Acute Hemodynamic Improvement With Percutaneous Mechanical Thrombectomy in a Real-World Pulmonary Embolism Population: Interim Results of the FLASH Registry

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Disclosure Statement of Financial Interest

I, Catalin Toma DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

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Unmet Needs in Pulmonary Embolism

- **High acute mortality**
  - Up to 40% mortality for high-risk PE and 15% for intermediate-risk PE at 90 days[1]
- **Advanced treatment options previously reliant on thrombolytics**
  - Major bleeding rates across large studies converge at ~10% and 2% for ICH[2,3]
- **Optimal treatment solution for at risk patients would be:**
  - **Safe** from a procedural and bleeding risk standpoint
  - **Effective** with an immediate improvement in hemodynamics which can be crucial to interrupt the PE death spiral, especially in patients with signs of cardiac shock[4]

1. Secemsky et al., Contemporary Management and Outcomes of Patients with Massive and Submassive Pulmonary Embolism, The American Journal of Medicine. 2018:131(12): P1506-1514.
2. Chatterjee et al. Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage: A Meta-analysis, JAMA. 2014; 311(23): 2414-2421.
3. Giri et. al, Interventional Therapies for Acute Pulmonary Embolism: Current Status and Principles for the Development of Novel Evidence: A Scientific Statement From the American Heart Association. Circulation. 2019;140:e774–e801
4. Toma et al., Percutaneous thrombectomy in patients with massive and very high-risk submassive acute pulmonary embolism. Catheter Cardiovasc Interv. 2020; 1– 6

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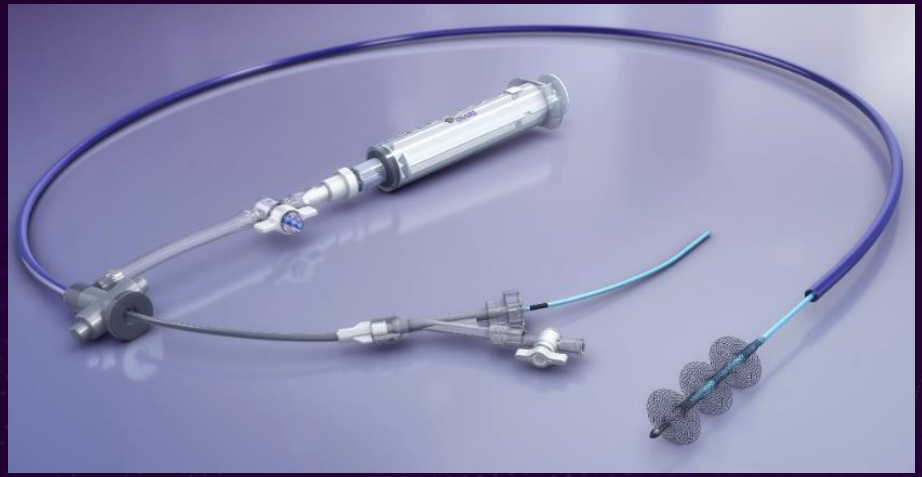
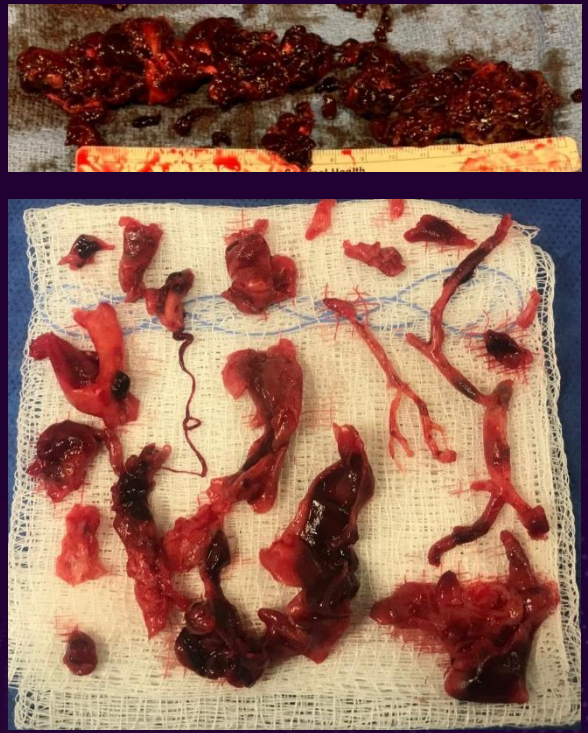
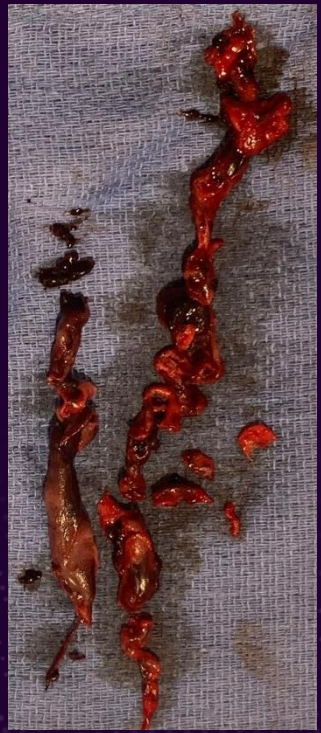
FlowTriever System

