Title: HF 22: Rebalance-HF: Catheter-Based Ablation of the GSN in Pts with HFpEF
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- My name is Marat Fudim. I'm a Cardiologist at Duke University, I'm a Heart Failure Cardiologist to be specific, and the name of my study is Rebalance-HF. It's the endovascular ablation of the greater splanchnic nerve, and it's the role in cohort that we presented today.

Background

Dr Fudim: The intent of the endovascular ablation of the splanchnic nerve surrounds the concept of volume distribution. We now know that cardiac decompensation is not just the result of volume overloads, but it's a result of volume distribution, and that's a concept that is based in the vasoconstriction of vasculature.

So, when you vasoconstrict, particularly the venous vasculature, you are causing distribution of blood volume from the periphery into the chest, which then causes elevation of filling pressures and can exert itself either as exertional limitation with exercise, or maybe even a cardiac decompensation, these heart failure hospitalisation. So rather than the addition of water and salt, here it is simply the distribution effect that leads to this concept.

So we have done series of studies in the past, they were short-term studies, few hours, a day, and also surgical resection of the same nerve, which have demonstrated as a proof of concept that we can lower pressures in the heart, we can lower pressures in the heart during exercise and we can sustain the lowering of pressures throughout 12 months when you resect that nerve with direct visualisation.

So we know that the splanchnic nerve induces some of these distribution effects, and if you get rid of the nerve you might prevent some of the distribution effect, thus, it's a declared target. So enemy number one now.

Patient Population & Study Design

The study population here is heart failure with preserved ejection fraction, with HFpEF, specifically it's patients with the ejection fraction of 50 and greater. They had to have some

form of cardiac decompensation in the past, whether it's IV diuretic administration of last year, hearth failure hospitalisation, or they simply had an elevated NT-proBNP. Having said that, the exclusion and inclusion criteria for this study are not very stringent, but the key inclusion criteria is that they had to go on the cathlab table and do supine ergometry, so bike exercise, supine, with a catheter in place to measure the pressures, they need to have it elevated filling pressures.

This is how we really, really know as a gold standard, whether a patient had heart failure with preserved ejection fraction, by meeting this. It's not an arbitrary cut-off, but certainly very well-established cut-off to determine heart failure preserved ejection fraction. So 25 and greater, they had to meet that, that was the hardest criteria to meet.

GSM Ablation

Dr Fudim: The procedure in this study, we refer to as SAVM, it's splanchnic nerve ablation. And here we take a transvenous femoral approach. So, you enter the vein in the groin, you drive it up to the SVC and then down the azygos vein, the azygos vein is a branch that leads into the SVC.

You can drive this catheter all the way down into the intercostal vein of T10 and T11, those are the vertebral levels. At that location, the veins intersect with the nerve, the greatest splanchnic nerve for GSN in a relatively fixed anatomical position.

You know, there have been enough cadaver study, preclinical studies and clinical studies that indicate that the anatomy of the nerve and the veins is relatively fixed, and because they're fixed, we can simply use landmarks to position an RF catheter, RF means radiofrequency, you turn on the device and it heats the tissue.

The nice thing is there's not much down there besides the nerve, the vein you in located and then the pleura that's close by, but the heating is not that high to induce any damage really beyond the local nerve that is very close in proximity, a couple millimetres to the vein.

So, you heat up the nerve, you destroy the nerve on one side, just the right side, and that's the entire procedure. Procedure duration is anywhere between 20 to 40 minutes in the study, for the entire procedure.

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Key Findings

Dr Fudim: The population was predominantly female, they met all the inclusion criteria of sort of "true HFpEF", they had an average age that was above 70, they had a lot of comorbidities as it's typical for a 70-year-old patient with HFpEF.

The NT-proBNP was only in the three hundreds, not that high. This was a predominantly exertional population with class two, three heart failure. We found that when we ablate the nerve at one month follow up, which was the predefined time point where we again repeat the hemodynamic testing, we found that there was a drop in wedge pressure, that's the left sided pressure in the heart, that wedge pressure dropped by about eight millimetre Hg in average, in those 18 patients, with either low grade exercise, which is 20 Watts or with peak exercise, which was around eight as well. The median was lower, was five in two of those individual time points, it was highly statistically significant between those two endpoints.

And then we also looked at quality of life. There was an improvement in quality of life at the one in three marks. There was an improvement in six-minute walk, but it was not statistically significant. There was an improvement in NYHA scale by about one point and about third of population. And the NT-proBNP has not changed in the three months of follow up, following based on procedure.

Then also to speak of safety, which is probably something that your listeners would want to know about. As to safety, so all 18 patients had a successful ablation, so we were able to access the vein and ablate the nerve, we suspected what the nerve was ablated, in most cases there's no confirmation of technical success besides the actual pressure coming down at one month.

A, B, there were three device related complications, those were pain. One patient actually got admitted to the ET shortly after the procedure because he got a lot of fluid during the procedure, and the diuretics were withheld, is a mistake that we wouldn't repeat going forward. And that's pretty much it. And it was a hypertensive episode during the procedure, which is associated with pain, thus, we do the procedure under anaesthesia. So, all those procedure related effects were self-limited, not sustained, so that I think is very good testament to the procedure so far.

Conclusions and Next Steps

Dr Fudim: The conclusions to this is that this is the open label running to a larger pilot randomised controlled study. So, the role in cohort is now followed by an 80-patient randomised portion. That randomised portion we don't have currently the data; we are more than half enrolled into the study. We should have the data by the end of the year, and then follow up completed by next year. So the conclusion here is, you know, this is open label data, it sounds very reassuring because it confirms price single centre and dual centre data, so clearly encourages us that that signal we seize seems to be reproducible, but because it's open label and device procedures, certainly having a sham or a placebo effect, we need to do one or two randomised controlled studies to really in a large fashion to confirm the findings. So, a sham controlled study is following, and I'm excited to be able to share the results next time.