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The use of Tricuspid Annular Plane Systolic Excursion and Tissue Doppler Imaging Velocities for the Estimation of Pulmonary Hypertension and Right Ventricular Function in Mechanically Ventilated Patients

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1. Introduction

Right ventricular (RV) function can be seriously compromised due to either left ventricular (LV) failure or severe pulmonary hypertension (PH) and pulmonary vascular dysfunction of extra-cardiac origin, especially in critically ill patients, and can be associated with worse prognosis. Echocardiography in the Intensive Care Unit (ICU) can provide significant information to the caregivers, when confronted with a patient with unexplained hemodynamic instability. However, right ventricular echocardiographic assessment can be a challenge in day-to-day clinical practice in the ICU, mostly because of complex interactions between mechanical ventilation, fluid balance and critical illness *per se,* whereas right-to-left interdependence can lead to significant hemodynamic collapse in patients with severe respiratory diseases, septic cardiomyopathy or pulmonary embolism. Finally, the complex geometry of the chamber in association with lack of optimal visualization may limit the accuracy of conventional variables, which have bee proven to be reliable in other clinical settings. For the above reasons, novel indices have been adopted for easier, highly reproducible and less variable evaluation of RV function, such as the tricuspid annular plane systolic excursion (TAPSE) and the Tissue Doppler Imaging (TDI) velocities of tricuspid valve. Their accuracy has already been tested in patients with cardiovascular diseases. Nevertheless, their adoption as monitoring tools in critically ill patients under mechanical ventilation remains to be established. In this chapter we will review the different areas of application of TAPSE and TDI velocities and try to discuss their possible potential as accurate and reproducible diagnostic and prognostic techniques in adult critical care.

2. Conventional hemodynamic measurements in ICU

The pulmonary circulation is a high-flow and low-resistance system. Contrary to the left ventricle (LV) the thin-walled right ventricle (RV) cannot easily tolerate acute increase in afterload, leading to acute distention, paradoxic intra-ventricular septal movement and consequently, reduced LV filling and cardiac output (CO) (Pinsky, 2002, 2007; Sibbald & Driedger, 1983). Due to ventricular interdependence superficial myocardial fibers enrich both LV and RV. As a result, the two ventricles share the septum and are contained within the same pericardial cavity, explaining the decrease in LV output during positive pressure ventilation and application of different levels of positive end-expiratory pressure (PEEP) (Taylor et al., 1967; Fellahi et al., 1998).

Right ventricular dysfunction is common in critically ill patients. Any cause of RV pressure overload such as pulmonary hypertension (PH) or reduced RV contractility, such as RV infarction, sepsis, cardiomyopathy, myocarditis and pericardial disease may lead to RV failure in patients during their stay in Intensive Care Unit (Bunnell & Parrillo, 1996; Parker et al., 1990). Furthermore, pulmonary vascular dysfunction is associated with many disease processes in the ICU setting, whereas pulmonary embolism (PE) and acute respiratory distress syndrome (ARDS) are considered the two main causes of acute *cor pulmonale* (ACP) in adults (Jardin et al., 1985; Vieillard-Barron et al., 2002). The elevation in pulmonary vascular resistance (PVR) can increase the transpulmonary gradient and lead to RV failure. For these reasons, adequate assessment of RV function is very important, especially in hemodynamic unstable patients, since the presence of RV dysfunction may alter treatment and has severe impact upon final outcome (Beaulieu & Marik, 2005).

Pulmonary hypertension is defined at right heart catheterization with resting pulmonary artery systolic pressure (PASP) exceeding 35 mmHg, whereas absence of echocardiographic evidence of increased left atrial pressure or pulmonary artery occlusion pressure (PAOP) $<$ 15 mmHg, obtained through a pulmonary artery catheter (PAC), describes PH associated with primary pulmonary disease (Rubin, 1997; Berger et al., 1985). The gold standard for the diagnosis of pulmonary hypertension and RV dysfunction in ICU is considered to be the pulmonary artery catheterization (Price et al., 2010). However, different studies have shown that assessment of PASP, LV and RV with PAC seems to be inaccurate in patients under mechanical ventilatory support, whereas overall outcomes are not improved when the PAC is used in general in critically ill patients (Vieillard-Barron et al., 2002; Price et al., 2010; Hadian & Pinsky, 2006).

