Moderate or severe functional tricuspid regurgitation (TR) is commonly observed in patients with mitral valve disease and warrants concomitant or combined, at the same time, surgical correction. It is indeed well established that severe TR portends an adverse prognosis with an increase in mortality and morbidity and that TR only decreases temporarily and often worsens after the successful correction of the left-sided disease. Furthermore, short series have shown a 10% to 15% surgical mortality rate of isolated tricuspid valve surgery in highly selected patients. In contrast, tricuspid surgery eliminates TR and improves right ventricular function and this effect is durable over time.

See Clinical Perspective

However, moderate or severe late TR often develops despite successful mitral valve correction and absence of TR at the time of the index surgery. It has been suggested that tricuspid annulus (TA) enlargement may be a more sensitive criteria that may lead to the consideration of combined tricuspid surgery. Both the European Society of Cardiology and the recently published American College of Cardiology/American Heart Association guidelines recommend performing combined tricuspid surgery when the TA is enlarged even in the absence of significant TR (class IIa recommendation with a level C of evidence for the European Society of Cardiology and B for the American College of Cardiology/American Heart Association guidelines).

Nevertheless, several issues remain to date unsolved. First, the incidence in which TA measurement should be performed (two-dimensional [2D] transthoracic echocardiography (TTE) in the apical 4-chamber [A4C] view in the European Society of Cardiology guidelines) relies on limited evidence. Second,
the 3D shape of the TA is complex and whether currently performed 2D measurements accurately reflect the degree of TA enlargement has not been demonstrated. The 3D echocardiography now offers an accurate and real-time assessment of the size and shape of the TA\textsuperscript{14–16} to which both 2D and surgical measurements can be compared but such comparisons are seldom performed. Finally, recommended thresholds are not firmly established although they were evaluated in a few outcome studies.\textsuperscript{13,17,18} Thresholds of ≥40 mm or 21 mm/m\textsuperscript{2} of body surface are proposed both in the European Society of Cardiology and in the American College of Cardiology/ American Heart Association but it has also been suggested using direct surgical measurement but with a completely different threshold (70 mm) and the limitation of an obviously invasive method of measurement.\textsuperscript{9}

Thus, the aims of the present study were (1) to evaluate the feasibility and the reproducibility of the different 2D-TTE views for TA measurements, (2) to compare TA measurements performed using 2D echocardiography, real-time 3D echocardiography and surgery, and finally (3) to provide TA thresholds that can be used in clinical practice to guide indications for the performance of associated tricuspid valve surgery.

Methods

Population

Patients
In this first subset, we prospectively enrolled 282 patients referred to our echocardiography laboratory between January 2010 and November 2013 who underwent a transthoracic and a transesophageal echocardiography (TEE) the same day performed by the last author. When available, the 3D-TEE probe was used (n=194). TTE and TEE were all clinically indicated. Patients with poor 2D-TTE image quality were excluded, whereas those in atrial fibrillation were not. In 120 patients who underwent combined tricuspid valve surgery within 15 days, TA size was measured peroperatively. Surgical decisions were made by the physician in charge of the patients. All TTE and TEE were clinically indicated. The study was approved by our local ethical committee and informed consent was obtained from the patients.

Healthy Volunteers
In this second subset, we prospectively measured the TA size using 2D-TTE in 66 healthy volunteers. Healthy volunteers were mainly nurses, medical students, or physicians with no medical history, taking no medication and with no modifiable cardiovascular risk factors enrolled in an ongoing prospective study (GENERAC, clinical trial gov number NCT00647088). None of them had any echocardiographic abnormality including tricuspid valve or right-sided chambers abnormalities and thus could be surely considered as having normal tricuspid valve geometry.