Purpose-built PE thrombectomy system designed to rapidly extract thrombus for on-table hemodynamic restoration without the need for tPA



FDA cleared for pulmonary embolism on May 21, 2018 based on FLARE IDE Study Results: Tu et al., A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism J Am Coll Cardiol Intv. 2019 May, 12 (9) 859-869.





Thrombus images from It's Alive! The Evolution of Thrombus and Why Fast, Effective Removal Is Key, Inari sponsored EVT article, April 2020.

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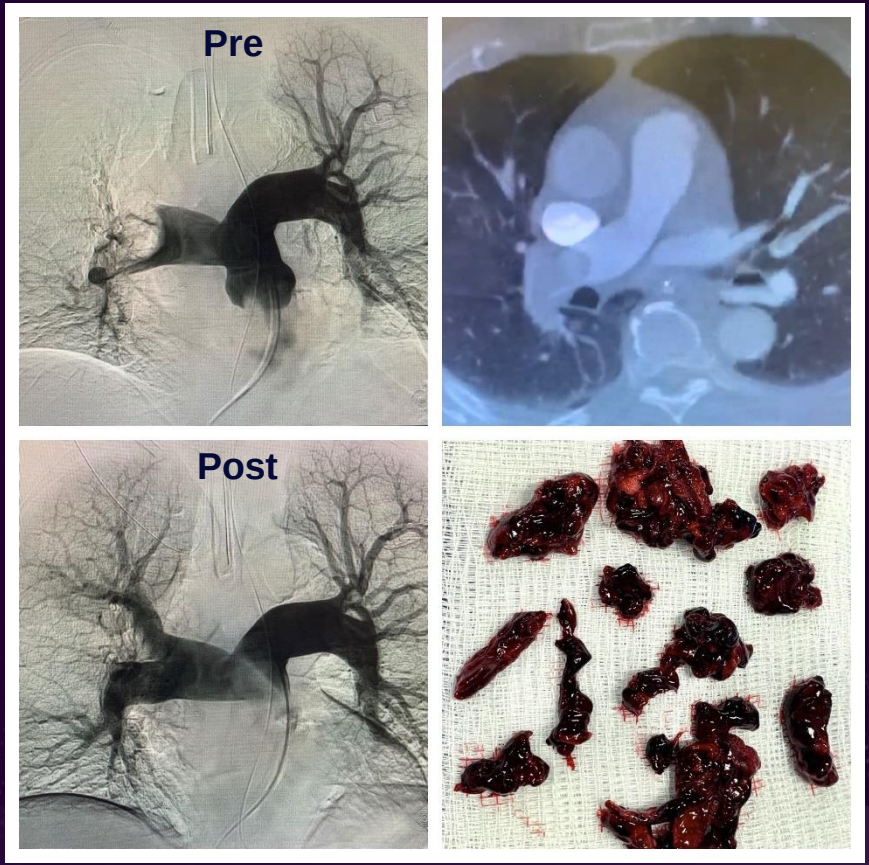
FlowTriever Case Example



Images courtesy of Dr. Igor Latich (Yale School of Medicine)

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FLASH Registry

Design	Goal	Enrollment
Prospective Multicenter Registry	Evaluate the safety and effectiveness of the FlowTriever System for treatment of PE in a real-world patient population	Up to 500 intermediate- and high-risk PE patients at up to 50 sites