For the above reasons, the role of both transthoracic and transesophageal echocardiography is increasingly recognized in assessing both RV and LV function in critically ill patients, providing significant information regarding RV geometry in different clinical scenarios. Normally, RV systolic function can be quantified using the right ventricular function area change (RVFAC) and ejection fraction (RVEF), whereas RV dilatation can be estimated by measuring RV end-diastolic area (RVEDA) in the long axis, from an apical four-chamber view. The ratio between RVEDA and LVEDA is one of the best ways to assess RV distention and quantify pressure and volume overload. A ratio ≥ 0.6 corresponds to moderate dilatation whereas a ratio ≥ 1 reflects a severe RV dysfunction (Jurcut et al., 2010). Moreover, in cases of severe RV overload, the septum becomes flat (in diastole indicating volume overload and in systole when there is pressure overload) and the LV takes the 'D' shape, limiting LV preload. In addition, the pulmonary pressures can be calculated using the modified Bernoulli equation by estimating the systolic-pressure gradient across the tricuspid valve and after measuring right atrial pressure (RAP) (Jurcut et al., 2010; Kaul et al., 1984).

2.1 Common limitations of traditional echo-derived measurements in ICU

However, the presence of tricuspid regurgitation (TR) varies among studies, based on different levels of severity of pulmonary hypertension. Furthermore, narrow acoustic windows due to lung hyperinflation or marked respiratory variations in intrathoracic pressure, particularly in patients with severe lung disease, may limit the ability to detect an adequate TR jet (Berger et al., 1985; Arcasoy et al., 2003). In a cohort study of 374 lung transplant candidates with a prevalence of pulmonary hypertension around 25%, it was found that estimation of pulmonary artery systolic pressure by echocardiography was frequently inaccurate, compared with data derived from right heart catheterization, leading to considerable overdiagnosis of pulmonary hypertension (Arcasoy et al., 2003).

Another possible limitation for PASP estimation with pulse wave (PW) Doppler is associated with the method used for RAP assessment. Right atrial pressure depends not only on RV preload but also on pleural pressures transmitted to the right atrium, leading to differences between intravascular and transmural pressures under mechanical ventilation. Only a few studies have evaluated different echo-derived measures for the assessment of RAP in mechanically ventilated patients (Lichtenstein & Jardin, 1994; Yock & Popp, 1984). Different techniques for calculating inferior vena cava (IVC) diameter have been proposed to impact on accuracy of RAP estimation (Bendjelid et al., 2003). The method that seems more accurate was developed by Lichtenstein, and calculates IVC diameter longitudinally at end-expiration and end-diastole and during the R wave on electrocardiogram (ECG), 2 cm before the right atrium and with the M-mode on short axis view (Lichtenstein & Jardin, 1994). The estimation of RAP using IVC diameter and its respiratory collapse has been shown to correlate better with central venous pressure (CVP) in patients with RV dysfunction and PH (Mintz et al., 1981). It seems that since the normal respiratory augmentation in venous return is limited by RV enlargement, normal IVC diameter variations are reduced, increasing diagnostic accuracy of this technique. Furthermore, measurement of distensibility index of IVC has been proposed for RAP calculation in mechanically ventilated patients (Barbier et al., 2004). Finally, traditional echocardiographic indices, such as RVFAC, are time-consuming and not always easy to perform because of difficulties to well delineate the RV endocardial border.

3. Estimation of TAPSE and RV TDI velocities in different clinical studies

For the above reasons, different methods have been suggested for echo-Doppler derived diagnosis of pulmonary hypertension and assessment of RV function in patients under mechanical ventilatory support, such as Tricuspid Annular Plane Systolic Excursion (TAPSE) calculation (Kaul et al., 1984; Hammarstrom et al., 1991) and recently, the ratio of peak tricuspid regurgitant velocity (TRV, ms) to the right ventricular outflow tract time-velocity integral ($TVI_{RVOT,}$ cm) that seems to accurately determines pulmonary vascular resistance (Abbas et al., 2003).

Moreover, tissue Doppler imaging (TDI) techniques that measure velocities of cardiac tissue have been studied for the assessment of left ventricular diastolic function in the ICU (Combes et al., 2004; Vignon et al., 2008), whereas only a limited number of researchers have investigated their diagnostic accuracy on right ventricular (RV) dysfunction, in different clinical settings (Meluzin et al., 2001; Sundereswaran et al., 1998; Moustapha et al., 2001).

Finally, an increased ratio of RV diameter to tissue Doppler velocity of tricuspid annular motion has been suggested by others as useful predictor of pulmonary hypertension (McLean et al., 2007)

3.1 Calculation of TAPSE in cardiovascular patients

Since RV muscle fiber orientation results in a contraction that occurs predominantly along the longitudinal plane, systolic displacement of the tricuspid annulus toward the RV apex closely correlates with right ventricular fractional area change. TAPSE as a measure of RV base-to-apex shortening during systole is recorded on M-mode using the 2D four-chamber view. The cursor is placed to the junction of tricuspid valve plan with the free wall of the RV, whereas data are averaged over five beats (Figures 1 & 2). Normal values for TAPSE are 15-20 mm (Price et al., 2010; Meluzin et al., 2001; Lang et al., 2005).

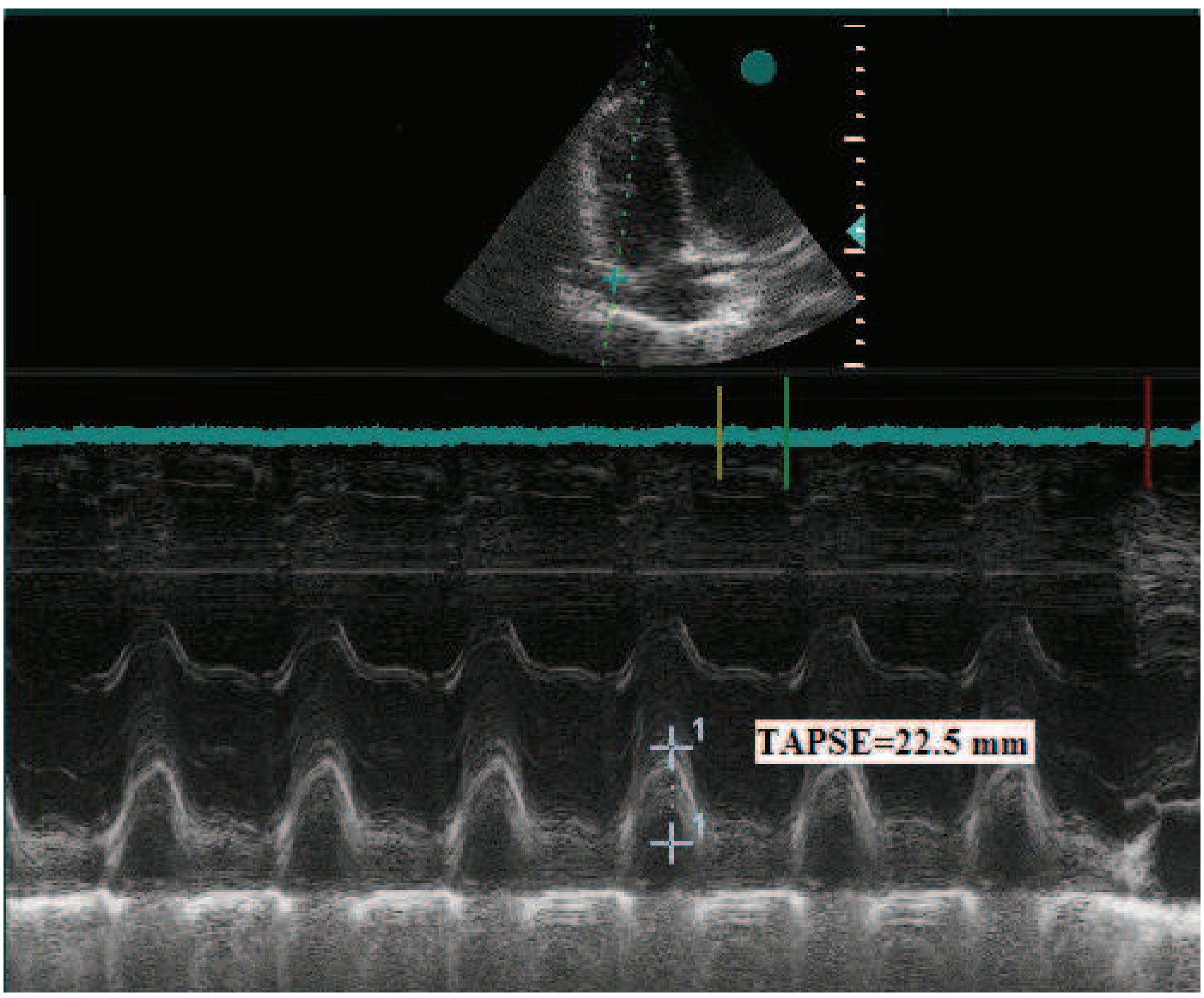

Fig. 1. Measurement of tricuspid annular plane systolic excursion (TAPSE)

TAPSE calculation in a patient under spontaneous respiration by M-mode, using the 2D four-chamber view. The cursor was placed to the junction of tricuspid valve (TV) plan with the free wall of the right ventricle (RV), whereas data were averaged over five beats. In this case, TAPSE value is normal (22.5 mm).

