Vascular Disease in Chronic Obstructive Pulmonary Disease

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Since the introduction of multi–detector row computed tomography (MDCT), most attention has been directed toward the use of this technique to improve the characterization of anatomic changes at the level of the airways and lung parenchyma in patients with chronic obstructive pulmonary disease. The introduction of fast rotation speed and dedicated cardiac reconstruction algorithms exploiting the multislice acquisition scheme of the data has opened new possibilities for thoracic imaging, starting with the possibility to integrate cardiac functional information into a diagnostic CT scan of the chest. Initiated with 16-slice MDCT, this concept of integrating morphology and function has been further simplified with 64-slice CT scanners, thus allowing radiologists to provide vital information in the management of patients with a wide variety of acute or chronic respiratory disorders. Because this CT technology also offers the possibility of generating high-resolution and motion-free images of the coronary arteries, evaluation of the coronary arteries in asymptomatic patients at risk for coronary artery disease during CT examinations of the chest can widen the clinical applications of CT for respiratory patients. More recently, the introduction of dual-source CT and its subsequent ability to apply dual energy to chest imaging has added another area of clinical interest at the level of the pulmonary capillary level. The purpose of this article is to review the potential applications of these technological developments in the population of patients with chronic obstructive pulmonary disease to provide a noninvasive depiction of the cardiovascular abnormalities known to occur in this subset of patients.

Keywords: chronic obstructive pulmonary disease; pulmonary arteries; bronchial arteries; coronary arteries; multi–detector row CT angiography

Chronic obstructive pulmonary disease (COPD) is “a new name for an old malady” (1), caused primarily by cigarette smoking, with diagnostic criteria based on pulmonary functional characteristics (2). Despite their key diagnostic role, these criteria do not allow a comprehensive approach to COPD because of the poor correlation between disabling symptoms and airflow obstruction as well as the wide variability in the rate of decline of lung function between smokers. As reflected by numerous publications, there is a need for a better understanding of the underlying respiratory lesions that could participate in the phenotypic characterization of COPD (3). Moreover, more recently there has been an increasing number of publications that have emphasized the systemic nature of COPD and the significant contribution of chronic comorbidities in COPD severity and mortality (4). Among them, the cardiovascular diseases play an important role, currently recognized as the leading causes of death among patients with COPD (5). Keeping in mind these needs for the comprehensive management of COPD, the only imaging test recommended for the assessment of a patient with COPD is a chest X-ray, “seldom diagnostic in COPD but valuable to exclude alternative diagnoses such as pulmonary tuberculosis, and identify comorbidities such as cardiac failure” (2). In the era of computed tomography (CT), it is surprising to observe that no particular interest has been developed toward the utilization of this imaging modality in the management of COPD (2, 4, 6), despite its obvious superiority over chest radiography to provide not only anatomic details of target organs but also functional information. The purpose of this presentation is to review the CT technological developments currently applicable to the evaluation of the various aspects of vascular disease in COPD. Because of the interrelation of vascular and cardiac disease in COPD, right and left heart alterations are also considered.

MULTI–DETECTOR ROW COMPUTED TOMOGRAPHY ANGIOGRAPHY OF THE CHEST IN 2008

In 2004, all major CT manufacturers introduced multi–detector row computed tomography (MDCT) systems with simultaneous acquisition of 64 slices. The fast rotation times of these scanners have greatly improved the temporal resolution of cross-sectional imaging of the chest, which opened new possibilities in routine clinical practice. One immediate consequence was that the entire thorax could be scanned with submillimeter resolution in about 5 seconds, a breath-hold duration acceptable for the majority of patients, including dyspneic patients. Using a standard 64-slice MDCT protocol, high-quality images of all thoracic organs, including small-sized pulmonary and systemic arteries, can be obtained in the vast majority of respiratory patients. Thirty-four–slice CT scanners have also made it possible to cover the entire thorax in an ECG-gated mode with submillimeter collimation. This scanning mode makes it possible to combine evaluation of the underlying respiratory disease with the acquisition of functional information in the same examination (7, 8). Whenever clinically relevant, high-resolution imaging of the coronary arteries is also accessible from the same data set (9, 10). The introduction of dual-source CT and its further improved temporal resolution opens the field for greater applicability of ECG-gated 64-slice MDCT examinations of the entire thorax in respiratory patients, even with relatively high heart rates (11). ECG-gated MDCT examinations can be obtained without beta-blockers and allow radiologists to provide high-quality images of the thoracic organs, as previously obtained with nongated scans, but also coronary artery imaging and functional information from the same data set. Dual-source CT opens another major field of application linked to the possibility to apply a different energy on each of the two X-ray tubes and, thus, to analyze the spectral characteristics of a given anatomic or chemical structure within the thorax (12). The first clinical application of this technology for chest imaging has focused on the analysis of lung perfusion, based on the possibility to generate iodine maps of the lung microcirculation. From this brief review of CT technological advances, several messages should be emphasized for the medical community in charge of respiratory diseases in general, and COPD in particular. The main message is that a chest CT examination in 2008 is no longer limited to morphologic analysis. Additional information can be generated from the same data set without any impairment in the quality of morphologic imaging. The patient’s clinical situation and the additional information expected by the clinician will

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dictate the optimal scanning protocol to the radiologist. In the context of evaluating patients with COPD, there are numerous reasons to consider CT an essential tool not only to characterize the nature and extent of both parenchymal and airway disease (13) but also to provide a noninvasive approach to the cardiovascular changes observed in this disease. More frequent recommendations for CT in COPD populations cannot be considered without careful consideration of the radiation dose delivered during these examinations, owing to the interactions between radiation and smoking (14). All of the above-mentioned protocols, including ECG-gated scans, deliver radiation doses lower than the European reference value of 650 mGy cm for a standard non-ECG-gated chest CT examination (radiation dose expressed as dose–length product) (15, 16). From personal experience with CT angiography (CTA) of the chest, the average dose–length product value for standard CTA is 150 mGy · cm, 300–400 mGy · cm for ECG-gated CTA, and 300 mGy · cm for dual-energy CTA (17–19).

**BRONCHIAL ARTERIES AND COPD**

CTA is a unique noninvasive means of evaluating bronchial arteries in smokers with various stages of smoking-related disease. As described from preliminary studies (20), normal bronchial arteries have a diameter of less than 2 mm. They possess tortuous but predictable trajectories that can be easily analyzed with a thorough knowledge of bronchial artery anatomy (21–23). The most frequent situation leading to bronchial artery evaluation on CT scans of patients with COPD concerns those presenting with hemoptysis. MDCT can help (1) evaluate the airways and lung parenchymal changes related to COPD and search for an additional etiology for hemoptysis, in particular early carcinoma; (2) assess the consequences of hemorrhage into the alveoli and the airways, which may mask subtle underlying abnormalities; and (3) provide a detailed roadmap of the thoracic vasculature by means of two-dimensional reformatted maximal intensity projection images and three-dimensional reconstructions, encompassing not only the bronchial arterial circulation but also the nonbronchial systemic circulation at the level of the suprarenalic vessels and infradiaphragmatic arteries, thus allowing early identification of nonbronchial systemic collateral circulation requiring embolization (24, 25). To our knowledge, the degree of bronchial artery hypervascularization according to COPD severity has not been evaluated on CT scans. However, one could extrapolate the angiographic findings reported in a cohort of 35 smokers presenting with cryptogenic hemoptysis (26). In this study, Menchini and coworkers reported moderate to marked bronchial hypervascularization in a majority of smokers classified as GOLD stages 2 and 3 but also in 10 of 12 smokers (82%) classified as GOLD stage 1 and 12 of 16 smokers (75%) with no airflow limitation, suggesting a lack of correlation between the

Figure 1. Standard 64-slice multi-detector row computed tomography angiogram of the chest. Maximal intensity projection, coronal view, illustrating the computed tomography depiction of a moderately enlarged right bronchial artery in its mediastinal (thin arrows) and hilar (large arrow) portions.

Figure 2. Standard 64-slice multi-detector row computed tomography angiogram of the chest. Maximal intensity projection, coronal view, showing a normal-sized right bronchial artery coursing in the mediastinum (thin arrows) and the right hilum (large arrows).
angiographic findings and the spirometric severity of COPD. Considering that the diameter of enlarged bronchial arteries varied between 2 and 4 mm for moderate hypervascularization and was greater than 4 mm for marked hypervascularization, their depiction on CT scans is clinically realistic (Figures 1 and 2). If CT angiograms are indicated in COPD, one should certainly add bronchial arteries to the list of vascular structures to be analyzed.

Figure 3. Dual-energy 64-slice multi-detector row computed tomography angiography of the chest in a 58-year-old patient with normal lung perfusion. Shown is a fused image of the native perfusion scan (gray-scale image) and the mediastinal diagnostic scan (color-coded image) at the level of the lower lung zones (2-mm-thick images). Note the presence of an asymmetric peripheral rim (arrows), devoid of perfusion information, due to the smaller field of view of the second X-ray tube.

Figure 4. Dual-energy 64-slice multi-detector row computed tomography angiography of the chest in a 60-year-old patient with chronic obstructive pulmonary disease. (A) Transverse perfusion scan obtained at the level of the right interlobar pulmonary artery and (B) coronal perfusion scan obtained at the level of the descending aorta, illustrating the heterogeneity of lung perfusion. The arrows point to the peripheral rim devoid of perfusion information.


**Imaging of Lung Perfusion**

On the basis of single-source CT, two approaches have been investigated for the detection of perfusion abnormalities, one using color-coded maps of lung density in humans (27–29) whereas other authors have investigated a subtraction technique using precontrast and postcontrast conventional CT images in experimental animal studies (30, 31). Although both approaches demonstrated the detectability of perfusion defects by CT, the feasibility of this approach in clinical practice has substantial limitations pertaining to scanning times and levels of radiation exposure to the patient. The availability of dual-source CT and the subsequent possibility to scan patients with dual energy offers another alternative for lung functional imaging (Figure 3). Preliminary experiences have shown that this technique could be applied to the analysis of lung perfusion in the context of pulmonary embolism levels (12, 19). COPD treatment could also benefit from this technique by improving our understanding of functional impairment in patients with COPD. While investigating a cohort of 32 patients with COPD, Pansini and coworkers evaluated the regional distribution of lung perfusion according to the presence of emphysematous changes in the lung parenchyma (Figure 4). These authors found that a gradient of perfusion greater then 5% enabled depiction of patients with significant differences in the extent of emphysema between the apex and lung base (right lung, $P = 0.017$; left lung, $P = 0.015$) (32). Moreover, alterations of lung perfusion can be detected in areas devoid of emphysematous changes, raising questions concerning the detectability of perfusion changes secondary to narrowing of pulmonary arterioles that could precede the development of emphysema (33).

**Assessment of Pulmonary Hypertension**

Pulmonary hypertension (PHT) is frequently observed in patients with advanced COPD. However, structural and functional changes in pulmonary arteries have also been observed in normoxic patients during the initial stages of the disease (34). Using ECG-gated MDCT, it is possible to evaluate parameters such as right ventricular outflow tract systolic shortening and myocardial thickness, and pulmonary artery distensibility, reported to be abnormal on echocardiography and/or magnetic resonance imaging (MRI) in patients with PHT. In a study based on 64-slice MDCT, Revel and coworkers demonstrated that pulmonary artery distensibility, defined by the change in cross-sectional area between diastole and systole, was the most reliable parameter for identifying patients with PHT (35) (Figures 5 and 6). In addition, they found that mean positive airway pressure was closely related to pulmonary artery distensibility. This functional approach overcomes the well-known limitations of PHT diagnosis based on the CT measurement of pulmonary trunk diameter (36–41). It is also possible to calculate pulmonary vascular resistances with CT from noninvasive measurements of cardiac output and mean pulmonary transit times (42).

**RIGHT CARDIAC CAVITIES AND COPD**

**Patent Foramen Ovale**

Patients with COPD have increased patency of their foramen ovale (PFO), responsible for a right-to-left atrial shunt that contributes to chronic hypoxemia (43). The reference method for detecting PFO is contrast-enhanced transesophageal echocardiography. Arrival of bubbles in the left atrium during a Valsalva maneuver, or immediately at its end, after one or two cardiac cycles is the key point for PFO assessment. The high sensitivity of this method for detecting PFO is counterbalanced by the existence of some limitations and contraindications. Moreover, it is partially invasive and cough efforts during the procedure may artificially increase the right atrial pressure. Consequently, there is a need for alternative and less invasive diagnostic modalities. The same principle as that used for echocardiography can be used for MRI after administration of 10 ml of gadopentetate dimeglumine during a Valsalva maneuver (44–46). PFO can also be visualized during MDCT angiography with dynamic CT centered on the fossa ovalis after injection of 10 ml of iodinated contrast medium with a low-voltage technique (Figure 7). Images are acquired during the relapse of the Valsalva maneuver, showing the left atrial enhancement before the pulmonary venous return of iodine. An atrial septal aneurysm bulging in the juxtaatrial part of the left atrium or in the right atrium can also be identified. The sensitivity of MDCT ranges from 28% in grade 1 to 90% in grade 4 PFO; the reported specificity is 96% (47).
Right Ventricular Dysfunction

