TRENDS-in-MEDICINE

BULLETIN:

IMPLICATIONS OF THE FDA WARNING ABOUT MORTALITY WITH ABIOMED'S IMPELLA

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by Lynne Peterson

The FDA issued a safety alert letter to healthcare providers (what's referred to as a Dear Doctor letter), warning them that the interim results with 60 patients in a postmarketing study of Abiomed's Impella RP, a temporary, percutaneously-placed right ventricular assist device showed an increased rate of mortality (30-day survival of 17.4% vs. 73.3% in the pivotal premarket study). The Agency said that, although it is concerned about the mortality rate, it believes the benefits still outweigh the risks when the device is used as approved and in the patients studied in the premarket trials, noting that 70% of the post-approval patients would not have qualified for participation in the premarket studies.

The question is what the letter means for use of Impella PR going forward. ***Trends-in-Medicine*** reached out to three experts for their take on this issue. Basically, they don't expect the letter to affect use very much – unless insurers restrict use. And they don't expect the FDA to further restrict use at this point. It may impact patient consenting. They likened use of Impella RP in the off-label patients to a Hail Mary pass where it is great if it works (helps save the patient's life) but is not necessarily expected to work. There would be much more concern if the mortality rate were higher in the same type of patients studied in the premarket trials.

This is what they had to say:

- **Steven Nissen, MD, chief of cardiology at the Cleveland Clinic and a past president of the American College of Cardiology:**
  - "We are unlikely to change our practice based on the FDA analysis.
  - "The FDA report is not based on high quality data. In the real world, patients often do worse than those studied in clinical trials. Most observers think that the devices are probably being placed in patients who have already reached the point of no return.
  - "The widespread use of the device has been fueled in part by very aggressive marketing which has expanded usage beyond the population studied in the pre-approval clinical trial.
  - "I continue to believe that standards for approval of medical devices need to be higher. This is a chronic regulatory problem that needs to be addressed on a national level."
- **Mary Norine Walsh, MD, medical director of the Heart Failure and Cardiac Transplantation Programs at St. Vincent Heart Center in Indiana and the immediate past president of the American College of Cardiology:**
  - "I think the main thing…is if we compare the indications for which Impella RP was approved by the FDA to those in the [postmarketing] trial, those two are very disparate…Clinicians are using this for patients who would never have fit in the trial.
  - "There is evidence it is being used, for example, for patients who suffered cardiac arrest during hospitalization. Those patients were not included in trial. This is an example of what we sometimes call indication creep. The FDA approves something for a given indication, and once it is out and in the marketplace, clinicians use it as they see fit.

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- "So, rather than the device 'not working'…in these early reports it is not always being used for the indicated patients."
- "It is a good device for appropriate patients for whom it is indicated."
- *Should use be restricted?* "When you offer it to a patient, following the indication means the patient with whom you discuss the therapy knows the scientific data, that this device may help…But, on the other hand, how do we learn what other indications might eventually be approved…I'd say registry information and gathering information as the FDA is doing – we need to look at that."
- *Could insurers restrict use going forward?* "Most commonly insurance coverage for device therapy follows the FDA indications… depending on the response of insurers to this…Insurers will be the ones who control use."

Timothy Gardner, MD, chief of cardiothoracic surgery at the University of Pennsylvania School of Medicine and a past president of the American Heart Association:

- "I don't think [it will change use]. This is a device not used very often. It is a device to help bail out a patient who is in serious need, has severe left heart failure after a myocardial infarction or has a heart transplant and the right ventricle doesn't function well. It is a pretty rare circumstance. Anytime anyone puts in a right heart assist device, the patient is in pretty bad shape. It is a sort of rescue therapy.
- "The attraction of Impella RP is you can insert it without having to open the patient's chest. Mechanistically it is a great device. I think the surgeons and heart failure doctors dealing with severely ill patients look on it as a hopeful adjunct to what they have available.
- "I don't think this postmarketing study is going to blow it out of the water…but I do think it is a little bit of a wring from the FDA or a heads up from the FDA that, 'Don't put this device in patients who are so far gone you won't expect recovery.'
- "The device is fairly safe, and the attraction is you don't have to put the patient on a large right ventricular assist device through the chest…I think the FDA is just being appropriately thorough in alerting the public/users that, so far, expected results in salvage patients is not what they would have predicted."
- *Will the FDA restrict use?* "I doubt it seriously. The issue is not the safety of the device; it is the fact that in a patient whose situation is futile or whose long-term survival is not likely…that is a patient who is not going to be helped by the Impella device…I respect the FDA for doing these postmarketing studies, but I think, in this case, the results to date from the Abiomed database are so poor that they wanted to alert people. But I don't think the issue is the device doesn't work…It is you have to choose your patients carefully."
- *Will insurers restrict use?* "I don't think so. I think…if another year goes by and the results are equally poor – but I think they will be better – the FDA might suggest that this device looks fairly futile…But I don't think they will do that. They are more into safety and efficacy for the purpose for which the device is approved…The explanting here sounds like a lot of the patients in whom the device was implanted did not have good life expectancy potential…and the device shouldn't have been used."
- *Will the FDA letter have a chilling on Hail Mary use of Impella RP?* "No, because it is still so much easier to use…but I do think it is a very, very small patient group that is a candidate for it."
- *Asked about experts encouraging more use of Impella*, he said, "A message that you shouldn't wait to use it until the patient is at the last ditch because we have this device that allows us to intervene earlier, and it is less invasive, so use it when the right ventricle starts to fail – don't wait until the patient has horrible complications – that message is still appropriate."