【Original Article】 doi: 10.34376/jsachd.O-2021-0005

Severity classification of Fractional Area Change (FAC) in the left ventricle: A pilot study for evaluating systemic ventricular function by using FAC

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Abstract

Purpose: The disk summation method cannot assess systemic right ventricular function and single ventricular function because of its unique shape. Fractional area change (FAC) and eyeball ejection fraction (EF) methods are often used in such cases; however, the FAC cutoff value is vague. Estimation of left ventricular (LV) EF is classified into four stages; however, a severity classification system using the FAC method is lacking. This study aimed to assess LVFAC cutoff values based on systemic LVEF for evaluating systemic ventricle with complicated shape using FAC. We also evaluated the accuracy of the eyeball FAC method in the left ventricle because we are generally accustomed to evaluating eyeball right ventricle FAC, not LVFAC.

Methods: A total of 320 consecutive patients who underwent echocardiography were retrospectively enrolled. Eyeball LVFAC was estimated by well-trained sonographers. LVFAC was assessed simultaneously at the time of LVEF measurement.

Results: A total of 303 patients were classified as follows: 115 patients with normal contraction (LVEF>52%), 78 patients with mild dysfunction (40%<LVEF<51%), 62 patients with moderate dysfunction (30%<LVEF<40%), and 48 patients with severe dysfunction (LVEF<30%). The cutoff value of actual LVFAC measurements calculated from the receiver operating characteristic curve was 33% for mild dysfunction, 25% for moderate dysfunction, and 20.8% for severe dysfunction. The correlation between measured LVFAC and eyeball LVFAC was strong (r=0.94).

Conclusion: We classified LVFAC into four severity stages. LVFAC may be used as a simplified screening tool for any LV shape in local hospitals and emergency rooms, but further studies are needed.

Key words : Fractional area change, Eyeballing, Echocardiography

Introduction

Left ventricular ejection fraction (LVEF) estimation using the disk summation method (modified Simpson's rule) is a typical index for evaluating the contractile function of the systemic LV[1)], which is not always feasible to assess systemic ventricular function in complicated structures, such as systemic right ventricle (RV) or single ventricle with a rudimentary chamber.

Three-dimensional (3D) measurements may be used in cases of complicated morphology, but the analysis software is expensive and its availability is limited in local hospitals. Therefore, fractional area change (FAC) and visual estimation (eyeball) EF methods are often used; however, there is no severity classification of LVFAC[2)]. RV dysfunction is defined as FAC<35%; however, it remains unknown whether FAC is feasible to assess mild or moderate

Received June 4, 2021 Accepted September 23, 2021 Advance publication March 25, 2022
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RV dysfunction, and not severe RV dysfunction.

FAC assessment of complicated ventricular shape is preferred for the following reasons. 1) The regular use of 3D measurements is cumbersome in daily practice[3]. 2) FAC use is more practical in local hospitals. Therefore, we mainly evaluated the cutoff value of LVFAC severity based on LVEF using the disk summation method in this study. This is the first step in evaluating LVFAC in normal structural subjects, and we plan to evaluate LVFAC in complicated congenital heart disease (CHD) cases as a next step.

We also evaluated the accuracy of the eyeball FAC method in the left ventricle, because we are generally accustomed to RVFAC in CHD, but not LVFAC. Well-trained sonographers used this simplified method, because a good correlation between eyeball FAC and actual FAC is important to improve the measurement accuracy of sonographers.

Materials and methods

Patients

A total of 320 consecutive patients who underwent transthoracic echocardiography between July 2019 and October 2019 were enrolled. All 320 patients had systemic LV, and no cases of CHD were included in this study. Patients with atrial fibrillation or those with poor imaging findings were excluded. This study used the data obtained within the scope of routine medical care.

Echocardiography

Echocardiography was performed using EPIQ7 (PHILIPS) and an X5-1 transducer. Apical views were obtained with the patient in the left lateral recumbent position. An apical four-chamber view was recorded at a field depth of 12 cm and a frame rate of 70. Firstly, the apical four-chamber and two-chamber views were used to estimate left ventricular eyeball LVFAC. LVEF was calculated from the apical four- and two-chamber views using the biplane disk summation method. The LV function results were classified into normal, mild, moderate, and severe using the LVEF severity assessment values listed in the American Society of Echocardiography (ASE) guidelines[2]. LVFAC was calculated from LV end-diastolic area (LVEDA) and LV end-systolic area (LVESA) that were measured simultaneously with the disk summation method. LVFAC was calculated from the apical four- and two-chamber views using the following equation: $100\times(\text{LVEDA}-\text{LVESA})/\text{LVEDA}$. To avoid bias, measurements were taken only once.

