

AN INTERVIEW WITH...

Rebecca T. Hahn, MD

Dr. Hahn shares insights from the SCOUT tricuspid regurgitation trial, various valvular regurgitation guidelines, the formation of the interventional echocardiography subspecialty, and much more.



As the National Principal Investigator of the SCOUT trial, can you discuss its findings and their significance in the field? What specific quantitative measures and imaging techniques were used?

The SCOUT trial used the Trialign device (Edwards Lifesciences, formerly Mitralign, Inc.), which was the first transcatheter device for treatment of severe, symptomatic, functional tricuspid regurgitation (TR) to complete an early feasibility study in the United States. The report of the 30-day results documented what most subsequent trials confirmed were the unique baseline characteristics of these patients: a high prevalence of women, multiple comorbidities including liver and renal disease, and frequent previous left heart surgery.¹ Importantly, the trial excluded patients with significant pulmonary hypertension (systolic pulmonary artery pressure > 60 mm Hg), left ventricular dysfunction (ejection fraction < 35%), more than mild right ventricular (RV) dysfunction, or RV dilatation. The trial also excluded torrential TR by quantitative tricuspid effective regurgitant orifice area (EROA) > 1.2 cm² and tricuspid tethering distance > 8 mm at the time of enrollment.

The Trialign device successfully reduced TR severity by an average quantitative EROA of -0.22 ± 0.29 cm²

(ie, the equivalent of a full grade). However, the baseline quantitative EROA was 0.85 ± 0.22 cm² and the resulting EROA was 0.63 ± 0.29 cm². Using the American Society of Echocardiography's TR severity grading scheme at the time,² which remains unchanged in the newest updated guidelines,³ TR was "severe" at baseline, as well as following device implantation. The current grading schemes for TR thus failed to take into account the delayed presentation of these high-surgical-risk patients, and the "torrential" nature of TR in the patients currently enrolling in these trials. The SCOUT trial showed that the equivalent quantitative reduction of a "grade" of TR was associated with an increase in forward stroke volume and resulted in significant improvements in quality-of-life measures.

The SCOUT trial was also the first to use multiple methods of TR quantitation, including the proximal isovelocity surface area (PISA) method, quantitative Doppler method, and three-dimensional (3D) color Doppler planimetry of the vena contracta area.⁴ The study showed that the guideline-recommended quantitation of EROA by PISA underestimated the quantitative EROA and that different cutoffs for these methods may be appropriate. Based on the patients presenting for treatment with these novel transcatheter devices, a proposal was put forth to increase the grades to include massive (already included in the European society

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TABLE 1. PROPOSED EXPANSION OF THE "SEVERE" GRADE

Variable	Mild	Moderate	Severe	Very Severe or Massive	Torrential
VC (biplane)	< 3 mm	3–6.9 mm	7–13 mm	14–20 mm	≥ 21 mm
EROA (PISA)	< 20 mm ²	20–39 mm ²	40–59 mm ²	60–79 mm ²	≥ 80 mm ²
3D VCA or Quantitative EROA*	–	–	75–94 mm ²	95–114 mm ²	≥ 115 mm ²

Abbreviations: 3D VCA, three-dimensional vena contracta area; EROA, effective regurgitant orifice area; PISA, proximal isovelocity surface area; VC, vena contracta.

*3D VCA and quantitative Doppler EROA cutoffs may be larger than PISA EROA.

Hahn RT, Zamorano JL. The need for a new tricuspid regurgitation grading scheme. *Eur Heart J Cardiovasc Imaging*. 2017;18:1342-1343, by permission of European Society of Cardiology.

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guidelines⁵) as well as torrential (Table 1).⁶ The cutoffs for these grades were based on the ranges of values for the current grades of mild or moderate.

Since the publication of the SCOUT trial and the proposed new grading scheme, other trials have used the extended grading scheme and have successfully shown clinical improvement with other transcatheter devices⁷ and important differences in outcomes between severe and torrential grades in natural history studies.⁸ The Trialalign device has been acquired by Edwards Lifesciences; however, there is no current plan to proceed with further trial development for this successful therapy. This may be, in part, related to its early groundbreaking findings of single-grade reductions resulting in significant clinical benefit, as well as the use of novel methods of quantitation, which since then have been validated in other studies. In addition, its surgical predicate, the modified Kay procedure,⁹ is infrequently used and perhaps was not accepted as an adequate model for a transcatheter device like the Cardioband annular device (Edwards Lifesciences).⁷ Nonetheless, since the first early feasibility study of the Mitralign device was published, other novel devices are now in clinical trials, such as the TriCinch percutaneous annuloplasty device (4Tech Cardio Ltd.),¹⁰ and the Forma repair system (Edwards Lifesciences),¹¹ which have no surgical predicate.