Samad assessed TAPSE in patients after a first myocardial infarction and showed that values ≤ 15 mm were associated with increased mortality (45% at 2 years) compared with patients having TAPSE > 20 mm (4%) (Samad et al., 2002). Kaul and coworkers found that TAPSE was more closely related with the RV area change during systole compared with radionuclide estimation of RV ejection fraction (Kaul et al., 1984). Both of these studies have shown that TAPSE is decreased in patients with depressed right ventricular function (RVFAC< 25%), whereas low TAPSE values have been found to predict a poor outcome in patients with dilated cardiomyopathy and pulmonary hypertension (Ghio et al., 2000; Forfia et al., 2006). In 63 patients with PH, Forfia and colleagues found that a TAPSE ≤ 18 mm was associated with greater RV systolic dysfunction (RVFAC 24 vs 33%), right heart remodeling and RV-LV disproportion (RVEDA / LVEDA: 1.7 vs 1.2). In addition, for every 1-mm decrease in TAPSE, the unadjusted risk of death increased by 17%, which persisted after adjusting for other hemodynamic and echocardiographic measurements and treatment regimens. Finally, one year survival in patients with TAPSE of 18 mm or greater was 94% versus 60% in subjects with TAPSE less than 18 mm, respectively.

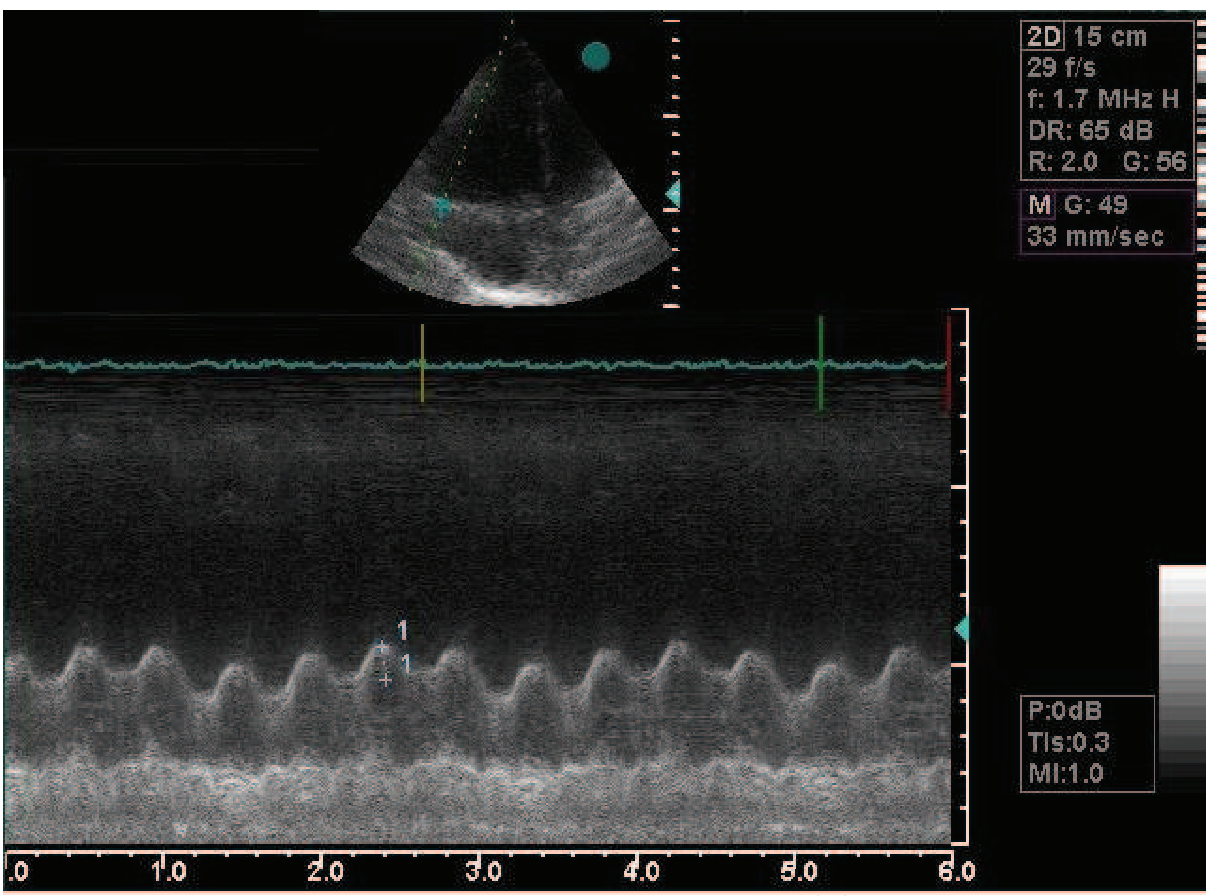

Fig. 2. TAPSE calculation. in a mechanically ventilated patient with severe pulmonary hypertension and RV failure due to acute respiratory distress syndrome (ARDS). TAPSE values were 9.8 mm