Two-Dimensional Transthoracic Echocardiography
Two-dimensional-TTE was performed using a commercially available ultrasound system (S5-1 probe, IE33, Philips, Andover, MA or M4S probe, Vivid 7, General Electric, Fairfield, CT). TA diameter (TAD) was measured in 4 echocardiographic views: the parasternal long axis (LA) view of the right ventricle inflow (PSRVI), parasternal short-axis view (PSA) at the level of the aortic valve, A4C, and the subcostal view (SC). Images were acquired in each view using the zoom mode focused on the tricuspid valve. Measurements of the TAD were performed offline by the first author at the time of the maximum TV diastolic opening between the 2 hinge points at the junction between the valvular leaflets and the TA (Figure 1). Three to 5 cycles were analyzed in each view and averaged. TR degree was semiquantitatively graded with color Doppler in 4 grades (absent, mild, moderate, and severe).\textsuperscript{19} Left ventricular systolic ejection fraction and systolic pulmonary artery pressure were measured as recommended.\textsuperscript{20} Right ventricular dilatation was semiquantitatively assessed visually and graded as none, moderate, or severe.

Real-Time 3D-TEE
Three-dimensional-TEE was performed after topicalization using Xylocaine\textsuperscript{2} and intravenous injection of midazolam using a commercially available matrix array transducer (X7-2t, Philips). Volumes were obtained using the zoom mode (1 beat) focused on the tricuspid valve in real-time 3D-TEE and digitally stored. The view was optimized for depth and gain setting before 3D acquisition and particular attention was given to including the entire TA in the sector boundaries. Measurements

Figure 1. Measurements of the tricuspid annulus diameter using 2-dimensional transthoracic echocardiography. Measurements were performed in 4 views: (A) left parasternal long-axis view of the right ventricular inflow, (B) left parasternal short-axis view at the level of the aortic valve, (C) apical 4-chamber view, and (D) subcostal view.
of the TA were performed offline on a workstation using QLab7 software (Philips) by the first author in a random order and blinded to any clinical or echocardiographic information. Measurements were performed at the time of maximum diastolic leaflet opening. The plane of the TA was obtained by cutting the TA at its junction with the valvular leaflets in the different axes. From this plane, we measured the long axis (LA) as the largest TAD, the short axis (SA), as the diameter perpendicular to the LA and the TA area (Figure 2). Measurements were performed in 3 to 5 cycles and averaged. TA eccentricity index (EI) was calculated as the LA/SA ratio. TA orientation (Figure 3) was evaluated by the angle between the LA and the vertical axis at the level of the interatrial septum in the surgical view (aortic valve on top, mitral valve on the left, and tricuspid valve on the right).

**Surgical Measurements**

TAD was measured in the operating room in unloaded conditions using a supple ruler as the maximal diameter from the interatrial septum to the opposite side in a so-called neutral position. A second measurement of the TA was also performed after slight traction was applied by the surgeon on the tricuspid valve (stretched measurement). Peroperative measurements were performed blinded of echocardiographic measurements.

**Statistics**

Quantitative variables were expressed as mean±SD. Comparison of the feasibility of the different TTE views was performed using the Cochrane Q test and the McNemar test for pairwise comparisons to determine the most feasible view. A repeated measure ANOVA was performed to compare TA measurements performed in each TTE view and paired t tests and Pearson correlations for comparison between 2D-TTE, 3D-TEE, and surgery. Agreement between methods of TA measurements was assessed as described by Bland–Altman. Reproducibility of TA measurements, calculated as the absolute difference±SD, was evaluated for both 2D-TTE and 3D-TEE in 30 randomly selected patients a few weeks after the initial measurement for intraobserver variability (first author) and by a second observer (second author) for interobserver variability. Comparison of the differences between measurements (intra- and interobserver variability) was evaluated using a repeated measure ANOVA and paired t test for pairwise comparisons. Intraclass correlations within each of the 4 views were also calculated. Pathological thresholds for TAD enlargement were defined as mean+2 SD of normal values obtained in the healthy volunteer subset. Time needed for 3D-TEE TA measurements was also evaluated in 30 patients. All tests were 2-sided. Statistical significance was defined with $P<0.05$. Statistics were performed using JMP software and MedCalc.

**Results**

**Population**

We prospectively enrolled 282 patients. Mean age was 60±16 years, 158 patients (56%) were women, 191 (68%) were in New York Heart Association functional class 3 or 4, 127 (45%) were in atrial fibrillation, and 180 (64%) had a rheumatic valve disease. The main reason for echocardiography was mitral valve disease (90 mitral stenosis [32%] and 89 mitral insufficiency [32%]). Moderate or severe TR was present in 118 patients (42%) and mean systolic pulmonary artery pressure was 49±15 mm Hg. Left ventricular ejection fraction was normal (≥60%) in 212 patients (75%). Right ventricular size was normal in 91 patients (33%), moderately enlarged in 118 (42%), and severely enlarged in 73 patients (26%).

**Two-Dimensional TTE Measurements**

Feasibility of TAD measurements in the 4 2D-TTE views was evaluated in the first 100 patients. Measurements were considered feasible in 1 view if image quality allowed clear measurement of the TAD. Agreement between methods of TA measurements was significantly different between the 4 views (PS$_{RV}$: 76%, PS$_{SA}$: 65%, A4C: 92%, and SC: 73%, respectively; $P<0.0001$) with the A4C view being the most feasible ($P$ versus the 3 other views all <0.001).
Comparison of TAD measurement was performed in 138 patients in whom the 4 TTE views were all feasible. There was a wide range of TAD from 2.5 to 5.9 cm. Correlations between views were excellent (from 0.69 to 0.85). TAD measurements were significantly different between views even if differences were minimal (PSRVI: 3.85±0.58 cm, PSSA: 3.87±0.61 cm, A4C: 4.02±0.69 cm, and SC: 3.92±0.65 cm; P<0.0001).

Intraobserver variability of TAD measurements between the 4 views was of borderline statistical significance (PSRVI: −0.03±0.21 cm, PSSA: −0.02±0.22 cm, A4C: −0.04±0.14 cm, and SC: 0.06±0.25 cm; P=0.07), whereas interobserver variability was significantly different (PSRVI: 0.07±0.25 cm, PSSA: 0.11±0.28 cm, A4C: −0.05±0.22 cm, and SC: 0.12±0.31 cm; P=0.007) and A4C achieved the highest reproducibility (all P<0.05). For intraobserver and for interobserver, intraclass correlations (95% confidence interval [CI]) for each of the 4 views were PSRVI: 0.94 (0.90–0.96) and 0.91 (0.85–0.95), PSSA: 0.92 (0.86–0.95) and 0.86 (0.77–0.92), A4C: 0.98 (0.97–0.99) and 0.96 (0.92–0.98), and SC: 0.93 (0.88–0.96) and 0.89 (0.80–0.94), respectively.

Thus, as the A4C offered the highest feasibility and reproducibility, A4C measurements were compared with 3D-TEE and surgical measurements.

**Comparison With 3D-TEE Measurements**

Evaluation of the TV using 3D-TEE was performed in 194 patients with feasible measurements of the TAD using TTE in the A4C view. Eleven patients (6%) were excluded because of poor image quality mostly related to an excess of gain (9 patients) or a truncated annulus (2 patients) thus leaving 183 patients who had both measurements of TA size using 2D-TTE in the A4C view and 3D-TEE.

TAD measured in A4C view correlated well with LA measured using 3D-TEE (r=0.84; P<0.0001) but was significantly smaller (3.90±0.63 and 4.33±0.62 cm; P<0.0001; Figure 4A and 4B). Correlation with the TA area was also excellent (r=0.84; P<0.0001). Thus, measurement of the TAD using 2D-TTE in the A4C view accurately reflected the degree of TA enlargement even if it did not measure its maximal diameter.

Intra- and interobserver variability of 3D measurements was good for diameters (0.02±0.15 and 0.09±0.19 cm for the
LA and 0.02±0.19 and 0.05±0.22 cm for the SA, respectively) and area (0.09±0.40 and 0.19±0.52 cm², respectively). The mean time required for 3D measurements of TA size was 3±1 minutes.

Impact of 3D Shape and Orientation of the TA on TTE Measurement

Shape
TA shape was generally oval (mean EI=1.35±0.22) but was markedly different among individuals from circular (EI=1) to severely oval (EI=2.15; median=1.31; 95% CI [1.07–2.04]; Figure 5A). TA dilatation seemed to occur homogeneously in all directions of the right ventricle free wall as suggested by the good correlation between TA area and both the LA (r=0.89; P<0.0001) and the SA (r=0.88; P<0.0001). Larger TA tended to be more circular with an inverse although modest correlation between TA area and EI (r=−0.21; P<0.0001). Accuracy of 2D-TTE measurements when compared with that of 3D-TEE was not influenced by the EI. When the population was dichotomized according to the median EI value (EI <1.31 or EI ≥1.31), excellent correlations between 2D-TTE and 3D-TEE measurements were observed in both subsets (r=0.87; P<0.0001 and r=0.83; P<0.0001, respectively) with a similar 4-mm systematic underestimation as shown by the Bland and Altman plots (Figure 6A–6D).

Orientation
Mean angle between the LA and the vertical axis at the level of the interatrial septum in the surgical view was 87°±57° (median, 70; 95% CI [10–175]) but different orientations were observed among individuals from 5° to 175° with a bimodal distribution (Figure 5B). The 2 most frequent orientations were around 40° and 140° (LA directed toward the anterior and lateral side or toward the posterior and lateral side of the TA). TA orientation also did not affect the accuracy of TTE measurements as attested by the excellent correlations between TAD measurements performed using 2D-TTE in the A4C view and the LA measured using 3D-TEE in the subset of patients above or below the median angle value (r=0.81; P<0.0001 and r=0.87; P<0.0001, respectively) and a similar 4-mm systematic underestimation as shown by the Bland and Altman plots (Figure 6E–6H).

Comparison With Surgical Measurements
Surgical measurements of the TA were performed in 120 patients in the neutral position. TAD measurements obtained using 2D-TTE in the A4C view were significantly smaller but were only moderately correlated to surgical measurements (4.11±0.61 versus 4.37±0.75 cm; P<0.0001; r=0.57; P<0.0001). More importantly, a large SD of the difference was observed, twice the SD of the difference between 2D-TTE A4C and 3D-TEE LA measurements (0.64 versus 0.35 cm; Figure 7). In the 39 patients in whom 2D-TTE, 3D-TEE, and

Figure 5. Tricuspid annulus shape and orientation. Distribution (A) of the eccentricity index and (B) of the orientation of the tricuspid annulus. C, Examples of shapes of the tricuspid annulus from circular to oval, with the most frequent morphology in the yellow box. D, Examples of orientations of the tricuspid annulus, with the 2 most frequent orientations in the yellow boxes.
surgical measurements of TAD were performed, 3D-TEE and surgical measurements were not different (4.47±0.63 versus 4.42±0.79 cm; \(P=0.68\)) but correlation between methods was moderate \((r=0.50; P<0.0013)\) and again a large SD of the difference was observed (0.71 cm). Finally, a slight traction applied on the TA orifice (stretched measurements performed in 91 patients) resulted in a >1 cm increase in surgical measurements of the TA (5.40±0.76 versus 4.25±0.76 cm, respectively; \(P<0.0001\)).

**Healthy Volunteers**

TAD was measured in the A4C view using 2D-TTE in 66 healthy volunteers. Mean age was 34±12 years, 56% were women, and mean body surface area 1.76±0.20 m². Normal values were 3.24±0.46 cm (median, 3.2; 95% CI [2.37–4.17]) and 1.85±0.23 cm/m² (median, 1.86; 95% CI [1.36–2.42]) and thresholds for TA enlargement, defined as mean normal value+2 SD, were 4.2 cm and 2.3 cm/m², respectively.
Discussion

The main results of the present study can be summarized as follows: (1) 2D-TTE measurements of the TAD were statistically different but differences were small and the A4C offered the highest feasibility and reproducibility; (2) 2D-TTE measurements were systematically smaller than the LA diameter of the TA measured using 3D-TEE but still reliably reflected the degree of TA enlargement using this method; (3) shape and orientation of the TA were highly variable among individuals but did not affect the accuracy of 2D-TTE measurements; (4) using current methodology surgical measurements were poorly reproducible as a slight traction on the TA resulted in marked changes in TA measurements; and (5) in healthy volunteers, we defined normal (3.2 cm or 1.8 cm/m²) and pathological values (4.2 cm or 2.3 cm/m²) of the TAD that could be used in clinical practice to consider the performance of a combined tricuspid annuloplasty.