- **Primary endpoint**: MAE composite through 48h
  - Device-related mortality
  - Major bleeding
  - Intraprocedural device or procedure-related AEs, including clinical deterioration and device-related pulmonary vascular or cardiac injuries
- **Secondary endpoints**: impact on acute hemodynamics, procedural measures, 48h all-cause mortality, and longer-term patient outcomes

Timeline	Variables
Baseline	Detailed medical history
On-table	Invasive hemodynamics, procedural data
Through 48 hours	MAE, Non-MAE bleeding, laboratory markers
Discharge	Hospital and ICU stays
Out to 6 months	Vitals, anticoagulation, AE, readmissions, QoL, 6MWT, PE relevant symptoms (e.g., dyspnea)

FLASH Registry – Baseline Characteristics

230 patients enrolled at 19 US sites

Characteristic	n (%) or mean ± SD
Age (Years)	60.7 ± 13.9
Male Sex	120 (52.2%)
History of DVT	51 (22.2%)
History of PE	31 (13.5%)
History of PHTN	32 (14.0%)
Concomitant DVT	159 (69.7%)
Active Bleed	6 (2.6%)
History of Cancer	55 (23.9%)
Active Cancer	19 (8.3%)
Lytics Contraindication	88 (38.3%)

Characteristic	n (%) or mean ± SD
Intermediate-risk (Submassive)	212 (93.0%)
High-risk (Massive)	16 (7.0%)
sPESI	1.6 ± 1.1
Positive Biomarker(s)*	211 (96.3%)
RV/LV (CT or Echo)	1.6 ± 0.5
Saddle PE	90 (39.1%)
Unilateral PE	28 (12.2%)
Bilateral PE	112 (48.7%)

*troponin and/or BNP

Note: Sample size for each characteristic ranged from 217 to 230 patients

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FLASH – Procedural Data

Characteristic	n (%) or median [IQR]
Access Site	Femoral: 226 (98.7%) Jugular: 3 (1.3%)
Access Site Complications	1 (0.4%)
FlowTriever Device Time (min)	46.0 [26.0 - 71.5]
Estimated Blood Loss (mL)	250 [100 - 400]
Adjunctive Therapy	11 (4.8%)
Hospital Length of Stay (days post-procedure)	3.0 [2.0 - 5.1]
ICU Length of Stay (days post-procedure)	0.0 [0.0 - 1.1]

Note: Sample size for each characteristic ranged from 201 to 230 patients

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FLASH Registry – Safety

Mortality through 48 hours: 0/230 (0%)

Primary Endpoint 48h MAE: 3/230 (1.3%)

- 0 device-related deaths
- 3 major bleeds (non-ICH)
- 0 intraprocedural device or procedure-related AEs
  - 0 clinical deteriorations
  - 0 device-related pulmonary vascular injuries
  - 0 device-related cardiac injuries

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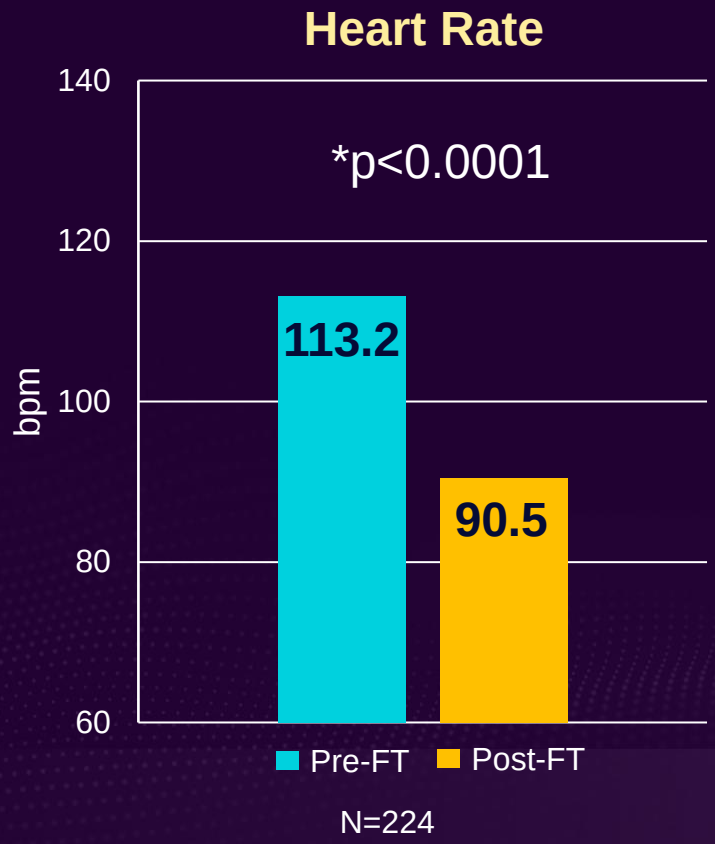
FLASH Registry – Heart Rate



