

## In memoriam, Professor Alain Cribier, 1945-2024: the heart of medicine

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Alain Cribier was an interventional cardiologist who played a key role in innovations that changed the way medicine is practised today, revolutionising the management of heart valve disease forever. He will always be remembered for his discoveries, and he belongs to that exclusive group of doctors and scientists who have pioneered life-changing techniques – which are the foundation of the modern treatment of heart valve disease. Alain Cribier worked tirelessly to translate his ideas into reality with his ongoing commitment to treating aortic stenosis using percutaneous techniques, from balloon aortic valvuloplasty (BAV) to transcatheter aortic valve implantation (TAVI). He thus played a key role in the initiation and the development of interventional cardiology for structural heart disease to where it stands today – with continually expanding treatment options for an increasingly large percentage of the population worldwide.

Born in Paris, France, in 1945, he studied medicine at the University of Paris, and, following a determinant cardiology fellowship at Cedars-Sinai Medical Center with Jeremy Swan and William Ganz, Los Angeles, CA, USA, he joined the Rouen University Hospital, Rouen, France, later serving as Director of the Cardiology Department.

Above all, Alain Cribier was deeply committed to his patients and could not bear to see those contraindicated for valvular surgery struggling with aortic stenosis and dying. To find a solution, Alain Cribier developed the technique of BAV, which consisted of enlarging the narrowed calcified aortic valve by a balloon using standard catheterisation techniques under local anaesthesia. And though this concept was considered unrealistic for degenerative calcified aortic stenosis, Alain Cribier performed the very first case in September 1985 in Rouen on a 72-year-old highly symptomatic woman who had been turned down for surgical valve replacement because of her age at that time. When this first BAV resulted in the disappearance of all symptoms – and allowed the patient to resume a normal life

– the response was quick and passionate, with the publication of this first Rouen BAV series in 1986 in *The Lancet* creating overwhelming enthusiasm in the medical community.

BAV was subsequently evaluated in large international European and US registries and reported in hundreds of articles. Cardiologists were coming from all over the world to participate in international workshops and patients coming to be treated in Rouen. However, after a few years, despite the undeniable beneficial effects this technique had on symptoms, the benefits themselves were short lived because of early valve restenosis.

Refusing to abandon his search for offering a non-surgical treatment to patients denied surgery, Alain Cribier developed the concept underlying TAVI, i.e., to replace the diseased native aortic valve itself with a new bioprosthetic valve using solely percutaneous cardiac catheterisation techniques. He had observed during BAV procedures that a balloon could be inflated completely and circularly, pushing aside the valvular calcifications, offering him proof that a frame could maintain the diseased valve open: adding a bioprosthesis inside the frame would be the solution. What Alain Cribier had in mind was a balloon-expandable, metallic, large-diameter “stent” containing a valvular structure that could be delivered within the diseased valve by balloon inflation. He started exploring this idea in the early 90s, by performing stent implantation in cadavers of patients with severe aortic stenosis, demonstrating the feasibility of his “crazy” concept.

I worked closely with Alain Cribier and was able to attest to and admire his perseverance for almost a decade in order to find a company to develop a prototype. It is also admirable that during these difficult years, he developed another innovation, the metallic mitral commissurotomy to treat percutaneously patients with mitral stenosis with a reusable device, which led us to teach the technique in various countries, particularly in India.

Finally, in 1999, a start-up named Percutaneous Valve Technologies (PVT) was created by the engineers Stan Rabinovitch and Stan Rowe, Martin Leon, the well-known US cardiologist, and Alain Cribier, and the first model of a percutaneous balloon-expandable valve was developed in Israel (ARAN Company).

Together with Alain Cribier, we then conducted important *in vivo* preclinical studies in Paris, implanting more than 100 prostheses at various cardiac sites in sheep models over a two-year period in both acute and chronic studies.

And the day came - a sunny Tuesday morning in Rouen on 16 April 2002 - when the first-in-human aortic valve implantation was successfully performed in Rouen in a 57-year-old patient with severe aortic stenosis who was dying, in cardiogenic shock, inoperable because of multiple comorbidities. That patient was admitted to our institution for BAV as a last-resort procedure. Due to persistent shock despite BAV, he was the first-in-human case. When it was published in *Circulation*, the reaction of the world medical community to this first case defies imagination, even today. TAVI was born.

In the practice of medicine, only a few medical discoveries and their subsequent technologies have been subjected to such an outstanding scientific evaluation as TAVI.

Twenty years after the first-in-human case, indications for TAVI, originally limited to “compassionate” use in high surgical risk patients, have been enlarged by the American and European guidelines to include patients at intermediate risk and finally, in 2021, to include low-risk patients as well.

At the present time, throughout the world, the number of TAVI procedures now exceeds surgical valve replacements – an impressive fact related to the outstanding combination of excellent clinical results and the simplicity of the procedure

for the patients. For these patients, this far less invasive approach requires no sternotomy and only local anaesthesia, offering a short hospital stay and, most importantly, a rapid return to normal life. This was the achievement of Alain Cribier’s dream to offer a “stent-like” treatment to patients with severe aortic stenosis denied surgery.

The impact of Alain Cribier’s innovations and subsequent work is not limited to cardiology or valvular disease alone but has rippled through many areas of the practice of medicine today. From inspiring countless young doctors to train in these innovative and effective techniques, to the reorganisation of hospitals and healthcare services around constantly evolving cath labs, to the widespread developments in imaging technologies, the footprint of TAVI can be seen in healthcare worldwide. Multidisciplinary teams, the Heart Team concept that grew out of TAVI, are now the basis for a more holistic approach to individual patient care.

Alain Cribier transformed and improved cardiovascular care through his dedication to medicine and his commitment to his patients and to the generations of specialists he trained and inspired. His unrelenting faith in a pioneering concept, TAVI, has now proven its value, and we join the millions of patients who have been successfully treated worldwide to whom he devoted his life in offering our profound thanks to Alain Cribier – a kind, simple, generous, caring and thoughtful individual, and an exemplary doctor beloved by his patients.

He will be deeply missed.

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