Besides the aforementioned novel findings, the SCOUT trial focused attention on the role of imaging in the successful implantation of these devices.^{4,12} New imaging planes (the deep esophageal level⁴) and reliance on previously underutilized transgastric views¹³ are required to image the anteriorly-inferiorly positioned tricuspid valve. In addition, advances in imaging including real-time, 3D, multiplanar imaging have significantly changed the implantation of tricuspid valve devices.¹²

Can you tell us about your work as Director of the Echo Core Laboratory for the Cardiovascular Research Foundation's (CRF) Clinical Trials Center and efforts to improve the quality of clinical research?

I am currently the Chief Scientific Officer for the Echocardiography Core Laboratory at the CRF. Core laboratories are essential not only in ensuring expertise and consistency during the assessment of safety and efficacy endpoints for clinical trials,^{14,15} but they are also frequently involved in trial design and conduct where a reduction in measurement variability could result in reduced sample sizes.¹⁶ The Echo Core Lab at CRF serves as one of the core labs for the PARTNER trials as well as that of nearly all the currently enrolling transcatheter TR device trials. Comparisons of echocardiographic param-

eters across trials^{1,7,17} could be made given the consistent use of a single core lab. In addition, insight into the novel methods for assessing TR severity¹⁸ may result in modifications to the current guidelines.

Why do you think that concomitant valve surgery for TR has continued to be underutilized, despite findings that intervention prevents progressive disease?

The underutilization of concomitant TR intervention at the time of left heart valve surgery can be attributed to a number of issues¹⁹: our limited guideline recommendations for quantitation of TR severity, the underestimation of TR severity under varying hemodynamic loads,²⁰ the misconception that TR resolves following mitral valve surgery,^{21,22} the overestimation of surgical risk when concomitant tricuspid valve surgery is performed at the time of mitral valve surgery,^{23,24} and the underappreciation of benefits from RV remodeling and functional improvement following correction of TR.^{25,26} At least for the first issue related to the underestimation of TR at the time of surgery, investigators are currently testing the use of concomitant tricuspid valve repair for less than severe TR (NCT02675244). In this trial, concomitant tricuspid repair will be performed in patients with moderate TR by transthoracic echocardiography or less than moderate TR with tricuspid annular dimension ≥ 40 mm (index ≥ 21 mm/m²) undergoing mitral valve surgery for degenerative mitral regurgitation. Because of the significant variability of TR severity due to loading conditions, use of annular size as a surrogate for severe TR makes sense given the relationship of TR with annular size²⁷; however, the use of a single linear diameter measurement fails to take into account the complex 3D shape and dynamism of the annulus.^{28,29} Loss of tricuspid annular shape and dynamic changes throughout the cardiac cycle are associated with more severe TR.²⁹⁻³¹

Do you foresee a time when guidelines in the United States will recommend standalone transcatheter tricuspid repair or replacement? What level evidence would be needed to change this, and in what time frame do you think might this occur?

It is clear that the current guidelines (United States and European) are far too limited, with only one class 1 indication for isolated tricuspid valve surgery. Because of these limitations, referrals for operative correction of functional TR is often delayed until intractable right heart failure occurs, increasing the surgical risk and affecting long-term outcomes. Transcatheter solutions may allow for a lower-risk, effective therapy to be introduced initially in the high-

risk population and move into the lower-risk population over time, as we saw with the transcatheter aortic valve replacement experience. Due to the long natural history of the disease, however, studies on outcomes may need to focus on soft endpoints such as rehospitalizations, functional status, quality of life, or other secondary anatomic or hemodynamic parameters that determine outcomes (eg, RV function and pulmonary artery pressures). The first randomized trial of a transcatheter tricuspid valve device has just been approved by the FDA. The primary objective of the randomized TRILUMINATE pivotal trial is to demonstrate the safety and effectiveness of the TriClip device (Abbott Vascular) compared with medical therapy in improving clinical outcomes in symptomatic patients with severe TR, who are at intermediate or greater estimated risk for mortality with tricuspid valve surgery (NCT03904147). Given the 12-month endpoint and need to randomize 700 patients, the trial will not likely be completed for 3 to 4 years.