Heart rate improved on average 22.7 bpm (20.1%) from a pre-procedural high of 113.2±16.8 bpm to 90.5±16.5 bpm

77.0% of patients were tachycardic (>100 bpm) pre-procedure compared to 24.6% immediately post-procedure (p<0.0001)

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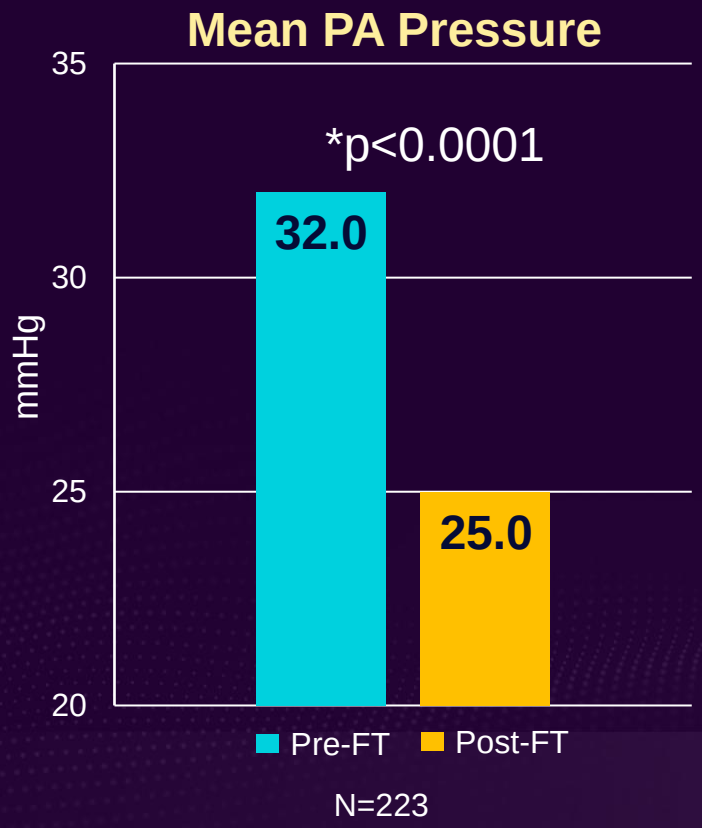
FLASH Registry – Acute Hemodynamics



On-table mean PA pressure dropped on average 7.0 mmHg (21.9%) from 32.0±8.2 mmHg to 25.0±8.2 mmHg

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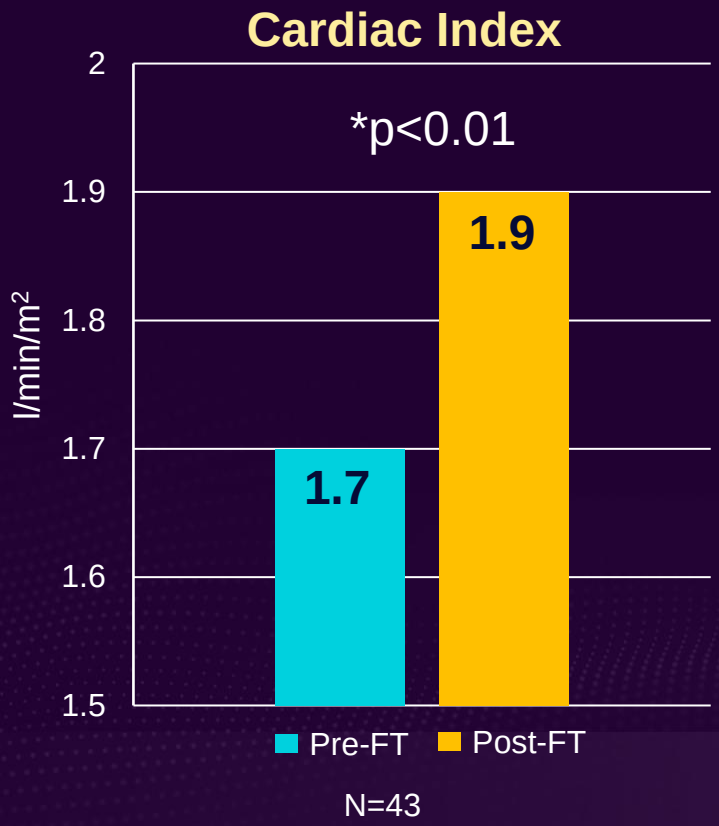
FLASH Registry – Acute Hemodynamics



23.5% of patients had a low baseline cardiac index < 2.0 l/min/m^2

These patients had an average on-table CI improvement of 0.2 l/min/m^2 (11.8%) from 1.7±0.2 l/min/m^2 to 1.9±0.4 l/min/m^2

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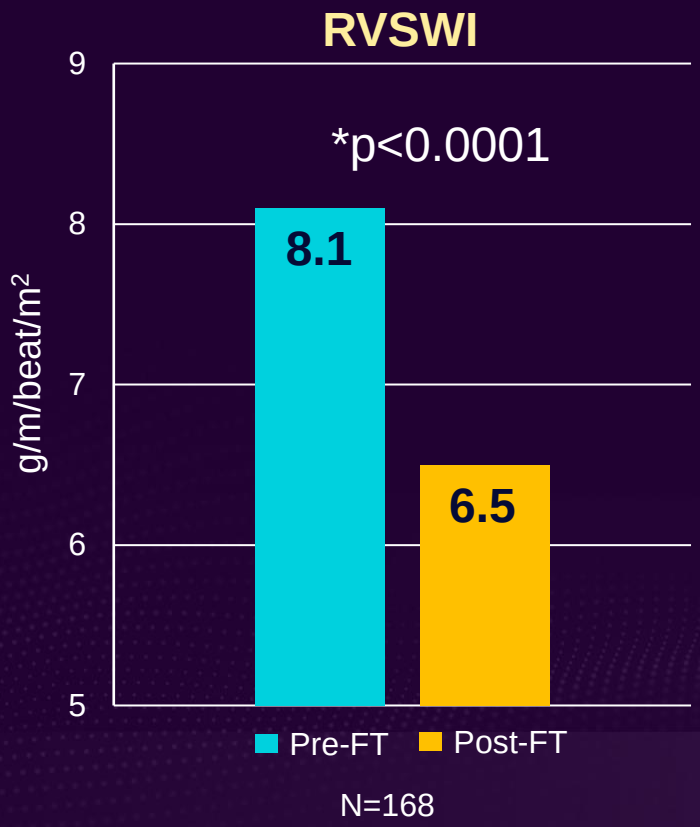
FLASH Registry – Acute Hemodynamics



Right ventricular stroke work index decreased on average 1.6 g/m/beat/m^2 (19.8%) from 8.1±4.0 g/m/beat/m^2 to 6.5±4.4 g/m/beat/m^2

