Ballooon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension
A Need for Further Dialogue, Development, and Collaborative Study

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“The historian of science may be tempted to claim that when paradigms change, the world itself changes with them. Led by a new paradigm, scientists adopt new instruments and look in new places ... see new and different things when looking with familiar instruments in places they have looked before.”1

Chronic thromboembolic pulmonary hypertension (CTEPH), increasingly recognized as occurring in some 2% to 4% of people experiencing pulmonary embolism, rivals idiopathic pulmonary arterial hypertension (PAH) in its poor untreated outcome, with rapid progression to increasing fatigue, breathlessness, right-ventricular dysfunction and failure, and untimely death.2 Intraluminal thrombus organization is accompanied by fibrous and inflammatory narrowing of directly affected vessels and is accompanied by inflammatory remodeling effects in overcirculated and pressurized pulmonary arterial segments that were not mechanically obstructed. Effects on pulmonary blood flow distribution, ventilation and gas exchange, and right-ventricular afterload and function are profound.3 To date, therapy for CTEPH has largely focused on surgically based pulmonary thromboendarterectomy (PEA) followed by adjunctive chronic anticoagulation.4 (Targeted medical therapies designed for PAH seem to have real, but limited, benefit for individuals with CTEPH.)5 When PEA is performed in centers with combined medical, surgical, and perioperative experience and expertise, results may be highly favorable, particularly in individuals with fewer medical comorbidities, with more proximally located obstruction, with greater preoperative efficiency of ventilation or vascular responsiveness to pulmonary vasodilator testing, and with lower preoperative pulmonary vascular resistance.5 However, heterogeneity of pathological and clinical presentation, combined with lack of uniform access to high-volume expert surgical centers, continues to contribute to 10% to 50% of patients with CTEPH classified as inoperable; an additional 10% to 15% of individuals, after PEA, are left with significant elevation in pulmonary artery pressures and resistance, either at rest or with exercise, contributing to poorer long-term outcome.5

Articles see p 748 and 756

The initial care paradigm for CTEPH required surgical removal of essentially all obstructive intraluminal debris from the entire pulmonary arterial circulation (a typically intricate and involved task, if accomplishable). Of note, a number of important findings from related fields challenged aspects of this model of care.

(1) Results from balloon pulmonary angioplasty (BPA) for pulmonary vascular obstructions associated with congenital heart and lung disease suggested that restoration of flow to particular segments of lung vasculature held greater potential for reduction in pulmonary vascular resistance; complete restoration of normal flow to all segments, although desirable, was not necessarily a requisite for return to reasonable functional ability and long-term survival.

(2) Coronary and peripheral angioplasty and stent implantation underscored that restoration of most normal intraluminal diameter and flow could be achieved with mechanical compaction, rather than physical removal of intravascular debris.

With this recognition, Voorburg and colleagues7 in 1988 (in single application), followed by Feinstein and our group8 in 2001, reported, and then demonstrated, an initial cohort of individuals effected by distal CTEPH treated with BPA, outlining a strategy that incorporated both physiological and methodological principles of flow restoration to targeted pulmonary artery segments via dilation and stenting; these investigators documented improved hemodynamic and functional outcomes as well as preserved vascular patency, thereby allowing a changing set of ideas and possibilities for individuals with CTEPH.7,8 Scientific and clinical promise was identified, with potential to bridge a gap of suboptimal outcomes. As with surgical PEA, performance of catheter-based restoration of flow via BPA seemed to be limited to extremely selected centers of experience and expertise; subsequent reports of additional attempts at BPA for CTEPH, and of procedural outcomes, were extremely limited.

This issue of Circulation: Cardiovascular Interventions contains 2 important additions to the experience of CTEPH care, cataloging improved definition of technique, long-term outcome, and more widespread application of BPA in the management of CTEPH.9,10 Both cohort series emanate from centers with past experience in the study and care of CTEPH and idiopathic PAH, as well as in diagnostic and interventional catheterization of the pulmonary arteries.

Mizoguchi and colleagues9 during a period of 7 years, offered BPA to 68 consecutive patients (who already were...
using targeted PAH medications) with CTEPH deemed inoperable by experienced surgeons.9 Standardization of preprocedural testing and management, intraprocedural lesion assessment with hemodynamics and imaging (angiography and intravascular ultrasound), BPA technique, postprocedural follow-up, and both indication and nature of subsequent reinter-vention, vastly overshadows the study’s primary limitations of (a) whether patients receiving BPA might have been considered candidates for CTEPH at other expert centers, (b) the questionable need for preoperative or subsequent targeted PAH and inotropic medical supportive therapies, and (c) the relative benefit of intravascular ultrasonography compared with standardized angiography. The investigators demonstrated technical feasibility of serial BPA in all patients, immediate and sustained (measured on average 1 year after final series of dilations) improvement in hemodynamics (approaching the boundaries of normal pressures and rivaling successes noted with surgical PEA), as well as both subjective and objective measures of volume retention and functional capacity, with reductions in both oxygen and targeted PAH medication requirement, all regardless of the significantly aged nature of this cohort. Periprocedural risk of reperfusion pulmonary edema remained significant, but was not determinant of outcomes, and did not seem limited by intervention with either intravenous steroid or positive pressure ventilation.

In a significantly smaller study of much shorter duration, Kataoka and colleagues,10 roughly during a 2-year period, offered BPA to 29 patients, who largely were thought to be candidates for surgical PEA, or who had significant residual pulmonary vascular obstruction after PEA; decision to proceed to BPA was based upon physician and patient choice.10 In this extension of application of BPA, investigators showed technical feasibility of serial BPA; both immediate and short-term sustained improvement (measured at 6 months after first series of dilations) in hemodynamics, and subjective and objective measures of volume retention and functional capacity was demonstrated (although less robust than that noted by Mizoguchi and colleagues,9 but similar to that seen in our initial cohort series), with similar rates and significance of periprocedural reperfusion edema. This experience harbors diffuse and significant limitations in its structure and standardization, but, nonetheless, serves as a demonstration of potential benefit, and an impetus for further study, of the extension of BPA for this disease.

Spurred by lack of accessibility to, and by inconsistent outcomes of, PEA for a considerable proportion of individuals with CTEPH, clinicians and scientists with increasing discomfort with the existing care paradigm have moved from recognition of success of catheter-based relief of vascular obstruction for other diseases in the pulmonary circulation and elsewhere, to consideration and then demonstration of BPA for CTEPH. However limited, the 2 current cohort studies further demonstrate, refine, assess, and extend technique and outcomes for BPA in CTEPH. BPA is recognized as a complex procedure, available in limited centers, mandating an intensive and specialized skill set for understanding pulmonary and right-heart physiology, navigating pulmonary vascular anatomy, successfully intervening on such, when appropriate, and ensuring greatest access to supportive therapies during follow-up; multidivisional and departmental resources and expertise are required. Few CTEPH programs offer BPA; as such, temptation exists to view these current results with skepticism based on the original paradigm of care (eg, faulting residual debris or failure to approach all involved segments), rather than as extension of potentials for vascular remodeling that advances a common mission of improved ventilation, flow balance, and right-ventricular function. It is extremely important for proponents of PEA, as well as of BPA, to recognize these shared goals and to allow observational data to be examined critically, rather than to discard potential benefit because of viewing results through biased lenses. As we advance to registry and controlled trial of BPA for CTEPH, we are obliged to recognize that we are in an era of scientific and clinical revolution in the understanding and treatment of CTEPH; one that would make Thomas Kuhn, author of The Structure of Scientific Revolutions, proud.1

Disclosures

None.

References


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