学位論文の要旨

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学位論文名	Severity of Aortic Regurgitation Assessed by Area of Vena Contracta: A Clinical Two-dimensional and Three-dimensional Color Doppler Imaging Study
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論文内容の要旨

INTRODUCTION

Accurate quantitation of aortic regurgitation (AR) severity is essential for effective clinical management and surgical intervention timing. Conventional two-dimensional (2D) and color Doppler echocardiographic imaging modalities, incorporating the vena contracta width (VCW), regurgitant volume (RV), and effective regurgitant orifice area (EROA) measurement, are established methods for AR severity evaluation. However, accurate prediction of AR severity is often challenging. Three-dimensional (3D) echocardiography can directly measure the vena contracta area (VCA): 3DVCA measurement was proven superior to VCW measurement for AR quantitation because it provides reliable assessment of the regurgitant orifice shape. In contrast, 3DVCA processing after data acquisition is time-consuming, and the high-end echocardiographic machine capable of 3D color Doppler imaging is not always accessible. We evaluated the feasibility of measuring the cross-sectional VCA using 2D color Doppler imaging (2DVCA) in comparison with 3DVCA in assessing AR severity.

MATERIALS AND METHODS

We enrolled 61 patients referred to our institution for AR evaluation by echocardiography. Conventional echo Doppler imaging was performed using an IE-33 ultrasound machine with S5-1 and X5-1 probes (Philips Medical Systems, Andover, MA, USA). Standard measurements were performed according to American Society of Echocardiography guidelines. We measured 2DVCA, EROA, VCW, and RV using conventional 2D color Doppler imaging and described 2DVCA as the smallest area of the AR jet using the short-axis view during 2D color Doppler imaging while referring to a simultaneous gray scale image. Three-dimensional echo Doppler imaging was performed using the iE-33 ultrasound machine with X3-1 and X5-1 probes, and

3DVCA measurements made manually off-line (QLAB 8.1; Philips Medical Systems). From the 3D dataset, three orthogonal planes (x, y, and z) were constructed. The reference lines of planes x and y were adjusted according to the largest point on the AR jet to obtain a plane exactly perpendicular to the AR jet (z plane). We measured the cross-sectional area at the narrowest region of the AR jet (3DVCA) in the z plane. Informed consent was obtained from all patients, and the protocol was approved by the hospital ethics committee. Statistical analyses were performed using SPSS (SPSS, Inc., Chicago, IL, USA) and R (The R Foundation for Statistical Computing, Vienna, Austria). Data were expressed as mean ± standard deviation (SD), and p-values <0.05 were considered significant. To compare 2DVCA with 3DVCA and to correlate 2DVCA with EROA, we performed linear regression analyses and calculated Pearson's correlation coefficients. Interobserver and intraobserver variability were evaluated via the intraclass correlation coefficient. Percentages of intraobserver and interobserver variability were calculated as the absolute difference divided by the average of the two measurements. Agreement was assessed using the Bland–Altman analysis. Comparison of mean values was performed using the paired t-test. We conducted receiver operating characteristic curve analysis to determine the optimal cut-off values in identifying severe AR (EROA: $>30 mm^2$).

RESULTS AND DISCUSSION

Comprehensive 2D and 3D data evaluating AR severity was successfully obtained in 52 of 61 patients (85.2%). 2DVCA also correlated with EROA ($r = 0.89$; $p < 0.001$). Significant correlation also existed between 2DVCA and RV ($r = 0.80$; $p < 0.001$) as well as 2DVCA and VCW ($r = 0.78$; $p < 0.001$). 3DVCA correlated with EROA ($r = 0.89$; $p < 0.001$). The optimal 2DVCA cut-off for grading AR severity was 34 mm^2 (area under the curve: 0.95; 95% CI: 0.88-1; sensitivity: 78%; specificity: 95%) and the optimal 3DVCA cut-off for grading AR severity was 32 mm^2 (area under the curve: 0.96; 95% CI: 0.88-1; sensitivity: 89%; specificity: 98%); for reference, EROA was >30 mm^2. We demonstrated that 2DVCA correlates with 3DVCA and EROA. Three-dimensional echocardiographic imaging facilitates direct measurement of VCA. When measuring 2DVCA using conventional 2D color Doppler imaging, there are two major considerations. First, 2DVCA measurement must be performed at the level of the vena contracta. We primarily measured 2DVCA using the parasternal approach. We were careful to measure the cross-sectional plane of the vena contracta—the narrowest area of the jet—and not the crosssectional planes of the proximal flow convergence or distal expansion of the regurgitant jet spray during mid-diastole. If the flow convergence is visible in the short- axis view, the area upstream of the vena contracta, part of the proximal isovelocity surface area, is being imaged. On the contrary, the downstream area of the AR jet is bigger than the vena contracta. For reference, we attempted to describe the complete AR jet using the long-axis view, then calculate VCA by measuring the smallest area between the proximal flow convergence and distal regurgitant jet spray in the short-axis view. It is important to begin the 2D scan at the proximal flow convergence, moving the image plane toward the regurgitant jet spray to identify the smallest area of the vena contracta. Second, a 2D view exactly perpendicular to the AR jet is important for measuring 2DVCA. In patients with an eccentric AR jet, we cannot accurately measure 2DVCA using the conventional parasternal short-axis view. This may explain why 2DVCA is not widely accepted for accurate VCA evaluation. We attempted to project ultrasound perpendicular to the AR jet using multiple echo windows and measure 2DVCA similar to 3D imaging. Alignment of the 2D image planes was not always perfect in older patients with reduced aortoseptal angle and in patients with eccentric AR: we measured the smallest area of 2DVCA using alternative, similar images from limited acoustic windows. In this study, we have reported that optimal cut-off value of 3DVCA was >32 mm^2, 2DVCA was > 34 mm^2, for reference, ERO was >30 mm^2. These thresholds need to be confirmed in further studies. Figure 6 shows the relationship between EROA and VCW (left), 2DVCA (middle) and 3DVCA (right). All 6 patients with eccentric AR (red) had severe AR (EROA>30 mm^2). VCW was >6 mm in 3 of 6 (50%) patients with eccentric AR, 2DVCA was >34 mm^2 in 5 of 6 (83%) patients with eccentric AR and 3DVCA was >32 mm^2 in all 6 (100%) patients with eccentric AR. The measurement of the 2D or 3DVCA could be a useful and accurate method in patients with eccentric AR. In this study, interobserver and intraobserver variability were low and the intraclass correlation coefficient was good. To our knowledge, this is the first study to show that 2DVCA can evaluate AR severity as well as 3DVCA. Measurement of 2DVCA is a simple technique, feasible for use clinically at patients' bedsides or in the emergency room, during comprehensive Doppler echocardiographic AR severity assessment. VCA can be measured simply by calculating the shape of regurgitant orifice as an ellipse, using the major (VCW_1) and minor (VCW_2) axis of the regurgitant flow, two orthogonal VCW: $VCA = \pi \times (VCW_1) \times (VCW_2)/4 = 0.785 \times (VCW_1) \times (VCW_2)$, and this method may have a potential role as simple semiquantitative assessment of AR severity in patients with eccentric AR.

