Tricuspid regurgitation (TR) occurs in 65% to 85% of the population in the United States. Although mild TR in the setting of a structurally normal tricuspid valve apparatus can be considered a normal variant, progression to moderate-severe TR increases with age and is estimated to affect nearly 1.6 million adults in the United States. Echocardiographic data from the Framingham Heart Study reported an overall prevalence of moderate or higher TR of 0.8%, with a majority due to functional TR and only 10% due to an organic cause. Several studies suggest that significant TR is associated with an adverse prognosis. In addition, the surgical referral has been limited by concerns about short-term mortality, which is reported to be as high as 24%. It has been shown that comorbidities associated with late referral may have an impact on poor outcomes of tricuspid valve surgery, thereby confounding the analysis of short-term mortality. In patients with significant TR, there is an urgent necessity for a better risk assessment tool. An uncomplicated technique for general internists and cardiologists to assess the risk of TR would recognize individuals who would benefit from early referral and care, thereby providing meaningful differences in clinical outcomes.

In this issue of Mayo Clinic Proceedings, Lara-Breitinger et al describe a retrospective analysis of moderate or higher TR between 2005 and 2016 studied at a single quaternary center. The 5-year probability of death was 53% for moderate TR, 63% for moderate-severe TR (hazard ratio, 1.24 [1.17 to 1.31]; P<.0001 vs moderate), and 71% for severe TR (hazard ratio, 1.55 [1.47 to 1.64]; P<.0001 vs moderate). Factors associated with all-cause mortality on the multivariate analysis included age of 70 years or older, male sex, creatinine concentration greater than 2 mg/dL, congestive heart failure, chronic lung disease, aspartate aminotransferase activity of 40 U/L or higher, heart rate of 90 beats/min or more, and severe TR.

Using a derivation and validation cohort, they developed a clinical risk score, Tricuspid Regurgitation Impact on Outcomes (TRIO), by summing the scores associated with the 8 clinical variables (age, sex, creatinine concentration, congestive heart failure, lung disease, elevated aspartate aminotransferase, elevated heart rate, and TR severity), with a maximum possible score of 12. In the validation cohort, the score was associated with a C statistic of 0.67 for all-cause mortality. Score cutoffs for clinical use were defined as low risk (0 to 3), moderate-intermediate risk (4 to 6), and high risk (≥7), which equated to a 79%, 63%, and 40% risk of 10-year mortality. Increasing TR severity was associated with increased mortality in the low-risk group but had no impact on the high-risk group. This is a timely, important, and relevant study to the practice of valvular heart disease in the contemporary era, and we would like to commend the authors for their work. However, there are certain points that merit further discussion.

First, as mentioned in the Limitations, there are limited data on significant mortality predictors, such as the severity of hepatic disease, type of prior cardiac surgery, and medical therapy. The addition of these variables may help in further refinement of the scoring system, especially in high-risk patients. A major confounder is the impact of tricuspid valve surgery and the natural history of this patient population. However, as mentioned by the authors, overall, a tiny fraction of patients (0.7%) had surgical intervention, indicating a negligible impact on the score. Unfortunately, this is also a testament to the current practice, highlighting the unmet need for tricuspid valve interventions. The observations align with the exceedingly low volume of isolated tricuspid interventions reported nationwide. Although not included in the current model severity of right-sided heart failure, use of guideline-directed heart failure therapy,
implantable cardiac devices crossing the tricuspid valve, and the presence of atrial fibrillation or flutter have been associated with changes in the natural history of TR. It is difficult to ascertain the chronology of TR and right-sided heart failure, and further data are needed to understand whether the TR was the cause or effect of right-sided heart failure. Nevertheless, the study was inclusive of all patients despite comorbidities and was validated in a second, independent, and geographically distinct cohort with nearly identical results, suggesting that the predictors for the TRIO score are robust. Tricuspid regurgitation in the absence of significant comorbidities has been studied with 10-year survival rates as low as 63%, reflecting its significance as an independent predictor of outcome.5

Second, the TRIO score had a C statistic of 0.67. This implies a modest association and may make the model difficult to apply in designing study populations or predicting individual patient management. The absence of information on the management of cardiomyopathy or heart failure including the use of guideline-directed medical therapy is a significant confounder. In the absence of this information, we are unable to judge whether the progression of TR is basically because of medication noncompliance or intolerance as against progression despite optimal medical therapy. A large portion of the patient population did not have information on comprehensive blood work and medications such as diuretics, which may have also affected the degree of TR at the time of echocardiography. The modest discrimination of the TRIO score might have further attenuation as it is applied to other populations that are demographically and geographically distinct. Further independent analyses of the TRIO score are needed before widespread adoption.

Finally, the survival analysis does not account for the cause of TR (primary vs secondary TR), nor does it account for surgical intervention during follow-up, which may have a differential impact on long-term outcomes. The lack of quality of life and symptoms, which are considered important in patients with TR, limits its usefulness.

Despite these stated limitations, the TRIO score, because of its intrinsic simplicity, makes it more likely to be adopted in the primary care setting by the general physician. The largest impact of TR on mortality was observed in patients with a low TRIO score, which suggests that this population may benefit most from early tricuspid intervention. The tricuspid valve is truly the forgotten valve, and studies like these from Lara-Breitinger and others are needed to improve clinical outcomes in this population.

POTENTIAL COMPETING INTERESTS
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