In patients with COPD, right ventricular (RV) dysfunction is the expected consequence of long-standing PHT, but it is also present in less severe forms of COPD. According to Vonk-Noordegraaf and coworkers (48), RV dysfunction is present in 20% of normoxemic or mildly hypoxemic patients with COPD. The concept of RV dysfunction rests on a right ventricular ejection fraction (RVEF) lower than 45% on isotopic ventriculography (49). This parameter can also be evaluated by ECG-gated MDCT angiography on the basis of segmentation of the right ventricular cavity on systolic and diastolic short-axis images. Several studies have reported reliable estimation of RVEF by MDCT when the latter technique is evaluated in correlation with myocardial scintigraphy (50–52), MRI (53), and echocardiography (54). From a practical standpoint, cardiac functional information is derived from the same data set as that used for assessing the underlying respiratory disease acquired without β-blockers. The use of ECG-controlled dose modulation, known to deteriorate systolic images secondary to dose reduction during this cardiac phase, has no deleterious effect on RVEF assessment (55). These scanning conditions make RVEF accessible to unselected patients undergoing ECG-gated MDCT angiography and open the possibility of including functional imaging as part of CT examinations of the chest. Because of the complex geometry of the right ventricle, segmentation of the right ventricular cavity cannot be automated and requires manual drawing of the ventricular contours in systole and diastole. The overall duration of postprocessing to calculate RVEF by this method is approximately 15 minutes. A more rapid means of estimating RVEF by CT has been investigated, based on the measurement of tricuspid annulus displacement between systole and diastole. Because of the orientation of muscle fibers, RV contraction occurs mainly along its longitudinal axis, between the tricuspid annulus and the RV apex. Consequently, measurement of the tricuspid annulus excursion, known by the acronym TAPSE (tricuspid annular plane systolic excursion), reflects the strength of RV contraction. On the basis of transthoracic echocardiography, this parameter has been found to provide reliable estimation of RV systolic function (56, 57). Using ECG-gated 64-slice MDCT, Delhaye and coworkers have demonstrated that TAPSE measurements on four-chamber views of the cardiac cavities provide accurate and rapid estimation of RV function (58).

LEFT HEART, CORONARY ARTERY DISEASE, AND COPD

Patients with COPD with smoking history, systemic inflammation, artery stiffness, and other comorbidities such as diabetes are at high risk for heart attack. Moreover, dyspnea in patients with COPD may be related to left ventricular (LV) dysfunction, reported in 32% of patients with COPD exacerbation (59). Consequently, detection of cardiac and/or coronary abnormalities by CT should be considered in this population. Depending on the scanning mode, various aspects of functional and morphologic information can be approached. Nongated CT scans can demonstrate features of ischemic heart disease such as myocardial fat,
postinfarct aneurysms or pseudo-aneurysm aneurysms, sometimes thrombosed, as well as wall thinning. ECG-gated MDCT examinations have the potential to provide insight into left ventricular function, which can be calculated with dedicated cardiac software. Contrary to the right ventricle, LV shape allows automated (or semiautomated) segmentation of the ventricular cavity, which simplifies and shortens postprocessing. Multiple studies have demonstrated that ECG-gated MDCT determination of LV volumes and consequently global LV function parameters is feasible and in good agreement with established modalities such as cineventriculography, echocardiography, and cine MRI (60). ECG-gated scans can also allow screening for coronary artery disease, as more than 90% of proximal and midcoronary segments can be analyzed in nonselected patients before chest surgery (61). While investigating a cohort of 87 consecutive patients with COPD with ECG-gated MDCT, Moraux and coworkers identified sequelae of myocardial infarction in 13 patients (15%) and coronary artery abnormalities in 75 patients (86%) (Figures 8 and 9). Among the 70 patients with no history of myocardial infarction, 58 of 70 patients (83%) had coronary lesions, including one patient with sequelae of unknown myocardial infarction (62). The ability of noncontrast and prospective ECG-gated acquisition to detect lipid-rich plaques has been emphasized (63). This area of investigation is worth considering in patients with COPD, as the presence of lipids in plaques increases biomechanical stress and their risk of rupture. The breakthrough of new CT technologies counterbalances the limitations of noninvasive cardiac tests in these populations. Stress tests with echocardiography, ECG, and nuclear medicine may be limited because of the patient’s inability to perform the

Figure 8. Coronary artery imaging obtained from 64-slice ECG-gated multi-detector row computed tomography angiographic examinations of the entire thorax in patients with chronic obstructive pulmonary disease. (A) Curved reformation of the left anterior descending artery showing multiple calcifications (arrows). (B) Curved reformation of the left anterior descending artery showing a mixed plaque (arrows).
a major role in routine chest imaging. The reasons behind this situation can be found partly in the limited morphologic analysis of thoracic structures provided by MRI as well as in the limited availability of the tools required to achieve functional imaging. In the current status of technological developments, the superiority of CT over scintigraphy and MRI rests in its ability to provide morphologic and functional information from the same examination, otherwise indicated as the primary imaging modality after chest radiography. This raises questions about the currently restrictive indications for CT in the management of patients with COPD, exclusively considered “when there is a doubt about the diagnosis of COPD” or “if a surgical procedure such as lung volume reduction is contemplated” (69). Not only can high-resolution CT play a role but more recently introduced technical modalities have already shown their clinical applicability.

CONCLUSIONS

In addition to the well-known possibility of CT to characterize lung parenchymal and airway changes in COPD (70), this technique can also contribute to a better understanding of COPD-related cardiovascular alterations (71). Far from being a research tool, CT can help improve patient management provided that interdisciplinary interactions among the respiratory community define the clinical indications for chest CT in the clinical setting of COPD.

Conflict of Interest Statement: Neither author has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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