In this study, no patient exhibited multiple regurgitant orifices or prosthetic paravalvular regurgitation; thus, we cannot extrapolate our results to such patients. In a recent study, 3DVCA was reported to be a useful technique in such patients, and further studies of 2DVCA are justified. For the clinical study, we chose Doppler-derived EROA as the independent reference standard. Further studies comparing 2DVCA with magnetic resonance imaging may provide insight for assessing AR severity. The number of patients enrolled, especially those with severe AR, was small. Further studies are necessary to definitively validate this method.

CONCLUSION

Significant correlation existed between 2DVCA and 3DVCA as well as between 2DVCA and ERO, RV, and VCW. Measurement of 2DVCA is a simple technique for clinical use during comprehensive Doppler echocardiographic assessment of AR severity.

論文審査及び最終試験又は学力の確認の結果の要旨

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論文審査の結果の要旨

大動脈弁閉鎖不全症(AR)の重症度の正確な定量評価は、臨床管理や手術決定時期に必要不可欠である。二次元心エコー法によるAR重症度評価には限界があるとされてきた。しかし、新たに登場した三次元心エコーはAR重症度評価に有用なvena contractaの断面積(3DVCA)を直接計測できるが、高価であり、計測が複雑で時間を要するという欠点が指摘されている。申請者は、これまで困難とされていた二次元心エコー法によるvena contractaの断面積（2DVCA）の新しい測定法を考案し、3DVCAと比較検討した。本研究は院内倫理委員会で承認後、ICを行って施行した。61名のAR患者を対象に、従来法とはアプローチ部位を変えることでAR jetに対して垂直な断面を描出して、vena contractaの断面積(2DVCA), vena contractaの幅(VCW), 有効逆流弁口面(EROA)と逆流量（RV）を計測すると共に、従来の方法で3DVCAを計測した。その結果、61人中52人(86%)でAR重症度が評価できた。2DVCAと3DVCAの間に強い相関が（r=0.97、p<0.001)見られた。2DVCAとEROA、RV、VCWそれぞれとの間でも有意な相関が見られた。3DVCAとEROAとの間にも有意な相関が見られた。重症ARの2DVCAの最適なカットオフ値におけるAUCは0.95で感度78%, 特異度95%であった。3DVCAの最適カットオフ値におけるAUCは0.96で感度89%、特異度98%であった。本研究はARの重症度評価が通常のカラードプラ法による2DVCAの測定でも、従来法とは異なるアプローチ部位を用いることで可能であることを初めて示した研究であり、循環器診療に大きなインパクトを与える知見であることから、学位授与に値すると判断した。

最終試験又は学力の確認の結果の要旨

申請者は二次元心エコーの手技で工夫することで新たな三次元心エコーと同等に有用な情報を得てARの重症度評価が可能であることを多数の臨床例で示した。公開審査における質疑にも的確に応答でき、周辺知識も豊富であることから、学位授与に値すると判断した。(主査：北垣　一)

申請者はアプローチ部位を変えることで、カラードップラー法による二次元エコーでもARの重症度評価を三次元の結果と同等に評価出来ることを示し、安価で短時間でのAR重症度判定に道を拓いた。公開審査の質疑応答も問題無く、学位授与に値すると判断した。（副査：廣田秋彦）

申請者は二次元心エコー法で精度の高いAR重症度評価法を考案し、臨床応用できることを示した。関連領域の知識も十分に有し、学位授与に値すると判断した。（副査：中澤芳夫）

（備考）要旨は、それぞれ４００字程度とする。