What do you think the biggest drivers are for the recent wave of increased interest in developing new therapies to address TR?

The drivers for transcatheter TR therapies include the multiple outcomes studies showing worse outcomes with TR, the previous development of devices for the mitral valve that can be transferred to the tricuspid valve, and the safety of working on the right heart valves.

As Course Director for the Annual State-of-the-Art Echo Course, can share with us how this meeting originated over 20 years ago?

The meeting originated as an effort to offer echocardiographic education in the Northeast (and specifically the New York area), which at that time was lacking. The course was designed to have a small but well-known, versatile faculty who would bring not only their expertise in the clinical practice of echocardiography but also the most up-to-date research. It was also designed to appeal to both sonographers and physicians and, therefore, included nuances of imaging acquisition as well as quantification.

Can you tell us about the recent American Society of Echocardiography Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement³² and how the field of interventional echocardiography came about?

This is the first version of this guideline to be published and it reflects the creation of this new field of interventional echocardiography. This term was first

used in 2010 by Dr. Martin Leon to describe my new position as Director of Interventional Echocardiography at Columbia University. Once promoted by Dr. Leon, the importance of imaging became a focus for the growing structural heart disease field and has since become its own subspecialty within echocardiography and multimodality imaging. In fact, without the development of imaging experts for intraprocedural guidance, many of the advances in the structural heart disease field would not be possible. Now, imaging companies have invested in the development of advanced imaging capabilities (ie, real-time, 3D, multiplanar reconstruction), making more complex procedures and devices possible. This new guideline will require frequent updates as new devices and new methods for assessing postprocedural device function are developed.

Do you have any advice for women fellows in particular who are interested in entering the interventional imaging field?

This is a great field for any cardiology fellow or cardiologist interested in structural heart disease. Because echocardiography and imaging have a greater percentage of women than some other subspecialties in cardiology, I believe more women will choose to focus on this rapidly developing field. We still need to develop training guidelines for both interventionalists and interventional imagers because this is a field where great expertise is required to perform relatively few procedures. ■

1. Hahn RT, Meduri CU, Davidson CJ, et al. Early feasibility study of a transcatheter tricuspid valve annuloplasty: SCOUT trial 30-day results. *J Am Coll Cardiol*. 2017;69:1795-1806.
2. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr*. 2003;16:777-802.
3. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr*. 2017;30:303-371.
4. Hahn RT. State-of-the-art review of echocardiographic imaging in the evaluation and treatment of functional tricuspid regurgitation. *Circ Cardiovasc Imaging*. 2016;9:e005332.
5. Lancellotti P, Moura L, Pierard LA, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr*. 2010;11:307-332.
6. Hahn RT, Zamorano JL. The need for a new tricuspid regurgitation grading scheme. *Eur Heart J Cardiovasc Imaging*. 2017;18:1342-1343.
7. Nickenig G, Weber M, Schueler R, et al. 6-month outcomes of tricuspid valve reconstruction for patients with severe tricuspid regurgitation. *J Am Coll Cardiol*. 2019;73:1905-1915.
8. Santoro C, Marco Del Castillo A, Gonzalez-Gomez A, et al. Mid-term outcome of severe tricuspid regurgitation: are there any differences according to mechanism and severity [published online March 4, 2019]? *Eur Heart J Cardiovasc Imaging*.
9. Ghanta RK, Chen R, Narayanasamy N, et al. Suture bicuspidization of the tricuspid valve versus ring annuloplasty for repair of functional tricuspid regurgitation: midterm results of 237 consecutive patients. *J Thorac Cardiovasc Surg*. 2007;133:117-126.
10. Latib A, Agricola E, Pozzoli A, et al. First-in-man implantation of a tricuspid annular remodeling device for functional tricuspid regurgitation. *JACC Cardiovasc Interv*. 2015;8:e211-e214.
11. Perlman G, Praz F, Puri R, et al. Transcatheter tricuspid valve repair with a new transcatheter coaptation system for the treatment of severe tricuspid regurgitation: 1-year clinical and echocardiographic results. *JACC Cardiovasc Interv*. 2017;10:1994-2003.
12. Hahn RT, Nabauer M, Zuber M, et al. Intraprocedural imaging of transcatheter tricuspid valve interventions. *JACC Cardiovasc Imaging*. 2019;12:532-553.
13. Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society Of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26:921-964.