Statistical analysis

Data was analyzed using the Statistical Program for Social Science (SPSS) version 24.0 (SPSS, Inc., Chicago, IL, USA). Categorical data were expressed as percentages, and continuous data were expressed as mean±standard deviation. The Kruskal–Wallis test was used to compare the four groups, while the Steel-Dwass method was used as a multiple comparison method. Linear regression was performed for correlation analysis. Bland–Altman plot analysis was used to assess the agreement between different methods. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cutoff value. The areas under the curve (AUC) and 95% confidence intervals were obtained to confirm the predictive power of ROC curve analysis. Intra- and inter-subjective errors were assessed using intraspecific correlation coefficients (ICCs) for 50 LVFAC values randomly selected from all cases. Statistical significance was set at $P<0.05$.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The ethics committee of our hospital approved this study (20-R004). The requirement for informed consent was waived owing to the retrospective nature of the study, with an opt-out option.

Results

A total of 303 patients (mean age, 66±16 years; 216 [71%] were men) were included in the analysis, excluding eight patients with poor image quality and nine patients with atrial fibrillation (**Table 1**). Using the LVEF severity assessment described in the ASE guidelines, the patients were classified into four groups: 115 patients with normal contraction, 78 patients with mildly reduced contraction, 62 patients with moderately reduced contraction, and 48 patients with severely reduced contraction (**Table 2**). The mean FAC of the normal group was 44±5%, mild systolic dysfunction was 32±4%, moderate systolic dysfunction was 23 ±5%, and severe systolic dysfunction was 14±6% (**Table 2**). A strong correlation was noted between LVEF and LVFAC ($r=0.96$, $p<0.01$) (**Fig. 1**). The

Table 1 Patient characteristics

	Normal (n=115)	Mildly reduced contraction (n=78)	moderately reduced contraction (n=62)	severely reduced contraction (n=48)	p-value
Age[years]	60±17	69±14	72±12	70±12	<0.001
Male(%)	65(57)	63(81)	47(76)	41(85)	<0.001
Body surface area[m²]	1.6±0.2	1.6±0.2	1.6±0.2	1.7±0.2	0.234
Heart rate[bpm]	69±10	69±12	74±12	73±9	0.009
primary cardiovascular diagnosis					
Normal(%)	89(77)	24(31)	0	0	
Coronary artery disease(%)	20(17)	47(60)	48(77)	30(63)	
Cardiomyopathy(%)	2(2)	7(9)	6(10)	14(29)	
Valvular heart disease(%)	4(3)	0	8(13)	4(8)	

Table 2 Echocardiographic measurements

	Normal (n=115)	Mildly reduced contraction (n=78)	moderately reduced contraction (n=62)	severely reduced contraction (n=48)
LVEF[%]	62±5	47±3	35±3	23±6
FAC[%]	44±5	32±4	23±5	14±6
Eyeball FAC[%]	41±5	30±3	24±3	15±5
LVEDV[ml/m²]	83±27	93±30	107±34	141±51
LVEDA[cm²]	28±6	30±6	37±7	38±9

LVEF, left ventricular ejection fraction; FAC, fractional area change; LVEDV, left ventricular end-diastolic volume; LVEDA, left ventricular end-diastolic area

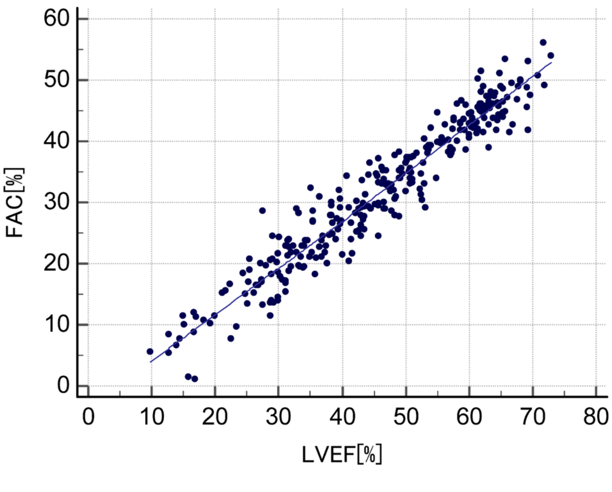

Fig. 1 Correlation plot: Fractional area change versus left ventricular ejection fraction.
The correlation between FAC and LVEF was strong (r=0.96, P<0.01).
LVEF, left ventricular ejection fraction; FAC, fractional area change

