

Appendix Table 4. Variable Definition for Large Shunt Size.

Systematic, Collaborative, PFO closure Evaluation (SCOPE)	Target: Large shunt size was defined in our database as >20+ bubbles (values below in BLUE coded as 'large' in our database)
CLOSURE	<i>Small: (1) None; (2): Trace, 1~10 bubbles, (3) Moderate, ~10-25 bubbles, Large: (4) Substantial, ~25 or more bubbles</i>
PC Trial	<i>Small: grade 0 = none; grade 1 = minimal (1-5 bubbles), grade 2 = moderate (6 to 20 bubbles), Large: grade 3 = severe (>20 bubbles)</i>
RESPECT	<i>Small: Grade 0 (none), Grade 1 = 1-9 bubbles; Grade 2 = 10 to 20 bubbles; Large: Grade 3 = over 20 bubbles</i>
REDUCE	<i>PENN RE-READ FROM TEE (IF MISSING (~20% of time), USED ORIGINAL DATA FROM GORE): Small :(0)Grade 0[no bubbles], (1)Grade 1 [1-9 bubbles], (2)Grade 2 [10-20] bubbles, Large: (3)Grade3 [>20 bubbles]</i>
DEFENSE	<i>Small: (<=20 Microbubbles), Large (>20 microbubbles)</i>
CLOSE	<i>Small : <=30 Bubbles on TTE or TEE, Large: >30 microbubbles on TTE or TEE</i>

PFO indicates patent foramen ovale; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram;