PREDICTION OF LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTIONS SIX MONTHS FOLLOWING MITRAL VALVE REPLACEMENT USING NEW ECHO DOPPLER INDICES

Moataz Abdelmonem Elkot, Msc, Ahmed Shafie Ammar, MD, Islam Abd-ELmoneem ELsherbiny, MD, Khaled Hassan Abdelbary*, MD.

Departments of Cardiology and Cardiothoracic surgery Faculty of medicine, Zagazig University, Egypt.*

ABSTRACT

Background: The development of left ventricular dysfunction is a major concern in the management of patients with severe mitral regurgitation. In the initial stages, contractility impairment may be ‘‘invisible’’ by the traditional methods to assess the ventricular function, because of different loading conditions. This fact can mask the presence of LV dysfunction. Sometimes, LV dysfunction may be ‘‘unmasked’’ only by change in loading conditions after surgical correction, leading to the development of overt LV dysfunction and congestive heart failure. The identification of contractile dysfunction at an early stage and surgical correction may avoid the development of irreversible postoperative LV dysfunction.

Objectives: To test the efficacy of new echocardiographic indices in predicting post operative left ventricular dysfunction and compare the diagnostic accuracy of these indices .

Subjects and Methods: The study included 41 patients with severe isolated Mitral regurgitation with ejection fraction > 50 %, prepared for mitral valve replacement. Patients were examined clinically and by Echocardiography pre and post operative. The following Echo Doppler modalities were done to the patients pre operative and 6 months post operative: Global longitudinal strain(GLS) , Modified Simpson ,dp/dt , IVRT/T(E-è) the early diastolic Driving Force , early diastolic and early systolic mitral annular velocity by tissue Doppler. Patients were then classified into Four sub groups according to post operative systolic and diastolic function, Group 1A were patients with normal post operative systolic function , Group 1B were patients with post operative systolic dysfunction , Group 2A were patients with normal post operative diastolic function , Group 2B were patients with post operative diastolic dysfunction.

Results: For prediction of systolic dysfunction ROC curve analysis showed high significant value of pre operative GLS in predicting post operative systolic dysfunction with cutoff value= -18.5 , high significant value of pre operative modified Simpson in predicting post operative systolic dysfunction with cutoff value=54.5, and significant value of pre operative dp/dt in predicting post operative systolic dysfunction with cutoff value=1166 mmHg/sec. The multivariate analysis showed that the independent variables for predicting post operative systolic dysfunction were pre operative GLS and dp/dt.

For prediction of diastolic dysfunction ROC curve analysis showed high significant value of pre operative GLS in predicting post operative diastolic dysfunction with cutoff value=-18.5, and significant value of pre operative IVRT/T(E-e\) in predicting post operative diastolic dysfunction with cutoff value=2.95. Multivariate analysis showed that the independent variables for predicting post operative diastolic dysfunction were preoperative GLS & preoperative IVRT/T (E-e\).

Conclusions: We can depend on pre operative Global Longitudinal Strain (GLS) and dp/dt in predicting post operative systolic dysfunction with cut off value=-18.5 and 1166 mmHg/sec respectively. We can also depend on preoperative GLS and IVRT/T (E-e\) in predicting post operative diastolic dysfunction with cutoff value=-18.5 and 2.95 respectively.

Keywords: Left Ventricular Dysfunction •Mitral Valve Replacment •Predictors.

Corresponding author: **Moataz Abdelmonem Elkot**,01068058518,mo3taz.elkot@gmail.com

INTRODUCTION

The development of left ventricular dysfunction is a major concern in the management of patients with severe mitral regurgitation. In the initial stages, contractility impairment may be ‘‘invisible’’ by the traditional methods to assess the ventricular function, because of different loading conditions. This fact can mask the presence of LV dysfunction. Sometimes, LV dysfunction may be ‘‘unmasked’’ only by change in loading conditions after surgical correction, leading to the development of overt LV dysfunction and congestive heart failure. The identification of contractile dysfunction at an early stage and surgical correction may avoid the development of irreversible postoperative LV dysfunction[(14)].

In spite of managing these patients according to the current guidelines, a notable incidence of postoperative LV dysfunction occurs, which worsens the early and long-term prognoses. The risk for postoperative myocardial failure is markedly increased by preoperative symptoms or reduced LVEF. Also LV dysfunction occurred in asymptomatic patients with severe MR managed according to current guidelines, this may be due to significant histological alterations of myocardial structures and functions in patients with severe MR and ejection fraction >60%[3]. This led some investigators advocate early consideration of surgical correction to preserve the contractile function and improve the long-term prognosis[9]

The major challenge for clinicians is the early detection of LV contractile impairment in patients with chronic severe MR. This would allow early surgical intervention to prevent the development of irreversible LV dysfunction. The traditional echocardiographic parameters to asses LV function, including LVEF and LV volumes, are load dependent. Thus, their applicability in patients with severe MR is reduced. Abnormal preoperative LVEF is a powerful predictor of postoperative LV dysfunction, which carries a poor prognosis, but its sensitivity to detect early contractile abnormalities is poor. LVEF frequently remains normal despite the presence of significant contractile dysfunction during the compensated phase of MR[12].

