

Global and local view of tricuspid regurgitation: a call for action

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Significant (moderate or severe) tricuspid regurgitation (TR) is a prevalent condition reaching approximately 4% of individuals aged 75 years or older,^{1,2} and may be even more prevalent when older people are systematically screened.³ TR prevalence is destined to increase with aging of the population, probably becoming the most frequently encountered valve disease in nonagenarians and certain patient subgroups.^{1,4} Even more impressive is the estimated incidence of significant TR, considerable at 200 000 new cases per year in the United States and probably 300 000 in the European Union.⁵ Certainly, it represents a currently sizable and growing clinical challenge for cardiologists.

Publications from leading journals have shown other peculiar characteristics of TR, including that it is chiefly functional, often associated with high comorbidity burden and frequent frailty, but despite these associations remains an independent determinant of adverse prognosis. We have also learned that TR is not only underdiagnosed but even more often undertreated.⁶ Surgical treatment of TR is associated with a high postoperative mortality rate, especially if patients are operated late in the course of the disease, and the repair, surgical or transcatheter, is often not durable.⁷ The lack of efficacy of current interventional options on hard end points combined with under-appraisal of the severe prognosis associated with conservative management partly explain the inertia toward addressing this condition. Given these premises, the last decade has seen a growing interest and an increasing volume of publications on this subject. However, the recent large cohorts reported all come from leading institutions in the world, that may have peculiar referrals and may not be representative of TR in the global population. High-quality data from a wider geographical location and more local recruitment are warranted to detect whether our new recognition of the poor prognosis of TR is true or results from a referral bias.

In this issue of *Polish Archives of Internal Medicine*, Piasecki et al⁸ presented a retrospective single-center study on 172 consecutive hospitalized patients with severe TR quantified by echocardiography, and showed high prevalence of clinical consequences of the disease, including congestion signs (ascites, peripheral edema, renal insufficiency, and diuretic dependence) and severe right heart dysfunction, but especially demonstrated that TR is detrimental in all settings. Although this was a high-risk cohort with numerous comorbidities and advanced right heart failure stage, greater degree of TR and echocardiographic parameters of right heart dysfunction could be used to identify patients with worse prognosis within 1 and 2 years.

Notably, this report considered patients with severe to torrential TR, categorized by quantitative assessment of severity by proximal isovelocity surface area method or vena contracta. Although this was a retrospective study, a standard echocardiographic protocol of image acquisition used at this tertiary care center encompassed routine quantitative methods to grade significant TR underscoring the feasibility of implementation of these methods in real-life practice. This is especially important in secondary TR whereby the severity of the disease may be under- or overestimated by relying on color jet area only. Indeed, severe pulmonary hypertension may lead to overestimation of TR by producing large high-velocity jets, while torrential TR, especially in the presence of severe right ventricular dysfunction, often produces low-velocity jets due to rapid equalization of filling pressures.^{9,10} The study by Piasecki et al⁸ confirms that, irrespective of the clinical context, severe TR is associated with dismal outcome with a graduation of risk even in patients with massive and torrential TR.

As many as 54% of the patients hospitalized for severe TR were women. Although this proportion is similar to other studies,^{7,11} it should be taken

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into account that most patients with TR were elderly, had atrial fibrillation, and heart failure with preserved ejection fraction, the conditions usually more frequently encountered in women. Indeed, community studies described a large preponderance of significant TR in women.¹ This issue needs further investigation, as it may reveal referral biases or may imply biological mechanisms that remain unclear, and is important, as undertreatment of women with valve diseases has been recently underscored.^{12,13} The most striking observation of the study is that 2 years after severe TR diagnosis nearly half of the patients had died. Several factors may explain this grim outcome. In this real-life cohort of patients followed at a tertiary center, notwithstanding the overt severity of TR, the patients were treated conservatively. If we are not mistaken, no patient underwent tricuspid valve intervention, either surgical or percutaneous, and a large proportion of patients showed signs of advanced and maybe irreversible right heart dysfunction. Thus, this single-center study confirms the observations of referral centers, that is, severe TR undertreatment, irrespective of where we are in the world, justifying continuing development of new and easier to implement therapeutic technologies.

