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EDITORIAL COMMENT

Left Main Coronary Artery Compression in Patients With Pulmonary Arterial Hypertension*

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Pulmonary arterial hypertension (PAH) entails a poor prognosis irrespective of the underlying etiology (1-3). Typical symptoms are largely nonspecific, including dyspnea, fatigue, and chest pain on exertion. Angina-like symptoms are frequent despite angiographically normal coronary arteries, and classically, have been attributed to right ventricular ischemia resulting from the increased metabolic needs of the overloaded, hypertrophied right ventricle or painful distention of the pulmonary artery (PA) (1-3). PAH constitutes the leading cause of PA enlargement (4). A severely dilated PA may compress adjacent anatomical structures including the left main coronary artery (LMCA) (causing myocardial ischemia), the left recurrent laryngeal nerve (causing hoarseness; i.e., Ortner's syndrome), and the tracheobronchial tree (large airway obstruction) (4). LMCA compression has been associated with ischemic left ventricular dysfunction leading to left-sided heart failure, which is frequently misinterpreted as an interventricular dependence phenomenon (1-4). Of concern, LMCA compression may present as sudden death, a major cause of death in these patients (1). However, post-mortem collapse of the PA may cause the condition to be overlooked during autopsy examination.

In the last decade, multiple single-case studies (5-9) and scarce small series (10-12) have been reported of patients with PAH presenting with extrinsic compression of the LMCA by a severely dilated PA. This unique complication has been described in patients with PAH, but also in patients with other forms of pulmonary hypertension (PH) (5-13). However, the prevalence and clinical implications of extrinsic LMCA compression in patients with PAH remain unclear. Currently, coronary computed tomography angiography (CTA) provides a precise assessment of the anatomical relationship between the LMCA and the enlarged PA (11,12). Additionally, advances in percutaneous coronary intervention (PCI) open new venues for treating these patients who usually have a prohibitive surgical risk (1-4).

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CURRENT STUDY

In this issue of the *Journal*, Galiè et al. (13) presented data on the prevalence of LMCA extrinsic compression by a dilated PA in patients with PAH and angina or angina-like symptoms. The usefulness of systematic coronary CTA screening and the value of PCI in this setting were carefully analyzed. Of 765 patients with PAH (48% secondary to congenital cardiac shunts) evaluated, 121 (16%) had symptoms compatible with angina. Of these, 94 patients (78%) with abnormal coronary CTA findings based on the relationship between the PA and LMCA underwent selective coronary angiography. The relationship between the PA trunk and the LMCA was categorized as: 1) normal distance (>1 mm); 2) contiguity (distance <1 mm without dislocation or stenosis); 3) dislocation (take-off angle <60°); and 4) significant LMCA stenosis (diameter stenosis >50%).

Significant LMCA stenosis was detected by invasive selective coronary angiography in 48 (40%) of the 121 symptomatic patients (10% of patients with

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continuity, 31% of those with dislocation, and 91% of patients with significant stenosis on coronary CTA). Surprisingly, baseline characteristics (including PA pressure and resistances) were similar in patients with and without significant LMCA compression. The best predictor of LMCA compression was a PA trunk diameter ≥40 mm. A total of 45 patients underwent PCI with stents (one-half received drug-eluting stents); procedural success was achieved in all cases, with no signs of acute recoil and no clinical complications. During follow-up, complete symptomatic relief was obtained in 91% of patients, of whom only 5 (11%) developed LMCA restenosis (2 with late recoil causing LMCA recompression) successfully treated with repeat stenting.

Of major clinical interest, this study suggests an unexpectedly high prevalence of LMCA compression in patients with PAH and angina-like symptoms. In this unique anatomic scenario, results of PCI were very favorable. Due to these findings' important potential clinical implications, some related issues also could be of interest.

First, although some previous studies already addressed this problem (5–12), the current series was not only the largest but also the most rigorous from a methodological standpoint. Moreover, the present study provided valuable clinical insights on predictors of LMCA compression, together with robust novel information on the prognosis of these patients after PCI.

Second, only patients with PAH and angina-like symptoms were studied. Although this appeared reasonable from a clinical perspective, the exclusion of patients without angina might be considered a potential source of bias. Indeed, many patients with severe PAH have a reduced exercise capacity and only complain of fatigue. Likewise, in these patients, dyspnea might be attributed to PAH rather than to heart failure even in the presence of depressed left ventricular systolic function (1–3). A high index of clinical suspicion is required for the diagnosis of LMCA compression, and a massively enlarged PA should be considered a red flag in this regard (1–4).