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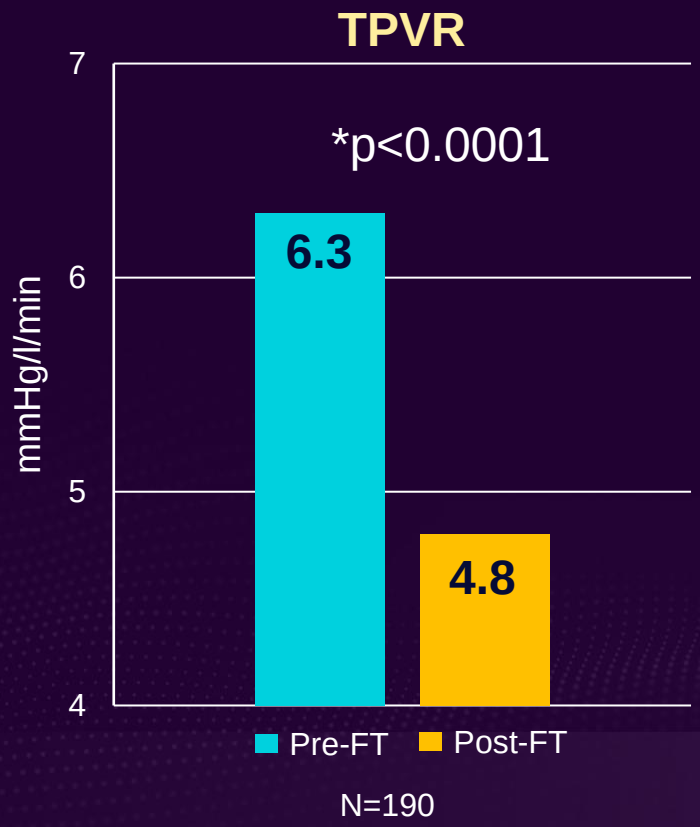
FLASH Registry – Acute Hemodynamics



Total pulmonary vascular resistance improved on average 1.5 mmHg/l/min (23.8%) from 6.3±2.8 mmHg/l/min to 4.8±2.1 mmHg/l/min

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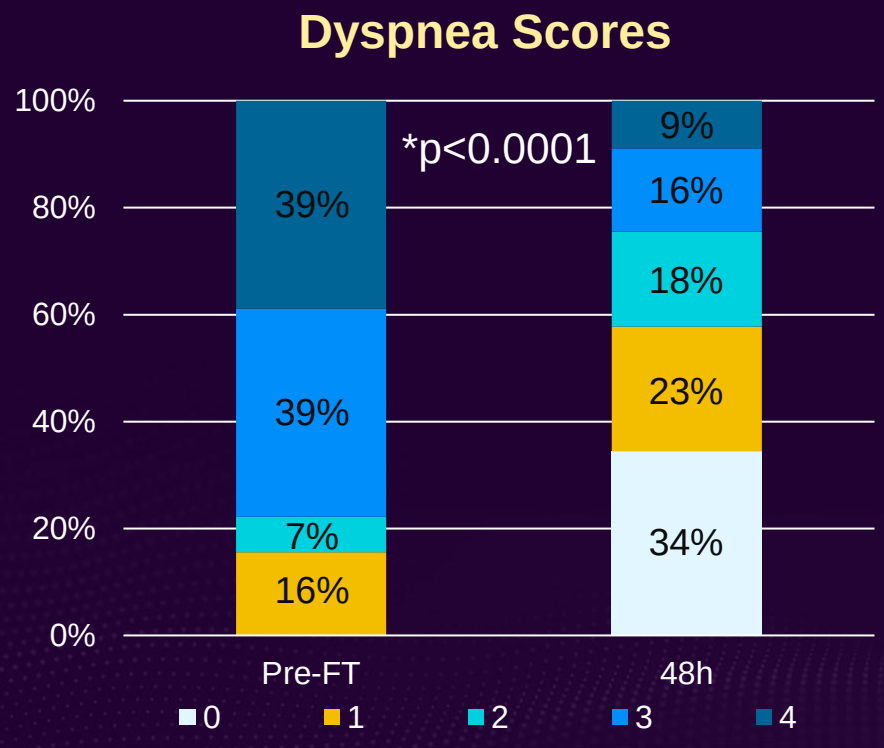
FLASH Registry – 48 Hours



Dyspnea scores using the mMRC scale (0-4 points) decreased on average 1.6 points from 3.0 to 1.4

Note: Sample includes 90 patients with available data confirming dyspnea at baseline

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FLASH Registry - Conclusions

- Interim results reinforce excellent FlowTriever **safety** in 230 real-world PE patients
    - No deaths at 48h, 1.3% 48h MAE rate, and only 1 access site complication
- Patients experienced significant on-table hemodynamic improvement compared to baseline
    - Mean PAP decrease: 7.0 mmHg; HR decrease: 22.7 bpm
- Dyspnea scores improved significantly at 48 hours
- Device time was short (median of 46 min) and most patients did not require an ICU stay post-procedure (median of 0 days)
- Further data will help design definitive studies in PE

Acknowledgements

Principal Investigators	Sites
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