Another important observation of this study is a late stage of TR at referral. More than half of the patients presented New York Heart Association (NYHA) class III–IV and all were on diuretic treatment. Moreover, most patients showed signs of right heart dysfunction, with almost half having dilated pulmonary trunk, short acceleration time, or right ventricular (RV) dysfunction/hypokinesis. This phenotype of advanced stage of TR, with most patients presenting late and treated late when RV remodeling has become irreversible, generates doubts on the benefit of any TR treatment, and shows strong association with excess mortality. Thus, this local study demonstrates that the late-stage TR clinical presentation is not a fluke of referral biases of major referral centers but warrants considerable efforts to improve the referral process of patients with TR to avoid the untoward consequence of the class IV functional status.¹⁴

As expected, this study has limitations, besides being retrospective and single-center, and including patients with heterogeneous TR mechanisms. Pacemaker leads were not excluded, and 4 patients had undergone previous tricuspid valve surgery. We do know that TR outcome is heterogeneous and influenced by valve morphology and TR etiology.^{1,2,15} Furthermore, a non-negligible proportion of patients was lost to follow-up, with 10% and 14% not reaching 1- and 2-year follow-up, respectively. This might have even contributed to underestimating adverse outcomes in the study cohort. It is surprising that, in a population of patients mostly with symptomatic heart failure, in NYHA class III–IV, and all on diuretics, only 2% received sodium-glucose transporter type 2 inhibitors. This may be partly related to enrollment

or reimbursement issues, but it may also denote a lack of awareness of the disease severity with consequent undertreatment. The small sample size may explain the lack of detection of more predictors of outcomes. Finally, the study did not use 3-dimensional imaging, which may have improved TR morphology and RV characterization. Irrespective of these limitations, the coherence of local and global data on TR is obvious, in terms of late presentation, poor outcome, and pervasive undertreatment, and gives us clear paths for improvement.

Once considered a consequence or a bystander of pulmonary hypertension or left heart disease, it is now widely evident that significant TR is associated with increased mortality independently of any background and warrants risk stratification and interventions. Among those, tricuspid annulus systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP) ratio is an emerging noninvasive marker of right ventricular-to-pulmonary circulation “uncoupling,”^{16,17} and may have independent prognostic value^{18,19} that warrants further testing. In the discussed study, TAPSE/PASP below 0.26 tended to be associated with higher mortality and this finding should be confirmed in larger samples. Defining new objective markers of clinical outcome is a task that needs to be actively pursued.²⁰ In that regard, risk-stratification tools, such as the TRI-SCORE may be helpful in identifying higher-risk patients even among those conservatively treated.⁸ Of note, in the study by Piasecki et al⁸ the average TRI-SCORE was intermediate-high, identifying patients in whom surgical or interventional treatment may be futile. However, to address how we should risk-score patients with TR, further validation is needed in prospective larger studies. To improve outcomes, we need a shift toward earlier diagnosis, better appreciation of the adverse prognosis with untreated TR, and improved innovative interventional techniques that offer more durable and effective results. While waiting for those, multidisciplinary Heart Team evaluation is essential to accurately analyze patients’ characteristic, including comorbidity and TR phenotype, and select the best approach from an increasing array of potential therapeutic, medical, surgical, and interventional strategies.⁶ In this critical task, again we need to think globally and act locally to improve our patients’ outcomes.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

