Tricuspid valve regurgitation in patients with heart failure: does it matter?

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This editorial refers to ‘Impact of tricuspid regurgitation on survival in patients with chronic heart failure: unexpected findings of a long-term observational study†, by S. Neuhold et al., on page 844

Tricuspid regurgitation (TR) aetiologies are currently divided into primary and secondary TR. Intrinsic abnormalities of the tricuspid valve leading to significant TR (primary) are rare and are seen in ~8–10% of patients with severe TR. In contrast, secondary TR is the most frequent form of TR requiring surgical intervention.

Secondary TR occurs mainly from tricuspid annular dilatation and increased tricuspid leaflet tethering due to right ventricular (RV) enlargement, which is often secondary to left heart failure (HF) from myocardial or valvular causes. As for secondary mitral regurgitation, secondary TR begets TR. Indeed, TR itself leads to further RV dilatation and dysfunction, right atrial enlargement, more tricuspid annular dilatation and tethering, and worsening TR. With increasing TR, the right ventricle dilates and eventually fails, causing increased RV diastolic pressure and, in an advanced situation, a shift of the interventricular septum toward the left ventricle. Such ventricular interdependence might reduce the left ventricular (LV) cavity size (pure compression), causing restricted LV filling and increased LV diastolic and pulmonary artery pressure. The resulting increase in left and right atrial pressures may promote atrial fibrillation and precipitate symptom onset (Figure 1).

When present, symptoms are often those of associated diseases. In fact, even if severe, TR may be well tolerated for years. Symptoms and signs of TR are those of RV failure, systemic venous congestion, and low cardiac output.

The natural history of secondary TR is still poorly understood. However, without treatment, TR may lead to irreversible RV dysfunction, HF, and death. In a large retrospective study including 5223 patients, Nath et al. underlined the strong relationship between severe TR and the increase in incidence of RV dilatation and dysfunction. They also identified that independently of age, LV function, and pulmonary arterial pressure, severe TR was a strong predictor of overall mortality. Following left-sided heart valve surgery, the recurrence or development of secondary TR is far from exceptional, especially in the presence of pre-operative atrial fibrillation. When not treated at the time of mitral valve surgery, and even when only moderate, secondary TR complicates the post-operative course and seems to be associated with reduced post-operative survival. These findings have encouraged some groups to perform tricuspid valve annuloplasty systematically at the time of left-sided heart valve surgery, even in the presence of mild TR, to avoid post-operative residual or development of TR and its negative impact on outcome. In this regard, the new European Society of Cardiology (ESC) guidelines have changed and consider that tricuspid valve annuloplasty is indicated in patients with severe secondary TR undergoing left-sided heart valve surgery (class I) and should be considered in patients with ≥mild secondary TR undergoing left-sided heart valve surgery (class IIa) when the tricuspid annulus is dilated (>40 mm or 22 mm/m²) in echocardiography. Of interest, all these recommendations are based on a level of evidence C, suggesting the urgent need for further prospective data on the natural history of TR.

In this regard, the study of Neuhold et al. provides a new contribution. The authors have conducted a long-term prospective observational study between 1995 and 2003, including 576 patients with chronic HF recruited through their tertiary care HF clinic. TR severity was assessed using an integrative approach respecting the most recent European recommendations. The population was divided into two groups: no/mild TR vs. moderate/severe TR. The outcome of these two groups was compared using a predefined combined endpoint of death, heart transplantation, or implantation of an LV assist device. According to this definition, 386 patients, during a mean follow-up of 69 ± 50 months, reached the combined endpoint. Interestingly, the authors first reported that the outcome of patients with moderate TR was similar to that of those with severe TR, allowing merging of these severities into one single group. However, after a robust adjustment, the multivariable Cox proportional hazard model revealed that TR was not an independent predictor of outcome. They did,
however, identify a significant interaction between TR and LV systolic function. They also separately analysed the impact of TR on outcome in patients with mild and moderately impaired LV function and in those with severely depressed LV function. By univariable analysis, significant TR was associated with reduced outcome in both groups (i.e. mild/moderate vs. severe LV dysfunction). In contrast, TR emerged as an independent predictor of outcome on multivariable analysis only in patients with mild/moderate LV dysfunction. Using the level of NT-proBNP as an estimate of the severity of HF, similar results were reported. Hence, TR was not an independent predictor of outcome in patients with advanced stage of HF. Overall, these results highlighted that in the case of severe LV dysfunction, other findings are more reliable to predict the outcome than the TR severity. For instance, ≏70% of patients with significant TR had concomitant ≥moderate mitral regurgitation; the vast majority of them were symptomatic and had severe LV dysfunction. It is well known that mitral regurgitation artificially increases LV ejection fraction, a volume-dependent parameter. Under these conditions, the LV depression can be much more severe than expressed by the ejection fraction, which may explain the low flow state resulting in lower systolic blood pressure and higher NT-proBNP release, two robust outcome parameters. All this might have overwhelmed TR in the multivariable model used for the subanalysis. On the other hands, these negative results may also be related to the relatively small sample size in this subset analysis (n = 89), leading to type II error. In addition, the inclusion of right atrial diameter in the multivariable model might have conveyed some degree of co-linearity with TR, masking its potential outcome effects.