In conclusion, patients with normal LV function and depressed TAPSE have increased pulmonary vascular resistance, reflecting afterload at the level of proximal pulmonary arteries. The increase in RV filling pressure and a trend toward a reduction in TAPSE can also be signs of right ventricular function deterioration in cases of preload increase and a reduction in contractility. We have observed a decrease in TAPSE during a trial of separation from mechanical ventilation (weaning trial) in a cohort of medical critically ill patients with different diagnoses of admission, associated with increase in RV preload that was estimated with RVEDA, probably due to augmented venous return during spontaneous negative pressure ventilation (unpublished data).

3.2 Use of Tricuspid annular tissue Doppler imaging in cardiovascular patients

Tissue Doppler is superior to blood flow Doppler as it reflects directly myocardial function and is less subject to preload changes. TDI imaging has been used for differentiating different levels of PASP and for assessing left and right ventricular systolic and diastolic functions (Isaaz, 2000, 2002). Low values of systolic (Sm) and diastolic [Em (early) & Am (late atrial)] velocities have been proposed to reflect systolic and diastolic RV dysfunction, respectively (Waggoner & Bierig, 2001). Figures 3 & 4 demonstrate TDI measurements at the level of tricuspid valve in two patients with normal PASP and RV function and pulmonary hypertension with RV failure, respectively.