TR has for a long time falsely been considered as a benign condition that could be neglected. In the past 15 years, there is a growing body of literature showing that not only is TR a marker/prognostic factor of poor outcome but also that TR by itself directly affects the outcome. There is now a consensus to correct moderate or severe TR at the same time as the mitral valve surgery and is associated with few complications. Such a preventive strategy is supported by a few nonrandomized studies showing that concomitant tricuspid annuloplasty prevents progression of TR and occurrence of late significant TR. As TA enlargement appears earlier in the course of the disease, current recommendations have incorporated, in addition to TR degree, enlarged TAD as an indication for combined surgery to avoid the occurrence of significant late TR and the need for a risky redo operation. It is worth noting that this combined surgery, mainly tricuspid annuloplasty, adds little time to the mitral valve surgery and is associated with few complications. Such a preventive strategy is supported by a few nonrandomized studies showing that concomitant tricuspid annuloplasty prevents progression of TR and occurrence of significant late TR and promotes right ventricular reverse remodeling and thus improvement of right ventricular function. Nevertheless, neither the methodology of measurement of the TAD nor thresholds have been firmly established.

The 2D-TTE is the most common echocardiographic modality and the most common method used to assess TA size. TAD can be measured in different views and comparisons between views as well as the reproducibility of TTE measurements are rare. In the present study, we show that overall the different views were statistically different but differences were minimal and the A4C view, which is indeed the most common used, provided the highest feasibility and reproducibility. An important finding of the present study is to show that TA measurements performed in the A4C using TTE accurately reflected the degree of TA enlargement. Using 3D echocardiography it is now possible to visualize, under physiological conditions, the TA with high image resolution and no need for complex and time-consuming reconstruction. With technological improvements, an image of the entire TA can be now be captured in 1 beat with no need for breath holding which is crucial as atrial fibrillation is common in patients with mitral valve disease. In the present study, feasibility of 3D-TEE was high and of the few patients we had to exclude most were at the beginning of our experience. TAD measured in the A4C was smaller than the TA LA diameter measured using 3D TEE but correlations were excellent and the Bland and Altman clearly show a systematic underestimation of TTE measurements validating 2D TEE in the A4C as an accurate method to assess TA size in a large series of patients with a wide range of TA values. In addition, 3D-TEE provided an assessment of TA morphology and orientation, both of which were highly variable from 1 individual to the other but did not affect the accuracy of TTE measurements.

Direct measurements by the surgeon are intuitively regarded as more reliable and often considered as the gold standard. The present study clearly shows the current limits of surgical measurements. In contrast to 3D-TEE, surgical measurements are performed under unloaded conditions and measurements are highly dependent on the force applied to the TA. Minimal changes in the traction applied to the TA resulted in important changes in the TAD. In addition, there is no commercial tool dedicated to the measurement of TA size in contrast to the aortic annulus. Measurements were performed with a simple ruler which was not always easy to precisely insert into the tricuspid valve. It is worth noting that we never achieved TAD values of 70 mm either using 3D or during surgery and most probably measurements obtained by Dreyfus and al reflected the maximum elongation of the TA. Overall our results are strong arguments to standardize surgical measurements using appropriate and dedicated tools for the assessment of TA size.

