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Shockwave Begins First All-Female Study Of Coronary Interventions

by Brian Bossetta

The EMPOWER CAD trial will evaluate Shockwave's intravascular lithotripsy system in female patients undergoing a percutaneous coronary intervention for coronary artery disease. Principal investigator Alexandra Lansky spoke to *Medtech Insight* about the first-of-its kind study in this understudied population.

A new study sponsored from *Shockwave Medical*, which specializes in coronary intravascular lithotripsy (IVL), is designed to close the deadly gender gap in coronary artery disease (CAD).

Heart disease kills more women in the US than any other disease — a fact not even many women are aware of. In 2020, heart disease accounted for one in five female deaths, according to the Centers for Disease Control, yet only 56% of women realize it's their number one killer.

Cardiovascular disease is the leading cause of death for European women as well, according to the European Society of Cardiology (ESC), which also notes that heart attacks in women "have worse outcomes and higher mortality than in men."

Women have historically been underrepresented in clinical trials for technologies that treat heart disease.

EMPOWER CAD will enroll 400 women with CAD across the US and Europe to determine whether positive results in

Key Takeaways

- Heart disease kills more women in the US than any other disease, but most people underestimate the risk for women.
- Clinical trials for cardiovascular technologies have traditionally enrolled few women.
- The EMPOWER CAD of Shockwave's

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both sexes from earlier studies with Shockwave's C2 coronary IVL catheter can be replicated in a large cohort of female patients undergoing a percutaneous coronary intervention.

The study's first patient was enrolled in May at St. Francis Hospital and Heart Center on Long Island, NY.

coronary lithotripsy system will enroll 400 women with coronary disesase to determine if the positive results from previous trials can be replicated in a large cohort of female patients undergoing a percutaneous coronary intervention.

Better Outcomes?

One of the study's lead investigators, Alexandra Lansky – a renowned interventional cardiologist and researcher at Yale University – told *Medtech Insight* that traditional CAD treatments have typically resulted in worse outcomes for female patients than for males.

Lansky said that after orbital or rotational atherectomies – in which plaque is either scraped or cut from the arteries – women often have higher rates of dissection, perforation, and other procedural complications compared to men.

This could be related to several factors such as women having smaller and more fragile blood vessels than men, she said.

> ***"EMPOWER CAD is all about taking better care of our female patients, but also to empower our female colleagues." – Alexandra Lanksy***

But patient-level analyses of prior trials of lithotripsy – a procedure that uses shock waves to break up calcifications – showed comparable outcomes for men and women without the complications seen in atherectomies.

"There were no complications, no dissections, no perforations, in female patients," Lansky said. "The outcomes were very similar between men and women."

Instead of scraping or cutting the calcified lesions, the Shockwave C2 coronary IVL catheter deploys a balloon to open the blood vessel then breaks up the calcifications with sonic pulses similar to those used to pulverize kidney stones.

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"It emits these waves into the coronary vessel once the balloon is inflated at very low pressure, and then fractures the calcium," Lansky said. "It basically causes these micro fractures within the calcium, which then enables better compliance of the vessel."

Further, because in most cases stents are placed in the artery to restore normal blood flow, Lansky said the device provides better stent expansion and acute results.

"The beauty of the device is that it's very easy to use," Lansky said. "It's not challenging for most interventional cardiologists."

However, Lanksy noted the analyses of prior lithotripsy trials were limited because they were retrospective and only included about 25% of women patients with limited follow up.

With 400 female patients across 35 sites in the US, 15 in Europe with a three-year follow up, EMPOWER CAD is designed to validate and confirm the positive results from earlier lithotripsy trials, Lansky said. "It's a very exciting new program and will provide more robust data to determine if IVL should be the front-line approach in female patients."

Shockwave's Progress

In 2021, the US Food and Drug Administration approved Shockwave Medical's C2 coronary intravascular lithotripsy system for lithotripsy-enabled, low-pressure balloon dilatation of severely calcified, stenotic de novo coronary arteries prior to stenting. (Also see "*FDA Approves Shockwave Coronary Intravascular Lithotripsy System*" - Medtech Insight, 18 Feb, 2021.)

The approval was based on the results of the *Disrupt CAD* III, a 431-patient prospective, single-arm trial comparing treatment of coronary calcification with IVL to a prespecified performance goal based on the *ORBIT II* trial of orbital atherectomy to treat coronary calcification. (Also see "*Shockwave Prepares For FDA Approval Of Coronary Intravascular Lithotripsy System*" - Medtech Insight, 11 Nov, 2020.)

Medicare approved transitional pass-through (TPT) payment for the Shockwave IVL catheter allowing coverage under government plans. (Also see "*New Treatment From Shockwave Medical For Clogged Arteries Gets CMS Pass-Through Payment*" - Medtech Insight, 18 Jun, 2021.)