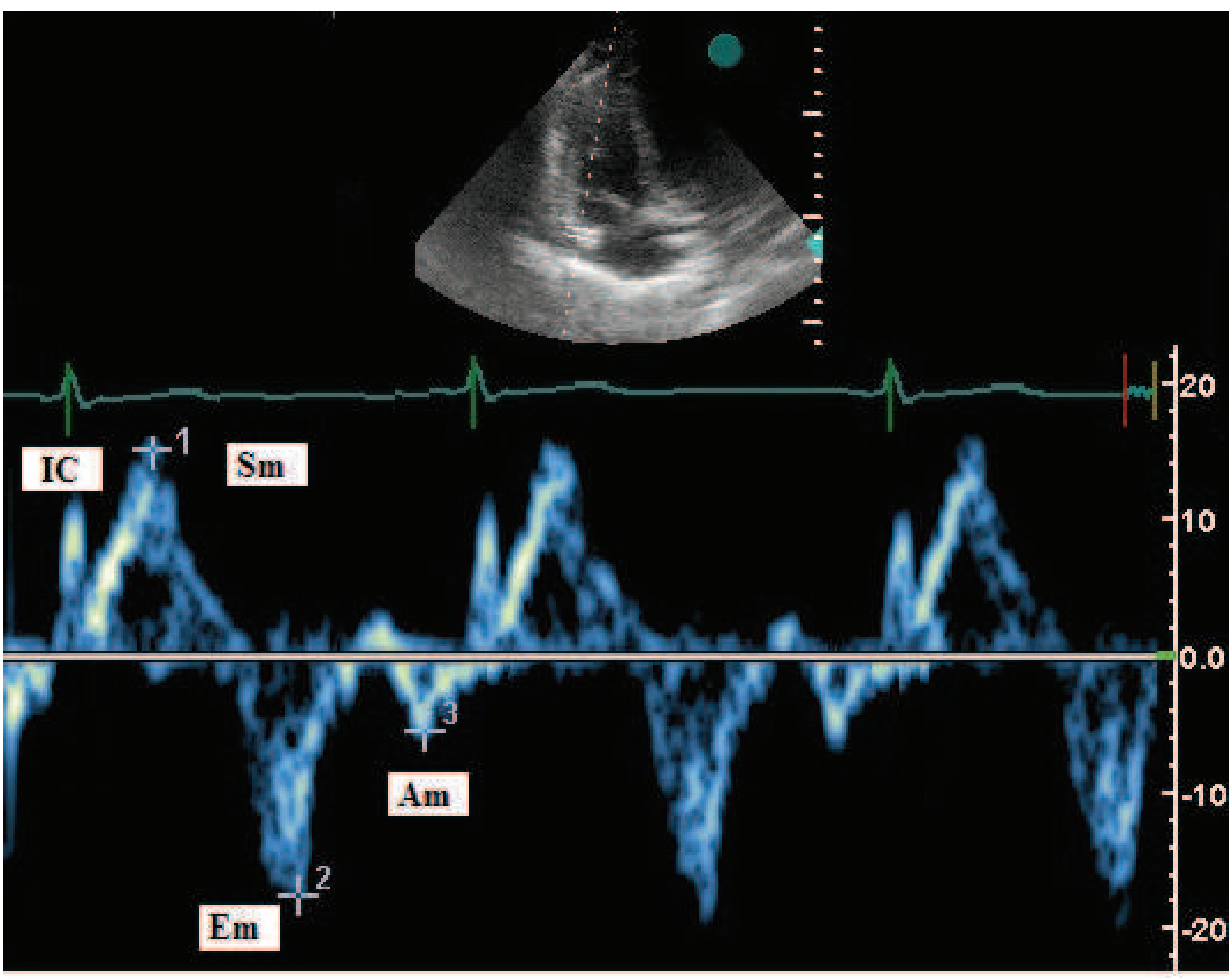

Fig. 3. Tissue Doppler Imaging (TDI) velocities of tricuspid valve.
After placing the cursor at the junction of the RV free wall and the anterior leaflet of the tricuspid valve, using the 2D four-chamber view. The systolic phase consists of two waves: 1. the first peak represents isovolumic contraction (IC) and 2. the second peak represents systole (Sm). Sm (1): Peak systolic velocity at the anterior leaflet of TV (15 cm/sec), Em (2): peak early diastolic velocity at the anterior leaflet of TV (18 cm/sec), Am (3): peak late diastolic (atrial) velocity at the anterior leaflet of tricuspid valve (6 cm/sec)

Meluzin J has shown that RV TDI systolic annular velocity correlated with RVFAC, assessed using radionuclide angiography and with prognosis, in 44 patients with LV heart failure (Meluzin, 2001, 2005). Moreover, a systolic annular velocity of less than 11.5 cm/sec predicted right ventricular dysfunction (RVEF < 45%) with a sensitivity of 90% and specificity of 85%. Dokainish has found that RV TDI systolic annular velocity detected mild degrees of RV dysfunction not yet apparent from visual assessment and concluded that Sm was an independent predictor of cardiac death or rehospitalization (Dokainish et al., 2007). Saxena demonstrated that the peak systolic tricuspid annular velocity (Sm) obtained from TDI measurements was able to determine RV systolic function, regardless of pulmonary artery pressures and was strongly correlated with both RVFAC and TAPSE, in 52 patients with varying degrees of pulmonary hypertension (Saxena et al., 2006). Similar results were found in a cohort of 22 heart transplant recipients, supporting that both Sm and TAPSE might be clinically useful for RV function determination (Doutreleau et al., 2007).