The present study deserves several comments. First, we used 3D-TEE as the reference method. In spite of the fact that we could not validate this method against a gold standard, validity and accuracy of 3D measurements are now well demonstrated. Second, no comparison with 3D-TTE was performed. In our experience, image quality of 3D-TTE is lower than that of 3D-TEE especially for posterior structures such as the mitral or tricuspid valve. Third, TR degree and TA size may vary according to loading conditions. In the present study, all TTE and TEE measurements were performed successively during the same examination and TEEs were performed under local anesthesia and midazolam. Fourth, for both TTE and TEE measurements, we assessed the intra- and interobserver variability of TA measurements but not of image acquisition. However, these acquisitions are standardized and poorly operator dependent. Fifth, our study cannot provide a definite answer on the anatomic correspondence between the 2D-TTE (A4C) and 3D-TEE (LA) measurements. Measurements in the A4C view are performed between the septal and anterior leaflet. In regard to the excellent correlation between both measurements, we may hypothesize that TTE measurements are performed in a direction grossly parallel to the LA. Further studies using ideally 3D-TTE may confirm or not this hypothesis. Sixth, not all examinations were performed in all patients. Surgical measurements were of course only performed in operated patients for whom the physician in charge asked for combined tricuspid surgery. Parts of the TEE were performed using a probe with no 3D capabilities because of logistic issues. Finally, as peroperative measurements were only performed in patients referred for combined tricuspid surgery, surgeons might have expected significant
TR or TA enlargement. Nevertheless, surgical measurements were performed blinded of echocardiographic measurements.

Accurate echocardiographic measurement of the TA has important clinical and surgical implications. Combined tricuspid valve surgery remains underused representing 10% of mitral valve operations and it is estimated that 75% of these patients have TA changes associated with functional TR. As mentioned previously, we filled several gaps in knowledge highlighted in the current guidelines. We validated a feasible and reproducible methodology to assess the TA size and proposed thresholds that could be used in clinical practice to recommend performing a combined tricuspid surgery. Using 3D as a reference, we validated measurements performed using TTE in the A4C view and defined thresholds of TA enlargement in a subset of healthy volunteers (>42 mm or >23 mm/m² of body surface area). These thresholds were close but not identical to those suggested in the guidelines. Thus, the present study offers the appropriate methodology and thresholds to validate in future randomized prospective studies whether a preventive strategy results in improvement of the outcome of patients who undergo a mitral valve surgery.

Conclusions

In a large cohort of patients with a wide range of TA size, we validated the measurements of the TAD using TTE and the A4C view. Two-dimensional measurements in the A4C were highly feasible and reproducible and despite being systematically smaller than 3D measurements, accurately reflect the degree of TA enlargement as assessed using this method. The accuracy of the A4C was not influenced by TA orientation and shape which were highly variable among individuals. In contrast, surgical measurements, performed in unloaded conditions, were highly variable depending of the traction strength applied to the tricuspid valve highlighting the need to develop a standardized method using dedicated tools for the assessment of TA size. We propose the thresholds of 42 mm or 23 mm/m² that may lead to consider tricuspid surgery at the same time as left-sided surgery. Further prospective studies using this methodology and those thresholds are now necessary to validate whether a preventive strategy can improve outcome.

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Disclosures

None.

References


**CLINICAL PERSPECTIVE**

Accurate echocardiographic measurement of the tricuspid annulus (TA) size has important clinical and surgical implications. Associated tricuspid annuloplasty is recommended during left-heart valve surgery in cases of moderate to severe tricuspid regurgitation or when the TA is dilated but combined tricuspid valve surgery remains underused and the methodology for the measurement of TA size and thresholds for TA enlargement are not clearly defined. Using 3-dimensional as a reference, we validated measurements performed using transthoracic echocardiography in the apical 4-chamber view and defined thresholds of TA enlargement in a subset of healthy volunteers (>42 mm or >23 mm/m² of body surface area). The present study thus may offer tools for future randomized prospective studies studying the impact of tricuspid annuloplasty in patients undergoing mitral valve surgery.
Comparison of 2-Dimensional, 3-Dimensional, and Surgical Measurements of the Tricuspid Annulus Size: Clinical Implications

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