Balloon 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...”

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. 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. To date, therapy for CTEPH has largely focused on surgically based pulmonary thromboendarterectomy (PEA) followed by adjunctive chronic anticoagulation. 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 could be achieved with mechanical compaction, rather than physical removal of intravascular debris. With this recognition, Voorburg and colleagues in 1988 (in single application), followed by Feinstein and our group 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. 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. 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 colleagues, during a period of 7 years, offered BPA to 68 consecutive patients (who already were...
using targeted PAH medications) with CTEPH deemed inopera-
table by experienced surgeons. Standardization of pre-
procedural testing and management, intraprocedural lesion
assessment with hemodynamics and imaging (angiography
and intravascular ultrasound), BPA technique, postproce-
dural follow-up, and both indication and nature of subse-
quent intervention, vastly overshadows the study’s primary limitations
of (a) whether patients receiving BPA might have been con-
sidered 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 re-
tative 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 out-
comes, 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, 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 pro-
ceed to BPA was based upon physician and patient choice.

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 capac-
ity was demonstrated (although less robust than that noted
by Mizoguchi and colleagues, 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 standard-
ization, but, nonetheless, serves as a demonstration of poten-
tial benefit, and an impetus for further study, of the extension
of BPA for this disease.

Spurred by lack of accessibility to, and by inconsistent out-
comes of, PEA for a considerable proportion of individuals
with CTEPH, clinicians and scientists with increasing discom-
fort with the existing care paradigm have moved from recog-
nition 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 demon-
strate, 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 spe-
cialized skill set for understanding pulmonary and right-heart
physiology, navigating pulmonary vascular anatomy, suc-
cessfully intervening on such, when appropriate, and ensur-
ging greatest access to supportive therapies during follow-up;
multidivisional and departmental resources and expertise are
required. Few CTEPH programs offer BPA; as such, tempta-
tion 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 reg-
istry 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

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