A History of Exclusion

"Women were not even included in clinical trials until 1993," Fayer said. "That seems like a long time ago, but it's not."

Though the National Institutes of Health (NIH) established a policy in 1986 encouraging researchers to include women in trials, it was not until 1993 that Congress made that policy law.

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> *"Women were not even included in clinical trials until 1993. That seems like a long time ago, but it's really not." – Marissa Fayer*

But lack of diversity in clinical trials is not uniquely American.

While the female enrollment in cardiovascular trials funded by the NIH between 1997 and 2006 was only 27%, according to ESC, it was even lower in European trials.

Misdiagnosis

Along with biological differences, such as smaller blood vessels, women often experience different cardiovascular symptoms than men.

Whereas men typically experience the "classic" symptoms of a heart attack, such as crushing chest pain, sweating, and nausea, women often have subtle symptoms that can be mistaken for something benign, like fatigue, or hormonal changes, or they might not have symptoms at all.

These "silent" symptoms also factor in as to why women often have less favorable outcomes in treating blocked arteries, Lanksy noted. Delayed diagnosis of CAD usually means the calcification has progressed making it harder to treat.

Research has consistently shown that women are more likely to be misdiagnosed after a heart attack than men.

For example, heart attacks are misdiagnosed more often in young women than in men, according to the American Heart Association (AMA), which notes that thinking differently about how symptoms manifest is key to reversing this trend.

In a 2019 *editorial*, *The Lancet*'s editors argued that women's heart health has been evaluated by a protocol geared toward men for decades.

"The historic failings of cardiology to take a balanced approach to research have led to fundamental flaws in the care for women with heart disease and has cost the lives of many women," the editorial concluded.

But in Fayer's view, societal prejudices are part of the problem as well.

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ALEXANDRA LANSKY

"When a man has certain symptoms, doctors know instantly it's a heart issue, but with a woman it might be the fourth thing they suggest. Palpitations or extreme fatigue is blamed on menopause or stress," Fayer said. "Well, maybe that's the case, but maybe not. Maybe it actually is the heart."

Fayer believes women also need to prioritize their heart screenings as they do with mammograms and Pap smears.

"So yes, cancer's incredibly important because it's the number two killer of women, but don't forget number one," she said. "There are things you can do. Know your risks, know your genetic factors, diet and exercise, and get your heart checked."

Postpartum

Screening takes on even greater importance for women after giving birth.

According to a new *study* led by epidemiologist Sadiya Khan and colleagues at Northwestern University, risk factors for heart disease increased among women who gave birth between 2016 and 2020. Despite the importance of assessing heart health after giving birth, only 60% of women reported heart health counseling in their postpartum visits, the study found.

Because 90% of US women have at least on postpartum visit – or "the fourth trimester" – they provide clinicians a golden opportunity to discuss heart health with their patients.

"We need to find ways to take advantage of this prime opportunity," said Kahn. "The fourth-trimester visit is an already-ready moment to prioritize maternal heart health."

Prioritizing heart health is especially true for Black women, who have a 50% higher risk of heart failure than white women, according to the Cleveland Clinic, and 59% of Black women between 20 and 59 have cardiovascular disease, according to the American Heart Association.

This speaks to the importance of diversifying clinical trials, which the federal government is trying to do at various levels. In April 2022, the FDA issued guidance to ensure clinical trials include a broader representation of underrepresented racial and ethnic groups. (Also see "*FDA Draft Guidance Takes Aim At Racial, Ethnic Disparities In Clinical Trials*" - Medtech Insight, 13 Apr, 2022.)

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Private industry is also stepping up. In June, Abbott announced it was investing $5m over the next five years to advance diversity in clinical trials among participants as well as physicians. (Also see "*Abbott Invests Millions In Clinical Trial Diversification Efforts*" - Medtech Insight, 8 Jun, 2023.)

Fayer also believes it would be beneficial if there were more female cardiologists.

The American College of Cardiology estimates only 10% to 15% of practicing cardiologists are women while only 4% of interventional cardiologists – such as those like Lansky treating CAD – are women.

EMPOWER CAD seeks to address that too.

Along with Lanksy and her co-principal investigator, Margaret McEntegart, an interventionalist at Columbia University Medical Center, 70% of the study's local investigators are women, according to Shockwave, providing a unique opportunity for many females to have a study leadership role for the first time.

"This is a field where women interventionalists represent a minority in the US. Women in the field are bypassed in leadership roles because we're simply outnumbered," Lansky said. "EMPOWER CAD is all about taking better care of our female patients, but also empowering our female colleagues."

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