Title: HF 22: 6M Results of a No-Implant Interatrial Shunt in Pts With Chronic HF

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My name is Lars Lund, I'm a Professor of Cardiology at the Karolinska University Hospital in Stockholm, Sweden. And I'm delighted to be at the 2022 HFA, Heart Failure Congress.

Aims of This Study

Prof Lund: The ALLEVIATE programme aims to treat and help patients with heart failure in a preserved ejection fraction. In heart failure with a preserved ejection fraction, patients we're learning have a reasonable prognosis, they do quite well, but they have poor quality of life. And this poor quality of life is very dominated by increased filling pressures in the heart during exercise.

Increased pulmonary capillary wedge pressure that could be almost normal at rest, but that increases very rapidly at exercise. An emerging concept to treat elevated filling pressures at exercise, or on exertion is to create a little hole in the septum, in the interatrial septum.

So, there are various approaches to creating a between 5- and 10-millimetre hole that allows blood to pass from the left to the right in a shunt. Like a PFO or ASD, something that we are taught to worry about. And by doing so we get approximately 1.2 ratio shunt where some blood is shunted over to the right, reducing pressure on the left, and improving symptoms and exercise capacity.

No-Implant Interatrial Shunt

Prof Lund: So, the emerging approach is to creating a hole in the septum, where initially, small devices that were placed as hardware in the septum to keep it open because when tissue does not have hardware normally it closes. In something like a balloon procedure for a valve or a septum or anything like that.

But the ALLEVIATE System is very unique in the sense that it uses off the shelf tools to go through the groin into the vena cava, into the right atrium, and cross the septum with off the shelf tools, and then with a unique sort of cutter puts a device, 16 french approximately, through the septum, and with radio frequency ablation cuts out a 7-millimetre diameter

piece of tissue. And we've seen in animal studies and now in, I believe in 32 patients, that this hole stays open, patent. You would worry that this hole was going to heal closed with fibrosis, but very quickly the edge of the hole endothelializes and there is tissue removed so there are no opposing edges, and nothing to fibrose.

So, in all the patients studied at 6 and 12 months to date, the shunt remains open, and there's no hardware left. And the other advantage with the with this approach is that many patients with heart failure and many patients with HFpEF will in their lifetime need additional procedures in the interatrial septum. You may need to cross the septum to do an atrial fibrillation ablation, pulmonary vein isolation. And there are many other conceivable procedures that all need access to this area in the septum. If there's already a device in place, that becomes difficult. If there's just a hole in place, that becomes easy.

Inclusion and Exclusion Criteria, Patient Cohort and Study Design

Prof Lund: So, the aims of the ALLEVIATE-HF-1 and ALLEVIATE-HF-2 pilot studies, which are non-randomized, open label without any SHAM control or without any control group, to test primarily the safety and feasibility of our new approach. And there have been approximately 30 patients in these 2 pilot studies, that have heart failure and a preserved ejection fraction defined as signs and symptoms of heart failure, elevated natriuretic peptides and an ejection fraction of over 40%.

In order to pick the patients, they need to, after consent and screening, they need to also have an invasive right heart catheterization to measure filling pressures, pulmonary catheter wedge pressure at rest and at exercise.

And if these are elevated, patients are then qualified to proceed with the procedure. And the endpoints in our study have been safety, so complications, which there have been none, patency, meaning feasibility of keeping a shunt open, which as I said at 6 and 12 months has been 100% in the patients studied so far. And then very, in a very exploratory fashion, some efficacy. And we've measured wedge pressure at exercise, which declines significantly by 6-millimetre mercury. We've measures NT-proBNP, which declines. And we've also assessed KCCQ quality of life, and 6-minute walk test, and they improved dramatically. Although we must describe that to a great part to the placebo effect in a non-randomized, non-blinded study.

Key Findings

Prof Lund: The key findings are a reduction in exercise pulmonary capillary wedge pressure by 6 millimetres of mercury, and of a resting PCVP of about 2 or 3. A reduction in NT-proBNP by about a third, and an improvement in KCCQ, a dramatic improvement of KCCQ of 10 to 20 points. Which is, would be considered highly clinically meaningful.
And similarly in increase in the 6-minute walk test from, if I recall correctly, roughly 250 to about 350, which is very, very good. But we must remember that this is a non-blinded study.

Take-Home Messages

Prof Lund: The take home messages are that patients with HFPEF have elevated filling pressures especially at exercise, even if they have near normal NT-proBNP.
This is what causes their poor exercise tolerance and their poor quality of life. And it's also associated with heart failure hospitalisation. This can be reduced by creating a hole, a shunt in the interatrial septum. And previous methods do so by inserting a device to keep the septum open. We do so by excising a piece of tissue. And we've seen that this teptechtomy, in other words, we've excised a bit of tissue, remains open 6-12 months, the duration we've studied. And reduces exercise wedge pressure, reduces NT-proBNP, improves quality of life and functional capacity, and we're now planning a double blind, or single blind, I should say, SHAM controlled, randomised study to begin in the fall.

Next Steps

Prof Lund: So, the next steps for us, after this very promising data in an unblinded setting of course, is to perform a randomised SHAM controlled study, which is critical, particularly if outcomes are subjected, such as quality of life, and very much determined by motivation, such as functional capacity, 6-minute walk test.