The first hybrid International CTEPH Conference concludes successfully

Basel, 6 January 2022

The 4th International CTEPH Conference (ICC), the first of its kind to be held in a hybrid format, took place on 10 and 11 December 2021. Despite the challenges related to the ongoing coronavirus pandemic, the conference attracted an international audience of over 350 health-care professionals involved in chronic thromboembolic pulmonary hypertension (CTEPH). Some participants attended the event in person in Bad Nauheim's charming Jugendstil setting, while others followed the presentations on a virtual conference platform. Seamless integration of live remote presenters, prompt availability of recorded live presentations as on-demand online content and the possibility for virtual participants to actively engage in Q&A sessions offered an enjoyable conference experience regardless of the mode of participation and enabled lively discussions. A virtual poster session with more than 50 contributions, including 11 posters on national CTEPH management strategies, three industry-sponsored satellite symposia and an industry exhibition complemented the 1.5-day plenary programme.

The recently proposed terminology of chronic thromboembolic pulmonary disease (CTEPD) includes patients with chronic thromboembolic disease with and without pulmonary hypertension (PH), in recognition of the fact that patients with CTEPD without PH represent an intermediate population between healthy controls and CTEPH patients. Treatment options for patients with CTEPD without PH are currently under investigation, including some case series of surgery in these patients.

In terms of pathophysiology, important insights have been gained on the role of the microvasculature in the response to pulmonary artery obstruction, both on the obstructed and the non-obstructed side of the lung, and recently, it has been implied that neutrophil extracellular traps may be involved in promoting fibrous vascular occlusions in CTEPH. It has also been elucidated that although right ventricular (RV) loads are similar in proximal and distal disease, RV wall stress is higher and RV ejection fraction is lower in proximal disease. Genome-wide association studies have confirmed similarities in the genetic signatures of CTEPH and pulmonary embolism, but not idiopathic pulmonary arterial hypertension, and it is hoped that eventually, genetic studies will also contribute to the development of new medical therapies.

There is still a considerable diagnostic delay in CTEPH, leading to worse outcomes and increased health care costs. This is particularly concerning considering the potential surge in CTEPH cases post-coronavirus due to the large number of patients with coronavirus-related venous thromboembolic disease. Advanced imaging technologies showing increased sensitivity and specificity in CTEPH, such as computed tomography (CT) pulmonary angiograms, dual-energy/spectral CT and perfusion imaging, have become available over the last years and may represent superior alternatives to standard ventilation-perfusion scans.

Patient selection for the two interventional treatment options, pulmonary endarterectomy (PEA) and balloon pulmonary angioplasty (BPA), is a point of ongoing debate, even among expert centres. Although many factors influence treatment decisions, which should ideally be made by multidisciplinary teams, the two key aspects are the localisation of the obstruction and the experience and practice of the treating centre. In the hands of an experienced surgeon, it is possible to surgically treat distal disease starting at the subsegmental artery level with similarly positive outcomes compared with more proximal disease. The main serious complications of PEA are airway haemorrhage, reperfusion injury, residual PH with RV failure and neurological injury. Extracorporeal membrane oxygenation can be used to manage severe complications; however, it is preferable to prevent complications in the first place by careful surgical management.

BPA is the modality of choice for the treatment of distal disease not amenable to surgery. The procedure can be used for total and subtotal occlusions and usually involves several sessions; the treatment goal should be complete revascularisation. As high mean pulmonary arterial pressure (mPAP) is a predictor of complications, efforts should be made to lower mPAP prior to the procedure. Lung injury, one of the main complications of BPA, can be prevented by treating vascular injury occurring during the procedure as early as possible. As for surgery, outcomes following BPA improve with growing experience of the operator. In a single-centre analysis, an impressive reduction in the overall complication rate was observed over time, together with a decrease in mortality and radiation dose, while the total number of sessions per patient and the overall haemodynamic

improvement increased. The ongoing International BPA Registry, which is led by the International CTEPH Association (ICA) and is collecting data on 500 patients enrolled at 18 expert centres in Europe, the US and Japan, is expected to provide further insights into current practices and outcomes in BPA.

Medical treatment targets the microvasculature, and there is evidence from randomised controlled trials that some therapies improve exercise capacity and haemodynamic parameters in patients with inoperable disease. Riociguat and subcutaneous treprostinil are the two therapies currently approved for CTEPH. Following positive Phase II data for macitentan in CTEPH, a Phase III study is ongoing.

In addition, there is increasing evidence for a combination of treatment modalities in certain patient subgroups, and many strategies are being tested by expert centres. Recently, the RACE trial has demonstrated that the combination of BPA and riociguat treatment shows comparable improvement in haemodynamics regardless of treatment sequence; however, the incidence of serious adverse events related to BPA was markedly lower when BPA was preceded by riociguat treatment. This is probably due to improved haemodynamics pre-BPA under medical treatment. Moreover, promising data on the efficacy of PEA followed by BPA or vice-versa, as well as hybrid procedures and novel approaches such as pulmonary artery denervation post-PEA, are emerging.

Life-long anticoagulation in CTEPH patients is recommended by clinical guidelines, but the question of whether vitamin K antagonists (VKA) or new oral anticoagulants (NOACs) should be preferred has not yet been conclusively answered. NOACs are easy to use and offer increased convenience, but data in CTEPH are limited, and some studies have shown a higher risk of recurrent thromboembolic events compared with VKA.

In conclusion, all experts agree that in light of the many available treatment options, multidisciplinary decision making is paramount to manage and treat patients with CTEPH. The combined efforts of the global CTEPH community in generating, disseminating and discussing scientific data continue to increase knowledge and advance patient management.

The ICA thank all presenters for their contributions and very much look forward to discussing new scientific findings at the next ICC in San Diego.

About the ICC

The ICC takes place triennially and is the largest gathering of CTEPH experts worldwide. It attracts an international and multidisciplinary audience of cardiologists, respiratory physicians and surgeons. The first ICC was held 2011 in Cambridge, followed by Paris in 2014 and Leuven in 2017. ICC 2021 was postponed by one year due to the coronavirus pandemic and was the first meeting to be held in a hybrid format. The next ICC is planned to be held in San Diego, USA.

About the ICA

The ICA is a non-profit organisation of physicians, surgeons and other medically qualified professionals committed to advancing the diagnosis and treatment of CTEPH, and thus improving the clinical outcome and long-term care for affected patients. ICA memberships are available to health-care professionals interested in CTEPH.

About CTEPH

CTEPH is a condition caused by a thromboembolism in the pulmonary arteries with incomplete resolution and remodelling causing permanent fibrous obstruction. The diagnosis is based on findings obtained after at least 3 months of effective anticoagulation therapy in order to discriminate this condition from ‘subacute’ pulmonary embolism. CTEPH is an orphan disease with an estimated incidence of 5 cases per million, but it is likely that CTEPH is under-diagnosed as symptoms are non-specific. The median age of patients is around 60 years, with paediatric cases being rare. Both genders are equally affected. Three treatment options (PEA, BPA and medical treatment) are currently available to improve symptoms and prognosis in patients with CTEPH.