The results reported by Neuhold et al. are in contrast to the current literature.1 These discrepancies may be explained by the different design and sample size, but also by the fact that, as emphasized by the authors, previous studies generally used different multivariable models, without inclusion of modern risk markers such as creatinine or NT-proBNP.

To date, the most important challenge is to know whether TR is a ‘real’ risk factor or a surrogate marker of other concomitant risk factors. In the former case, it is difficult to believe that chronic significant TR does not impact the outcome, even when LV function is markedly depressed, since the presence of only moderate residual TR following left-sided valve surgery has been associated with reduced survival. Moreover, the coexistence of these pathological conditions usually has a multiplicative effect on outcome rather than a subtractive impact. In the second hypothesis, if TR is simply a surrogate marker of concomitant advanced cardiac disease, the inclusion of several strong well-established risk factors of mortality in the multivariable model (i.e. LV function, creatinine level, NT-proBNP level, age, and NYHA functional class) may have mitigated the impact of TR on outcome.

In light of these results, we cannot draw a definite conclusion regarding the management of patients with HF and significant TR. On the one hand, the negative impact of TR on outcome in patients with mild LV dysfunction promotes, when possible, surgical correction of this valvular lesion. On the other hand, the lack of significant impact of TR in patients with advanced HF tends to encourage conservative management. Nevertheless, at the time of left-sided heart valve surgery, all significant TR should be corrected, consistent with current ESC guidelines, regardless of the level of LV dysfunction. The data reported by Neuhold et al. provide a further incentive for developing a large-scale multicentre clinical registry, which will aim to

Figure 1 Pathophysiology of tricuspid regurgitation (TR) secondary to left-sided heart valve disease (HVD) and cardiomyopathy. LA, left atrial; LV, left ventricular; RA, right atrial; RV, right ventricular.
assess the prognostic significance of moderate to severe TR in patients with HF.

Conflict of interest: none declared.

References

CARDIOVASCULAR FLASHLIGHT

Double-chambered right ventricle in adults: an ‘uncommon’ entity, new ways of imaging

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A 40-year-old man with previous cardiac surgery was referred to the adult congenital heart disease department at our hospital because of progressive dyspnoea during the previous 3 months. He had had successful pulmonary valvotomy when he was 9 because of a congenital pulmonary stenosis. As the initial approach in a patient with suspected heart failure (HF), a transthoracic echocardiography was performed in which a high-pressure gradient was measured by Doppler at the right ventricular outflow tract (RVOT) and a fibrotic structure, just below the pulmonary valve, could be seen. These findings led to the suspicion of a double-chambered right ventricle (DCRV).

Further evaluation by cardiovascular magnetic resonance (CMR) was conducted, as recommended in the recent HF guidelines (McMurray et al., Eur Heart J, 2012) and CMR recommendations for adults with congenital heart disease (Kilner et al., Eur Heart J, 2010). Cardiovascular magnetic resonance is a powerful tool for the confirmation of a suspected DCRV because it can help to distinguish between a jet through a ventricular septal defect, a subinfundibular stenosis or a possible infundibular or pulmonary valve stenosis, besides providing accurate measurements of biventricular function, myocardial viability, measurements of flow and angiography without ionizing radiation.

In our patient, CMR showed a fibrotic ring in the RVOT (Panel A and Supplementary material online, Video S1) that ‘closed’ in systole creating a proximal and a distal chamber. A turbulent jet emerged from the RVOT in systole (Supplementary material online, Video S2). Ventricular septal defect and pulmonary valve stenosis were excluded. A large right atrium and a severely dilated right ventricle (RV end-diastolic volume 256 mL/RV end-systolic volume 146 mL) with mild systolic dysfunction (RV ejection fraction: 43%) could be seen as well. The patient underwent successful surgical resection of the subpulmonary ring.

Panel A. Cardiovascular magnetic resonance cine-mode turbo-gradient-echo images showing a fibrotic ring (thin arrows) in the RVOT that ‘closes’ in systole creating a proximal (high-pressure) chamber and a distal (low-pressure) chamber. A large right atrium and a dilated right ventricle can be seen as well.

Supplementary material is available at European Heart Journal online.

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doi:10.1093/eurheartj/eht010
Online publish-ahead-of-print 23 January 2013