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FARAPULSE™ Pulsed Field Ablation System

MANIFEST-17K Multicentre Registry[1]

Multi-national survey on the safety of post-approval clinical use of Pulsed Field Ablation in 17,000+ patients (MANIFEST-17K)

OBJECTIVE[1]

- To assess if FARAPULSE Pulsed Field Ablation is:
  - Tissue-selective and spares the esophagus, pulmonary veins and phrenic nerve.
  - Associated with any unusual adverse events that would only be apparent after thousands of ablation procedures.

MANIFEST-17K REGISTRY DESIGN

- Retrospective observational study of the real-world commercial use of FARAPULSE Pulsed Field Ablation.
- Centre level data was collected from 106 centres (91.4% of all commercial centres using FARAPULSE) and 413 operators.
- The data expands beyond the previously published MANIFEST-PF registry to include a total of 17,642 (35% PersAF) patients.
- The initial MANIFEST-PF sites contributed 7,878 patients and the MANIFEST-17K sites contributed data from 9,764 patients.
- The results from MANIFEST-17K reflect a 2-year window of patients treated (3/2021-3/2023).

SAFETY

- The 3 adverse events classified as related to pulsed field energy delivery were transient phrenic nerve paresis (0.06%), coronary spasm (0.14%), and hemolysis/renal failure (0.03%). The remaining events (mortality, stroke, pericardial tamponade, TIA, and vascular access complications) were classified as non-PF energy related.

MAJOR ADVERSE EVENTS*

- The major adverse event rate was 0.98% with the most common complication being pericardial tamponade (0.36%).
- There were no reports of esophageal fistula or dysmotility, pulmonary vein stenosis or persistent phrenic nerve injury.
- **Mortality**
  - The mortality rate was 0.03% (n=5). Two deaths were procedure related (cardiac tamponade and post-procedure cardiogenic shock in a patient with cardiomyopathy and decompensated heart failure). The remaining three were not related to the ablation procedure.
- **Stroke**
  - The root cause analysis of the 22 (0.12%) stroke events was completed on 16 patients and showed that catheter exchanges, sheath management, ACT < 300, interruption of anticoagulation and uncontrolled hypertension accounted for 9 events, while 7 had no definitive cause.
- **Pericardial tamponade**
  - The pericardial tamponade rate was 0.36%, that number improved significantly from the initial MANIFEST-PF registry (0.97%).
- **Coronary spasm**
  - The rate of coronary spasm was 0.14% with a majority (88%) being proximity related occurring with off-label use of FARAWAVE™ during mitral isthmus (MI) or cavotriscupid isthmus (CTI) ablation. There were also 3 reports of generalised spasm (0.02%).
- **Hemolysis**
  - The rate of hemolysis was 0.03% and occurred in five persistent AF patients receiving complex lesion sets (PVI, PWI, MI, CTI)** with a large number of PF lesions (143 ± 27). Transient hemodialysis was used for all patients resulting in significant improvement of renal function at the time of discharge. Renal function normalised for all five patients in follow-up.
- **Vascular access**
  - Major vascular access complication rates requiring intervention (0.3%) were significantly lower in sites with routine use of vascular ultrasound. (0.17% in sites routinely using ultrasound versus 0.50% in sites not routinely using ultrasound).

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MINOR ADVERSE EVENTS*

- The minor adverse event rate was 3.21% with the most common complication being vascular access site complication (2.2%).
- There were 11 (0.06%) cases of transient phrenic nerve palsy with all cases resolving prior to hospital discharge.

LEARNING CURVE

- Comparing the MANIFEST-PF[2] registry of the first 1,758 patients treated with FARAPULSE to the MANIFEST-17K registry, there was:
  - A significant decrease in rates of pericardial tamponade and minor vascular complications.
  - Improvements in stroke and transient phrenic nerve paresis rates.

Complication rates improved between initial device use and continued device use		
	MANIFEST-PF[2] (Previously published, initial device use) **(n=1,758)**	**MANIFEST-17K (n=17,642)**
Pericardial tamponade***	0.97%	0.36%
Stroke	0.39%	0.12%
Transient phrenic nerve paresis	0.46%	0.06%
Minor vascular complications***	3.28%	2.20%

CONCLUSIONS

- This data expands beyond the initial 24 centres involved in the MANIFEST registry, showing that the low rate of safety events continues as the technology is adopted by additional centres.
- The major adverse event rate was <1% with no reports of esophageal fistula or dysmotility, pulmonary vein stenosis or persistent phrenic nerve injury.
- One of the goals of this registry was to look for any unusual adverse events that would only occur after thousands of procedures. Two rare events were noted, coronary spasm and hemolysis.
  - The rate of coronary spasm was 0.14% with a majority (88%) being proximity related occurring with off-label use of the catheter during mitral isthmus MI or CTI ablation. There were 3 reports of generalised spasm (0.02%) which is lower than the cited thermal (RFA/CBA) rate of 0.19%.
  - Hemolysis resulting in acute renal failure was rare (<1 in 1000) and were managed with hydration and associated with a high number of lesions applied.
- Evidence of learning curve at both the physician/site level and the EP community was seen in the significant decrease in rates of pericardial tamponade and minor vascular complications and improvements in stroke and transient phrenic nerve paresis rates from the initial MANIFEST-PF registry to MANIFEST-17K.

**Due to the retrospective nature of the registry, the adverse event rate was not reported at a pre-specified timepoint.*

***Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System.*

****Significant improvement (p<0.05).*

1. Reddy & Ekanem, *et al.* Multi-National Survey on the Safety of the Post-Approval Clinical Use of Pulsed Field Ablation in 17,000+ Patients (MANIFEST-17K). AHA 2023.

2. Ekanem, Emmanuel, *et al.* "Multi-national survey on the methods, efficacy, and safety on the post-approval clinical use of pulsed field ablation (MANIFEST-PF)." Europace 24.8 (2022): 1256-1266.

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