February 10, 2020

Dear Colleagues,

Today the Dhruva et al. paper analyzing CATH PCI and Chest Pain registry data published in *JAMA*. This paper has similar conclusions to Dr. Dhruva's presentation on this same topic last November.

The Abiomed Medical Office has reviewed the Dhruva paper and supplement and identified a number of limitations, including:

- This is a retrospective, observational study:
    - IABP AMI CGS unadjusted survival rate was 71% – a number not seen in any trial or FDA study.
    - The analysis excluded IABP patients escalated to other therapies.
    - The data mixes those who received Impella pre-PCI with those who received Impella as a bailout, rather than isolating the pre-PCI patients from those who had Impella support initiated after the PCI began.
    - The 16,227 patients making up 57.3% of the cohort in this shock population had a 20% mortality rate, substantially challenging the definition of shock in this data set. Not using inclusion criteria for cardiogenic shock established in multiple RCTs likely explains the low mortality in the medical treatment and IABP arms.

eTable 4: Unadjusted Outcomes Among Patients Undergoing Percutaneous Coronary Intervention for Acute Myocardial Infarction Complicated by Cardiogenic Shock from October 1, 2015 – December 31, 2017

	Medical Therapy Only (n=16 227)	Other or Multiple MCS Devices (n=1838)	Intravascular Microaxial LVAD (n=1768)	IABP Only (n=8471)
Outcomes, No. (%)				
Death	3,241 (20.0)	798 (43.4)	801 (45.3)	2,461 (29.1)
Major Bleeding	1,688 (10.4)	552 (30.0)	556 (31.4)	1,233 (14.6)

Abbreviations: LVAD, left ventricular assist device; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support

- The authors state, "there may be residual confounding whereby patients receiving intravascular microaxial LVADs had greater severity of illness than those receiving IABPs," which is certainly a limitation which Impella users are familiar with and likely substantially confounds these conclusions.

- The authors' conclusion conflicts with more than 10 years of outcomes data on Impella, which have been reported in more robust, previously published, FDA-audited, peer-reviewed, real-

world studies and randomized controlled trials, such as the INOVA Study, the NCSI Study and the STEMI DTU pilot study.

Without understanding of the flaws of this analysis, it has the potential to impact patient care and patient access to Impella. I hope these bulleted points will help educate those who may only look at the paper's title or abstract conclusion and are not familiar with the clinical, data and analytical limitations in this paper, and the prior data over the last decade that supports use of the Impella platform.

Thank you and please let me know if you have any feedback.

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