand, despite the improvement of medical awareness and diagnosis, venous thromboembolism remains the third most common cause of cardiac death.

Obesity and pulmonary embolism (PE) are not simply associated, because obesity can interact with other environmental or genetic factors [1]. The pathogenic relationship is multifactorial [2]. Various abnormalities of hemostasis have been described in obesity, mainly concerning increased levels of plasminogen activator inhibitor-1, as well as abnormalities of coagulation and platelet activation. Obesity itself is a hypercoagulable state, generating increases in coagulation factors, fibrin production and turnover, and also involves mechanical issues [3]. The clinical data have suggested a linear relationship between increasing of body mass index (BMI) and first occurrence of PE (a nearly sixfold greater risk when BMI ≥ 35 kg/m2) or recurrence, as well as for abdominal obesity and idiopathic PE [4,5].

The management of PE in obesity can be challenging. Many of the aspects involved in the care of obese patients are altered, from diagnosis and monitoring to medication pharmacokinetics [6].

First of all, the clinical diagnosis of PE is especially difficult, since normal obese patients have signs and symptoms similar to PE. Dyspnea, as the most frequent symptom, it is also a common complaint in obesity. Tachycardia, a common sign of PE, included in both the Wells and Geneva prediction rules, is nonspecific in obesity, because the heart rate increases in a linear fashion with BMI [3]. Signs of deep vein thrombosis are also difficult to interpret since lower limb edema and chronic skin changes are common in obesity. It’s worth mentioning that an acute worsening of preexisting signs or symptoms may be more suggestive for diagnosis of PE [3]. From a practical point of view, PE should be always considered when a pulmonary or cardiovascular disease is suspected.

Secondly, laboratory testing is difficult to interpret. D-dimer values have a linear relationship with waist circumference or BMI in obese patients [3], while BNP level, used as a marker for right ventricular dysfunction, is generally lower in obese patients. However, BMI increasing determines worsening of diastolic dysfunction, which is directly related to BNP values [7]. The performance of CT angiography is interfered by obesity because of weight limits, inability to physically fit into the scanner, and poor image quality. High weight capacity CT scanners, with larger gantry sizes are available since 2011, but the image quality is still a challenge. Recent studies have suggested that reducing the tube voltage from 120 to 100 kV allows a significant reduction of radiation dose without significant loss of diagnostic image quality [8,9]. Ultrasonography, a highly accurate and cost-effective method, is adequate for use in hemodynamically unstable patients in order to diagnose a proximal deep vein thrombosis. The transverse images are routinely obtained, but sagittal gray scale as well as color and spectral Doppler images may be particularly helpful in obese patients [10]. The multi modal imaging, combining CT venography and CT pulmonary angiography is considered a “one-stop examination” that serves as a road map for therapy, especially in high-risk patients [10]. Bedside echocardiography is a valuable diagnostic tool, because it is a non-invasive, simple and accurate, low cost, safe method. Unexplained pulmonary hypertension or right ventricular dysfunction may be due for PE in non-obese patients, but high pulmonary artery pressures are common in obesity [3]. Examining 3790 patients with normal echocardiograms, Mc Quillin et al., found a direct correlation between BMI and right ventricular systolic pressure, and suggested that values > 40 mmHg should be considered normal in obese patients [11].

Finally, the decision whether or not to anti-coagulate the obese patients with unconvincing or unavailable imaging diagnosis are empiric and based on clinical judgment. The clinician must evaluate the proper duration of therapy and the risk/benefit ratios of different approaches [3]. Obese patients have been excluded in many clinical trials, challenging clinicians on the appropriate strategy. Changes in pharmacokinetic parameters...
may be seen in any of the various classes of anticoagulants, so close monitoring is needed. For the novel oral anticoagulants (NOACs) small-scale studies suggested that fixed-dose regimens may not be sufficient in the obese patients, while an increased time to obtain target INR on initiation of vitamin K antagonists as well as higher maintenance doses are needed. ACCP practice guidelines recommend weight-based dosing of unfractioned heparin (UFH) over fixed dosing in obese patients and to monitor the therapy using aPTT [12]. Regarding the perioperative management of obese surgical patients, thromboprophylaxis should be initiated in obese patients [13]. The safety of using a low-dose of UFH, consisting of 5000 units 2 hours preoperatively, then either twice or three times daily postoperatively, is still questionable [12]. There are also some concerns for LMWH use, taking into account the lack of clinical data in obese patients, as well as variable absorption and distribution that requires optimal dosing and monitoring (anti-Xa). The recommended peak anti-Xa target range 4 hours after LMWH administration is 0.6–1.0 IU/mL. LMWH should also be adjusted based on total body weight without capping. The ideal dose or regimen for obese patients is unknown [12]. If higher prophylactic doses (weight-adjusted doses) without increasing the rate of major bleeding are recommended for surgical patients, the optimal regimen for medically ill patients is unclear [13]. Recently, the ITOHENOX study shows in medically obese in patients that thromboprophylaxis with enoxaparin 60 mg provides higher control of anti-Xa activity, without more bleeding complications, than the standard enoxaparin regimen (40 mg) [14]. Finally, NOACs are preferred as the first-line therapy over vitamin K antagonists. In the subgroup analyses of available clinical trials, it is likely that using higher doses of NOACs in obese populations may be more effective. Fixed doses for rivaroxaban, apixaban, and adjusted doses for dagibatran are recommended for thromboprophylaxis. However, further studies are required to establish the effective dose in this subgroup [15].

In conclusion, the diagnostic tests don’t replace clinical judgment, but can efficiently complete it in a safe manner for the obese patient. Anticoagulation is the first fast option in any situation, although the optimal regimen is under debate.

REFERENCES