correlation between LVFAC and eyeball LVFAC was very strong (r=0.94) (**Fig. 2a, 2b**). The correlation between LVEF and eyeball LVFAC was also very strong (r=0.957) (**Fig. 3**). ROC analysis of LVFAC cutoff showed mildly reduced contraction (LVEF<51%) in 33% of patients (AUC=0.999, p<0.001; sensitivity: 94.2%; specificity: 99%) (**Fig. 4a**), moderately reduced contraction (LVEF<40%) in 25% (AUC=0.978; p<0.001; sensitivity: 97.4%; specificity: 80.9%) (**Fig. 4b**), and severely reduced contraction (LVEF<30%) in 20.8% (AUC=0.974; p<0.001; sensitivity, 93.7%; specificity, 92%) (**Fig. 4c**) (**Table 3**). The intra-rater reliability for LVFAC measurements was ICC (1,2)=0.965, while the inter-rater reliability was ICC (2,1)=0.939, both of which are good results.

Discussion

Cardiac echocardiography is non-invasive, can be performed at the bedside, and is the first choice for imaging studies in cases of suspected cardiac disease even in small clinics without high spec machines; therefore, simple echo parameters are desirable to assess systemic LV contraction. To the best of our knowledge, this is the first study to examine the cutoff value of LVFAC and classify the

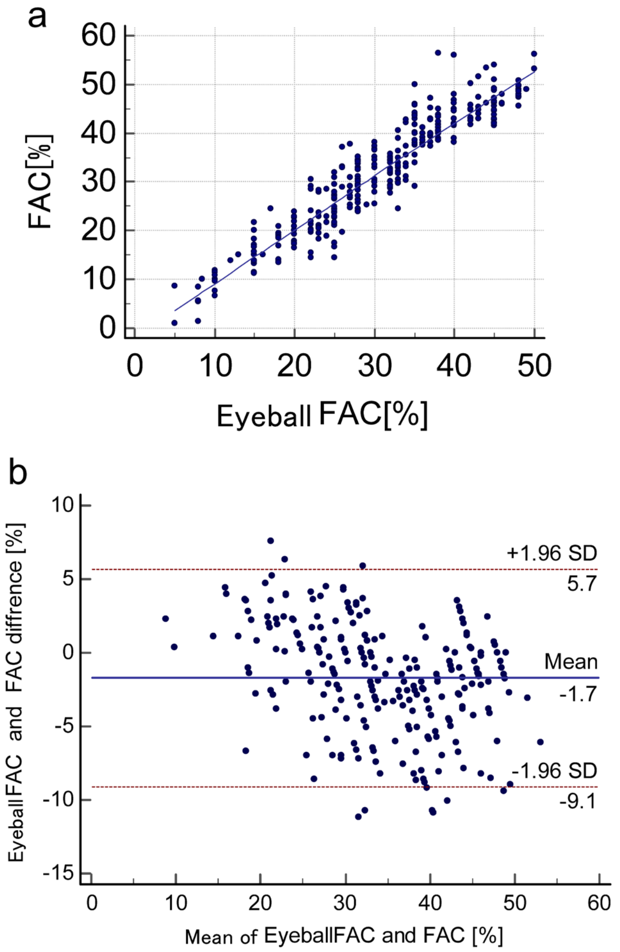

Fig. 2 (a) Correlation plot: Eyeballing fractional area change versus fractional area change. (b) Bland–Altman analysis comparing FAC and eyeball FAC.
(a) The correlation between FAC and eyeball FAC was strong (r=0.94, P<0.01). (b) Bland–Altman analysis comparing FAC and eyeball LVFAC (Bias=−1.7%, limits of agreement (LOA)=−9.1 to 5.7).
FAC, fractional area change

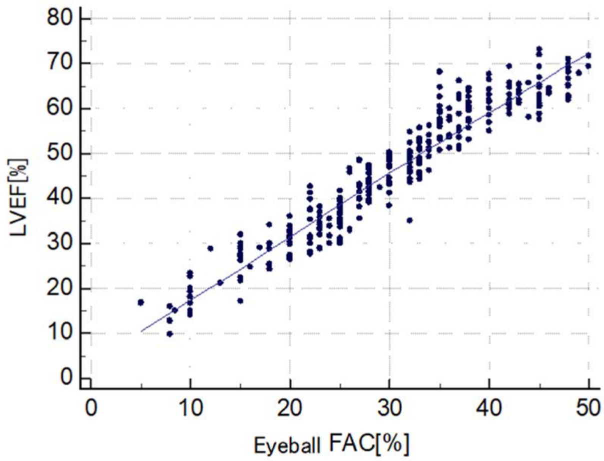

Fig. 3 Correlation plot: Eyeballing fractional area change versus left ventricular ejection fraction.
The correlation between eyeball FAC and LVEF was strong (r=0.957, p<0.001).
LVEF, left ventricular ejection fraction; FAC, fractional area change

severity into four levels.