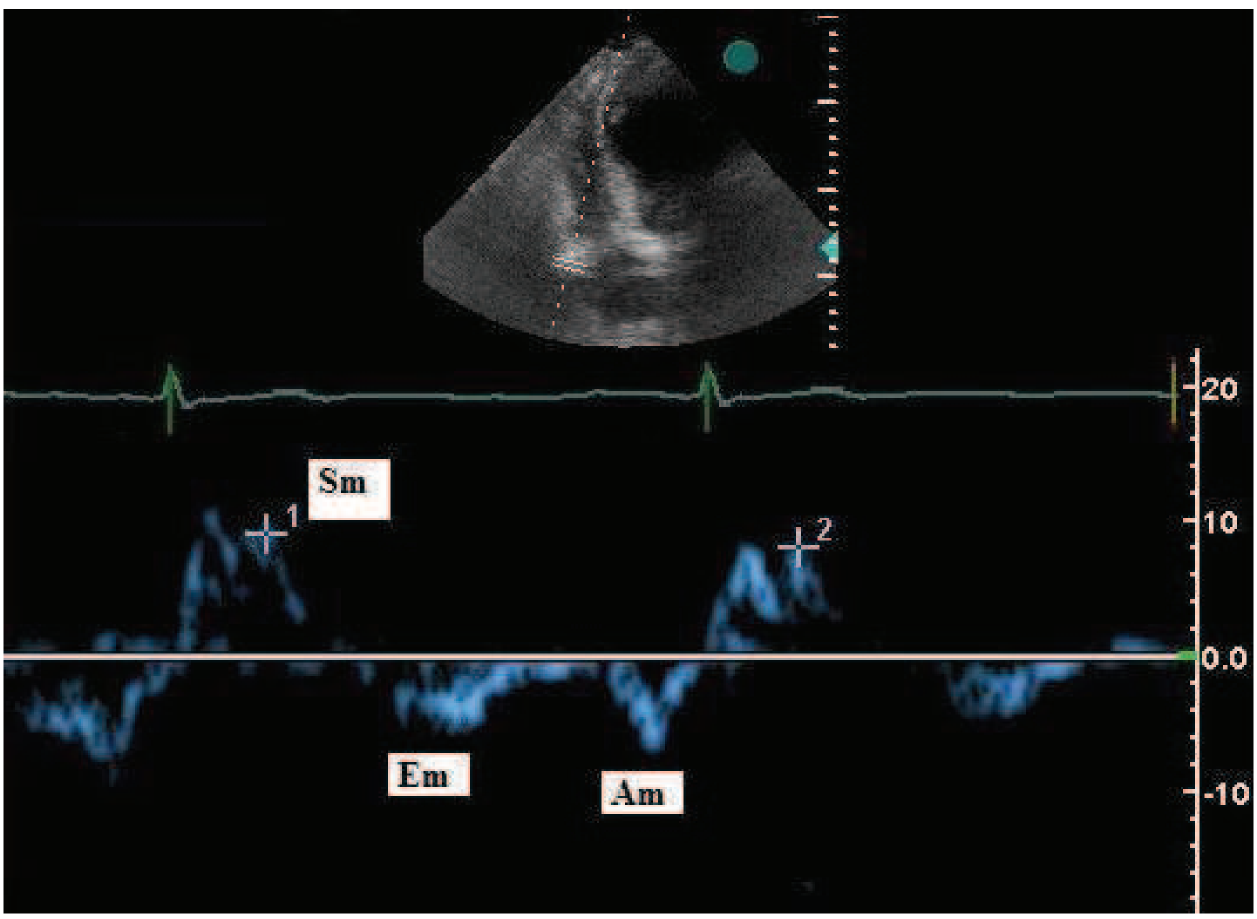

Fig. 4. Pulsed-wave tissue Doppler imaging (TDI) velocities of tricuspid valve in a patient with pulmonary hypertension and severe RV failure.
In this case, there is significant decrease in both systolic [Sm (1,2): 8-9 cm/sec] and diastolic velocities (Em, Am), indicating severe systolic and diastolic right ventricular dysfunction

3.3 Use of TAPSE and Tricuspid annular tissue Doppler imaging in the ICU

Recently, Sade showed that in ICU patients (35% under mechanical ventilation) the E (from the trans-tricuspid flow) /Em ratio was strongly correlated with right atrial pressure (Sade et al., 2007), whereas Denault proposed an algorithm for the diagnosis and classification of RV diastolic function during weaning from cardio-pulmonary bypass, based on a combination of indices derived from pulsed-wave Doppler of the tricuspid valve, hepatic vein flow and tricuspid annulus TDI velocities(Denault et al., 2005).

In a recent study we demonstrated that TAPSE and RV TDI velocities obtained by 2D echocardiography were significantly correlated with E/e' (transmitral early wave and mitral annulus motion ratio at its lateral aspect), left ventricular ejection fraction (LVEF), RVFAC, PASP and length of ventilatory support in a cohort of 32 mechanically ventilated patients with acute pulmonary edema (Papaioannou et al., 2010). Furthermore, these indices were proven to discriminate successfully patients with different duration of weaning. Liberation from mechanical ventilation can impose a significant load upon the cardiovascular system, especially in patients with heart disease. The shift from positive to negative intrathoracic pressure can augment venous return and central blood volume, increasing left ventricular preload and afterload. Moreover, high levels of catecholamines may reduce supply of oxygen to the heart due to tachycardia and decrease cardiac output due to increased pulmonary and vascular resistance (Lemaire et al., 1988).

Different studies in mechanically ventilated patients have confirmed that increased pulmonary artery systolic and occlusion pressures during weaning trials are associated with weaning failure (Schmidt et al., 1997 & Delooz, 1976) whereas only one study using echocardiography investigated the relation between the echo-derived index E/e' and PAOP during liberation from the ventilator, in patients without pre-existing heart diseases (Lamia et al., 2009). However, baseline filling pressures have not been proven to successfully predict weaning outcome (Lemaire et al., 1988 & Jubran et al., 1998), whereas early assessment of weaning readiness with echocardiography during the course of mechanical ventilation had not been studied previously. The direct correlations that were found in our study between low TAPSE and RV TDI velocities with LVEF reflect systolic ventricular interdependence, while the inverse correlations between the RV function parameters and E/e' indicate that LV filling pressures comprise an important part of RV afterload in the context of acute pulmonary edema.

In a similar study, Lamia and colleagues tested the hypothesis that TAPSE is related to RV function at baseline and increases in parallel with RVFAC following positive inotropic therapy, in 86 mechanically ventilated patients with varying diagnoses. Contrary to these initial hypotheses, they found that TAPSE was either weakly related or totally unrelated to RV systolic function, whereas a more significant correlation was found between TAPSE and left ventricular ejection fraction in comparison with RVFAC, especially after performing a set of dynamic maneuvers, such as fluid challenge, passive leg raising and dobutamine infusion (Lamia et al., 2007).