14. Douglas PS, DeCara JM, Devereux RB, et al. Echocardiographic imaging in clinical trials: American Society of Echocardiography standards for echocardiography core laboratories: endorsed by the American College of Cardiology Foundation. *J Am Soc Echocardiogr*. 2009;22:755-765.
15. Douglas PS, Waugh RA, Bloomfield G, et al. Implementation of echocardiography core laboratory best practices: a case study of the PARTNER I trial. *J Am Soc Echocardiogr*. 2013;26:348-358.e3.
16. Douglas PS, Hahn RT. Echocardiography in clinical trials for TAVR: getting to the core of the matter. *JACC Cardiovasc Imaging*. 2015;8:1376-1378.
17. Curio J, Demir OM, Pagnesi M, et al. Update on the current landscape of transcatheter options for tricuspid regurgitation treatment. *Interv Cardiol*. 2019;14:54-61.
18. Dahou A, Ong G, Hamid N, et al. Quantifying tricuspid regurgitation severity: a comparison of proximal isovelocity surface area and novel quantitative Doppler methods. *JACC Cardiovasc Imaging*. 2019;12:560-562.
19. Hahn RT. Current transcatheter devices to treat functional tricuspid regurgitation with discussion of issues relevant to clinical trial design. *Ann Cardiothorac Surg*. 2017;6:240-247.
20. Frater R. Tricuspid insufficiency. *J Thorac Cardiovasc Surg*. 2001;122:427-429.
21. Porter A, Shapira Y, Wurzel M, et al. Tricuspid regurgitation late after mitral valve replacement: clinical and echocardiographic evaluation. *J Heart Valve Dis*. 1999;8:57-62.
22. Onorati F, Santarpino G, Marturano D, et al. Successful surgical treatment of chronic ischemic mitral regurgitation achieves left ventricular reverse remodeling but does not affect right ventricular function. *J Thorac Cardiovasc Surg*. 2009;138:341-351.
23. Di Mauro M, Bivona A, Iaco AL, et al. Mitral valve surgery for functional mitral regurgitation: prognostic role of tricuspid regurgitation. *Eur J Cardiothorac Surg*. 2009;35:635-639; discussion 639-640.
24. Pfannmueller B, Verevkin A, Borger MA, et al. Role of tricuspid valve repair for moderate tricuspid regurgitation during minimally invasive mitral valve surgery. *Thorac Cardiovasc Surg*. 2013;61:386-391.
25. Desai RR, Vargas Abello LM, Klein AL, et al. Tricuspid regurgitation and right ventricular function after mitral valve surgery with or without concomitant tricuspid valve procedure. *J Thorac Cardiovasc Surg*. 2013;146:1126-1132.e10.
26. Chikwe J, Itagaki S, Anyanwu A, Adams DH. Impact of concomitant tricuspid annuloplasty on tricuspid regurgitation, right ventricular function, and pulmonary artery hypertension after repair of mitral valve prolapse. *J Am Coll Cardiol*. 2015;65:1931-1938.
27. Nemoto N, Lesser JR, Pedersen WR, et al. Pathogenic structural heart changes in early tricuspid regurgitation. *J Thorac Cardiovasc Surg*. 2015;150:323-330.
28. Ton-Nu TT, Levine RA, Handschumacher MD, et al. Geometric determinants of functional tricuspid regurgitation: insights from 3-dimensional echocardiography. *Circulation*. 2006;114:143-149.
29. Fukuda S, Saracino G, Matsumura Y, et al. Three-dimensional geometry of the tricuspid annulus in healthy subjects and in patients with functional tricuspid regurgitation: a real-time, 3-dimensional echocardiographic study. *Circulation*. 2006;114(1 suppl):I492-498.
30. Ring L, Rana BS, Kydd A, et al. Dynamics of the tricuspid valve annulus in normal and dilated right hearts: a three-dimensional transoesophageal echocardiography study. *Eur Heart J Cardiovasc Imaging*. 2012;13:756-762.
31. Maffessanti F, Gripari P, Pontone G, et al. Three-dimensional dynamic assessment of tricuspid and mitral annuli using cardiovascular magnetic resonance. *Eur Heart J Cardiovasc Imaging*. 2013;14:986-995.
32. Zoghbi WA, Asch FM, Bruce C, et al. Guidelines for the evaluation of valvular regurgitation after percutaneous valve repair or replacement: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Angiography and Interventions, Japanese Society of Echocardiography, and Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr*. 2019;32:431-475.

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