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REFERENCES

- 1 Topilsky Y, Maltais S, Medina Inojosa J, et al. Burden of tricuspid regurgitation in patients diagnosed in the community setting. *JACC Cardiovasc Imaging*. 2019; 12: 433-442. [↗](#)
- 2 Leonardi D, Bursi F, Fanti D, et al. Outpatient tricuspid regurgitation in the community: clinical context and outcome. *Int J Cardiol*. 2024; 396: 131443. [↗](#)
- 3 Gössl M, Stanberry L, Benson G, et al. Burden of undiagnosed valvular heart disease in the elderly in the community: Heart of New Ulm Valve study. *JACC Cardiovasc Imaging*. 2023; 16: 1118-1120. [↗](#)
- 4 Utsunomiya H, Itabashi Y, Mihara H, et al. Functional tricuspid regurgitation caused by chronic atrial fibrillation: a real-time 3-dimensional transesophageal echocardiography study. *Circ Cardiovasc Imaging*. 2017; 10: e004897. [↗](#)
- 5 Enriquez-Sarano M, Messika-Zeitoun D, Topilsky Y, et al. Tricuspid regurgitation is a public health crisis. *Prog Cardiovasc Dis*. 2019; 62: 447-451. [↗](#)
- 6 Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2022; 43: 561-632. [↗](#)
- 7 Sorajja P, Whisenant B, Hamid N, et al. Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med*. 2023; 388: 1833-1842. [↗](#)
- 8 Piasecki A, Tomaniak M, Gumiężna K, et al. Clinical and echocardiographic characterization of patients hospitalized for severe tricuspid valve regurgitation: a single tertiary-care center experience with 2-year follow-up. *Pol Arch Intern Med*. 2024; 134: 16752. [↗](#)
- 9 Praz F, Muraru D, Kreidel F, et al. Transcatheter treatment for tricuspid valve disease. *EuroIntervention*. 2021; 17: 791-808. [↗](#)
- 10 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.
- 11 Scotti A, Coisne A, Taramasso M, et al. Sex-related characteristics and short-term outcomes of patients undergoing transcatheter tricuspid valve intervention for tricuspid regurgitation. *Eur Heart J*. 2023; 44: 822-832. [↗](#)
- 12 Tribouilloy C, Bohbot Y, Rusinaru D, et al. Excess mortality and undertreatment of women with severe aortic stenosis. *J Am Heart Assoc*. 2021; 10: 1-13. [↗](#)
- 13 Avierinos J-F, Tribouilloy C, Bursi F, et al. Degenerative mitral regurgitation due to flail leaflet: sex-related differences in presentation, management, and outcomes. *Eur Heart J*. 2024; 45: 2306-2316. [↗](#)
- 14 Topilsky Y, Khanna AD, Oh JK, et al. Preoperative factors associated with adverse outcome after tricuspid valve replacement. *Circulation*. 2011; 123: 1929-1939. [↗](#)
- 15 Muraru D, Hahn RT, Soliman OI, et al. 3-Dimensional echocardiography in imaging the tricuspid valve. *JACC Cardiovasc Imaging*. 2019; 12: 500-515. [↗](#)
- 16 Guazzi M, Dixon D, Labate V, et al. RV contractile function and its coupling to pulmonary circulation in heart failure with preserved ejection fraction: stratification of clinical phenotypes and outcomes. *JACC Cardiovasc Imaging*. 2017; 10: 1211-1221. [↗](#)
- 17 Tello K, Wan J, Dalmer A, et al. Validation of the tricuspid annular plane systolic excursion/systolic pulmonary artery pressure ratio for the assessment of right ventricular-arterial coupling in severe pulmonary hypertension. *Circ Cardiovasc Imaging*. 2019; 12: e009047. [↗](#)
- 18 Fortuni F, Butcher SC, Dietz MF, et al. Right ventricular-pulmonary arterial coupling in secondary tricuspid regurgitation. *Am J Cardiol*. 2021; 148: 138-145. [↗](#)
- 19 Brener MI, Lurz P, Hausleiter J, et al. Right ventricular-pulmonary arterial coupling and afterload reserve in patients undergoing transcatheter tricuspid valve repair. *J Am Coll Cardiol*. 2022; 79: 448-461.
- 20 Grapsa J, Praz F, Sorajja P, et al. Tricuspid regurgitation: from imaging to clinical trials to resolving the unmet need for treatment. *JACC Cardiovasc Imaging*. 2024; 17: 79-95. [↗](#)