The cutoff value of LVFAC based on the severity of contraction

Determining EF using the disk summation method is recommended for LV assessment because it is ideal for obtaining a simple and non-invasive index of contractility[1]. This is the most accurate method in 2D LV volumetric measurement because it is less affected by LV morphology. According to the revised ASE criteria in 2015, the normal LVEF is 52%–72% in men and 54%–74% in women[2]. Conversely, ASE guidelines only state that an RV FAC≤35% is abnormal[2], suggesting that the normal and abnormal cutoff values of the RV are very ambiguous.

We believe that echocardiogram findings should describe whether a contraction is mildly, moderately, or severely reduced in the case of LVEF. However, the patient's habitus or complex anatomy limits the accuracy[4]. MRI is believed to be the gold standard for assessing ventricular volume and EF[5, 6]; however, MRI is not available in all cases. Therefore, the role of echocardiography in the follow-up of contraindicated cases is important. The AUC value of this study exceeded 0.9, suggesting that the severity classification of LVFAC based on LVEF was very accurate.

In children's hospitals, there are many well-trained sonographers for CHD, who can understand CHD abbreviations on case notes and can distinguish a single LV from a single RV. Conversely, there are a few trained sonographers and doctors for CHD in general adult cardiology clinics, local hospitals, and emergency rooms. It is sometimes very challenging for them to understand the diagnoses and anatomy of the case notes. Fontan patients sometimes present with breathlessness or palpitations at the emergency room at night, but they often cannot explain their initial diagnosis; therefore, ER doctors cannot know whether they have left- or right-dominant single ventricle. CHD education for sonographers or ER doctors, as well as patients themselves, is one of the key factors for a smooth transfer in CHD patients. In the case of complex morphology in CHD, standard LV measurements are sometimes challenging. In our hospital, the staff who treat adult CHD patients recom-