Although simple to use, highly reproducible and fast, especially in the ICU setting where it can be performed by less experienced practitioners, TAPSE has some inherent limitations as a measure of RV function. It may be difficult to obtain a clear visualization of the tricuspid annulus, particularly in obese patients and in those suffering from chronic obstructive pulmonary disease (COPD). LV failure may induces changes in TAPSE independently of RV dysfunction, whereas Lamia's finding of a cut-off value of 22 mm that identified patients with LVEF < 45% with 85% sensitivity and 62% specificity, makes this measure unsuitable for the assessment of LV function, at least in heterogeneous populations of critically ill patients (Lamia et al., 2007). In addition, RV assessment is restricted to the longitudinal movement of the RV free wall and does not measure the contribution of the intraventricular septum and RV outflow tract (RVOT) (Lopez-Candales et al., 2006). Finally, apical akinesis may preserve normal TAPSE values with impairment of RV function whereas severe tricuspid regurgitation can also underestimate RV dysfunction and correlation with RV ejection fraction (Lopez-Candales et al., 2006 & Hsiao et al., 2006).

4. Conclusions

The echocardiographic assessment of left ventricle in the ICU has gained increased interest in the last years. However, the estimation of both systolic and diastolic right ventricular function is much more difficult to perform in mechanically ventilated patients and is mainly based on hemodynamic data derived from right heart catheterization. Heterogeneous pathologic processes that may lead to pulmonary hypertension and ARDS, application of different levels of PEEP and models of mechanical ventilation and a continuous dynamic change in fluid balance may have profound implications in heart-lung interactions and finally, the estimation of cardiac output. Severe sepsis and septic shock can also impair both the left and right ventricle, through changes in contractility, venous return and dramatic decrease in systemic vascular resistance. Finally, the development of ARDS due to either pulmonary or extra-pulmonary causes (i.e., severe sepsis) can be associated with acute cor pulmonale, pulmonary hypertension, RV and subsequently LV failure and hemodynamic collapse.

For these reasons early and accurate assessment of cardiac function is urgently recommended in the ICU setting. Different Intensive Care Medicine Societies have already published guidelines concerning theoretical and practical education of intensivists in performing daily echocardiography (Cholley et al., 2006). The development of novel indices for the estimation of RV, such as TAPSE and TDI velocities seems very promising, since they are easily obtained at the bedside, they need less computational load and optimal visualization in comparison with conventional indices, such as RVFAC or RVEF and finally, can be performed by less experienced personnel, especially in the acute care setting (Salem et al., 2008). Moreover, intra- and inter-observer variability seems to be limited with the adoption of these techniques (Forfia et al., 2006).

Their value in the ICU needs to be further investigated for their future use as basic echocardiographic assessment tools, since there are only two studies in the literature exploring significance of TAPSE and RV TDI velocities, as diagnostic or prognostic methods in mechanically ventilated patients with different diagnoses of admission. Although their application for LV assessment seems scientifically ground, evaluation of RV function and primary PH using these tools can be biased by the presence of LV failure, excluding their possible adoption in patients with biventricular dysfunction. However, in cases with normal LV, TAPSE and RV TDI velocities could be of significant value for continuous and indirect evaluation of pulmonary hypertension and RV function, in patients with severe respiratory failure. New studies must be undertaken for assessing their accuracy for predicting successful or failed liberation from the ventilator and for evaluation of possible impact of high levels of PEEP upon RV contractility during ARDS. Finally, daily and sequential estimations can be adopted as an alternative method for therapeutic monitoring of positive inotropic treatment upon cardiac performance, during shock states of different origin.

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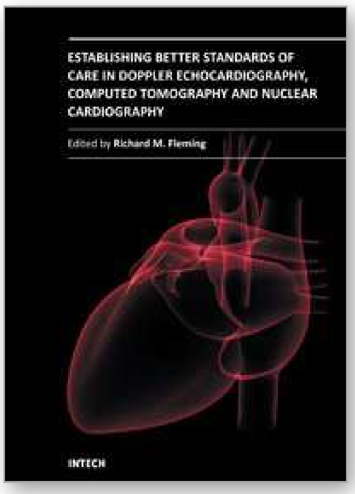

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Since the introduction of Doppler Echocardiography, Nuclear Cardiology and Coronary CT imaging, clinicians and researchers have been searching for ways to improve their use of these important tools in both the diagnosis and treatment of heart disease. To keep up with cutting edge improvements in these fields, experts from around the world have come together in this book to provide the reader with the most up to date information to explain how, why and when these different non-invasive imaging tools should be used. This book will not only serve its reader well today but well into the future.