Third, on angiography, LMCA compression is suggested by the presence of an eccentric "slit-like" lumen, usually detected in a single plane and associated with a downward displacement of the vessel (10). Although angiography remains the gold standard for diagnosis, findings of intracoronary imaging might have complementary value to further disclose the pathophysiology of LMCA compression (7,8). In patients with LMCA compression, these techniques have depicted an asymmetric, oval-shaped lumen and were able to exclude atherosclerotic plaque impinging into the lumen and negative vessel remodeling (7,8). Likewise, assessing the physiological significance of coronary lesions by angiography alone is particularly elusive in the LMCA. Therefore, in ambiguous cases, the use of invasive pressure-derived physiological indexes might have provided valuable additional information on the functional significance of LMCA compression (8).

Fourth, the association between LMCA compression and PA size was well expected. However, the lack of association between this finding and PH severity appears more difficult to understand. However, most previous studies consistently demonstrated the association of LMCA compression with PA size and PA-aorta ratio, and emphasized the lack of correlation with PH severity (10–12). LMCA compression due to massive PA has also been reported in patients with other types of PH, and even in patients with normal pulmonary pressures (9).

Last, but not least, PCI for unprotected LMCA is rapidly growing in popularity in patients with coronary artery disease based on currently available evidence (14). However, the optimal stenting technique in patients with extrinsic LMCA compression remains unsettled. Compression affects the ostium and the most proximal segment of the LMCA, but typically spares the bifurcation, thus facilitating stent implantation (10). Prolonged dual antiplatelet therapy might be a cause for concern in this scenario, as many patients require chronic anticoagulation for their underlying condition, whereas others experience recurrent hemoptysis due to hypertrophied but fragile bronchial arteries (1–4). This probably explains the use of bare-metal stents in one-half of the patients in the present study. However, it remains attractive to speculate that selecting devices with high radial force, resistant to acute and chronic elastic recoil, will be particularly beneficial in these patients.

PREVIOUS STUDIES

In 2001, Kajita et al. (10) reported on 12 adult patients with congenital heart disease with a dilated PA trunk causing LMCA compression. The narrowing was eccentric and was best visualized in a single projection (typically 45° left anterior oblique with 30° cranial angulation). Interestingly, the LMCA was displaced downward, in close contact with the left aortic sinus (narrowed angle: mean 23°). Surgical PA reduction was associated with stenosis relief and normalization of LMCA angle. The same year, Rich et al. (6) reported the value of stent implantation in 2 patients with primary PAH and LMCA extrinsic compression from a dilated PA. Ischemia relief and

left ventricular systolic function recovery was demonstrated after stenting. In 2004, Mesquita et al. (11) systematically studied the presence of extrinsic LMCA compression in 36 patients with PAH that was either idiopathic or secondary to congenital heart disease. Invasive angiography demonstrated LMCA compression in 7 of 26 patients (27%) with angina. LMCA compression was significantly related to PA trunk diameter and PA-aortic diameter ratio as measured by transthoracic echocardiography. Importantly, a PA trunk diameter >40 mm was identified as a strong predictor of LMCA compression. Indeed, none of the patients with a PA diameter <40 mm showed LMCA compression, whereas this finding was identified in 37% of patients with a PA diameter >40 mm. Recently, Lee et al. (12) used transthoracic echocardiography to prospectively screen for PA dilation (>40 mm) in a series of 298 patients with PAH. In the 46 patients (15%) showing PA enlargement, coronary CTA was performed to detect potential compression of the adjacent anatomic structures, including the LMCA. Major mechanical problems, identified in 16 patients (35%), were related to PA diameter but not to PAH severity.

CLINICAL IMPLICATIONS

Six decades after its initial pathological description by Corday et al. (5), extrinsic LMCA compression is increasingly recognized as a major cause of angina in these challenging patients. Currently, invasive coronary angiography is not routinely recommended in patients with PAH and chest pain. However, the findings of the study by Galiè et al. (13) suggest that, in patients with PAH and angina-like symptoms, coronary CTA should be systematically performed to unravel the presence of LMCA compression. Furthermore, the results of this study strongly suggest that PCI has a major role in treating patients experiencing this unique phenomenon. Further studies, however, are warranted to elucidate whether this management strategy can improve the dismal prognosis of patients with severe PAH.

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