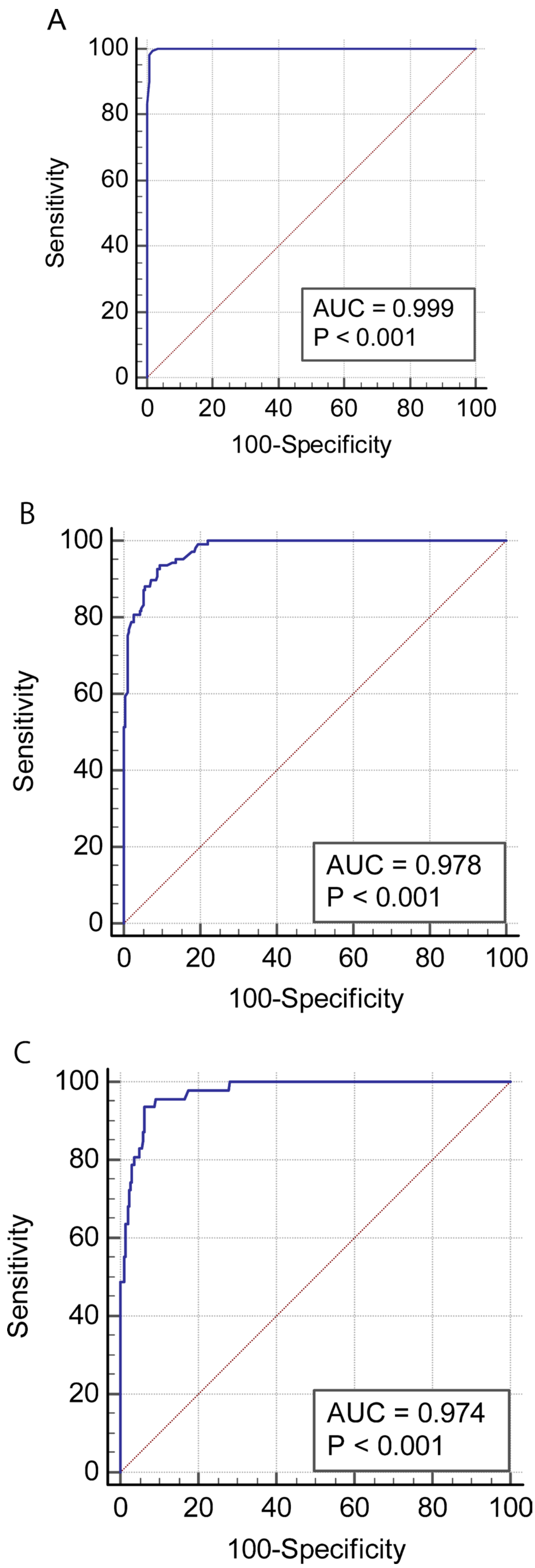

Fig. 4 (a) FAC cutoff showed mildly reduced contractility (LVEF<51%). (b) FAC cutoff showed moderately reduced contractility (LVEF<40%). (c) FAC cutoff showed severely reduced contractility (LVEF<30%).
(a) ROC analysis of FAC cutoff showed mildly reduced contractility in 33%. Area under curve (AUC)=0.999, p<0.001, sensitivity=94.2%, specificity=99%. (b) ROC analysis of FAC cutoff showed moderately reduced contractility in 25%. AUC=0.978, p<0.001, sensitivity=97.4%, specificity=80.9%. (c) ROC analysis of FAC cutoff showed severely reduced contractility in 20.8%. AUC=0.974, p<0.001, sensitivity=93.7%, specificity=92%.

Table 3 Receiver operating characteristics analysis

	AUC	AUC (95% confidence interval)	p-value	Sensitivity	Specifisity	Cut-off
LVEF threshold 51% FAC	0.999	0.975–0.996	<0.001	94.2	99.0	33
LVEF threshold 40% FAC	0.978	0.964–0.99	<0.001	97.4	80.9	25
LVEF threshold 30% FAC	0.974	0.959–0.992	<0.001	93.7	92	20.8

AUC, areas under the curve; LVEF, left ventricular ejection fraction; FAC, fractional area change

mend the measurement of both EF and FAC before a remote consultation when they cannot understand the CHD diagnosis in detail. Post-operative reports of complete transposition of the great arteries show a systemic LVFAC<33% with an LVEF<50% on MRI[7]. These results are similar to our cut-off values. The LVFAC measurement is a good parameter for both intra- and inter-test errors in terms of statistical reproducibility. The FAC is considered a simple measure of accuracy and ease of use if the cross-section of images to be drawn in the facility is unified. This study showed a good correlation between the LVEF and LVFAC. As a further study, we are planning to continue to investigate whether there is a discrepancy between eyeball EF and FAC in CHD, such as systemic RV or single ventricle.

Usefulness of eyeball LVFAC

Eyeball EF lacks objectivity; however, eyeball EF is widely used in local hospitals and emergency rooms because it can be used to visually verify a quantitative value[8, 9]. Even non-specialists can imagine the extent of the decline in cardiac function by determining the EF value. Moreover, eyeball EF and the disk summation method EF by a skilled evaluator are strongly correlated[10]. For the same reason, the accuracy of eyeball FAC is important because it enables us to judge the validity of actual FAC measurements. Even if FAC are carefully measured, they are meaningless if inaccurate. Based on the current guidelines, it is difficult to determine whether measured FAC is accurate and consistent with EF in mildly or moderately reduced contractions. In this study, the correlation between measured LVFAC and eyeball LVFAC was strong (r=0.94). Our findings suggest that eyeball FAC can be easily learned with experience as well as assessing eyeball EF.

Limitations

In this study, we assessed a highly authentic parameter, which is a non-novel marker. In many small clinics, high-specification echocardiographic equipment is not available; therefore, we believe that this basic study using a simple marker is still clinically informative. We investigated the correlation with LVFAC, using EF with the most commonly used disk summation method, rather than MRI, which is believed to be the gold standard. It is unknown whether the severity classification of this study can be applied to the systemic RV and single ventricle, so we plan to investigate these hypotheses in the future.

Conclusion

This study evaluated the cut-off values of LVFAC based on the severity of LV contraction: 33% for mild dysfunction, 25% for moderate dysfunction, and 20.8% for severe dysfunction. LVFAC may be used as a simplified screening tool for any LV shape in local hospitals and emergency rooms, but further studies are needed.

Acknowledgment: We appreciate that this manuscript was proofread for English language revision by Editage.

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