Several echocardiographic methods have been proposed to detect latent ventricular dysfunction in patients with severe MR eg. Exercise or dobutamine echo. However, most of these techniques have limitations that may reduce their applicability in daily clinical practice. Thus, there is a need for an accurate and reproducible echocardiographic parameters to predict early LV dysfunction in order to optimize the timing of surgery in this type of patients. Several methods have been studied with this aim, but none has been consolidated in the current clinical practice or appears in the current valvular heart disease guidelines[17].

Speckle-tracking strain analysis has been recently introduced as a novel echocardiographic technique for an accurate and angle independent assessment of myocardial deformation (strain), and is needed to detect subclinical preoperative LV dysfunction. Global longitudinal strain by speckle tracking (GLS) evaluates the shortening and lengthening of the myocardial wall, measured from the three apical views (long-axis and two-and four-chamber views), GLS was calculated by averaging the peak strain values of 18 segments[18]. Also we tested the capability of the early diastolic Driving Force (DF) -which is a novel index to assess diastolic function- to predict post operative left ventricular dysfunction. Early diastolic driving force (DF) is a new index derived from Newton's second law of motion[4]. We also tested the early diastolic mitral annular velocity(È value) and early systolic mitral annular velocity (S wave) measured by tissue doppler imaging as a predictor of post operative left ventricular dysfunction, in study of **Suehiro et al.,2014**[15] the patients with lower preoperative È value had greater decrease in ejection fraction after surgery and clinician can predict postoperative LV dysfunction with sensitivity of 80% in patients with preoperative È value less than 6.5 cm/sec[15].

SUBJECTS AND METHODS

The study included 41 patients with severe isolated Mitral regurgitation with ejection fraction > 50 %, prepared for mitral valve

PATIENTS EXCLUSION CRITERIA

1. Another significant valve disease.
2. Congenital heart disease.
3. Coronary artery disease patients.
4. Patients with cardiomyopathy.
5. Previous cardiac surgery.
6. Unsuccessful or complicated mitral valve replacement.

The patients were classified into:

Post operative LV systolic function into:

Group1A:with normal postoperative LV systolic function

Group 1B:with post operative LV systolic dysfunction

Post operative LV diastolic function into:

Group2A:with normal postoperative LV diastolic function

Group 2B:with post operative LV diastolic dysfunction

All patients were subjected to the following 48 hours preoperative and 6 months post operative:

Complete history taking , clinical examination and echocardiographic examination.

The echocardiography was done to assess severity of MR by venacontracta and EROA , to assess LV systolic function by Teicholz formula , modified simpson and dp/dt , and to assess diastolic function by E/A ratio, E wave deceleration time(DT), iso volumetric relaxation time(IVRT), E/è by tissue doppler imaging, ratio of IVRT:T(E-è) and TR peak velocity.

Also the Echocardiograhic predictors of post operative LV dysfunction were done 48 hours preoperative and 6 months post operative, these predictors are the global longitudinal strain , early diastolic driving force , early diastolic mitral annular velocity(È value) and early systolic mitral annular velocity.

RESULTS

In group 1 there were stastistically high significant difference between ages of two sub groups(group 1A and group 1B) with higher ages in Group 1B . Also there were signifinant difference in risk factors between the two groups(HTN and DM) , these risk factors were found only in Group 1B. The etiology of mitral regurge was significantly different between the two groups with more patients with degenerative MR in Group 1B. No significant difference in sex of the two groups.

In group 1 there was significant difference between pre and post operative Ejection fraction by both Teicholz method and modified simpson with high significant difference in the change of modified simpson between the two sub groups(group 1A and group 1B). Also there was high significant difference between pre and post operative GLS with significant difference in the change in GLS between the two sub groups. And also significant difference in pre operative dp/dt ratios.

ROC curve analysis revealed high significant value of pre operative modified Simpson in predicting post operative systolic dysfunction with cutoff value=54.5% , with sensitivity=91% and specificity=77%. Also the test revealed high significant value of pre operative GLS in predicting post operative systolic dysfunction with cutoff value= -18.5 , with sensitivity=87% and specificity=78%. It also showed significant value of pre operative DP/DT in predicting post operative systolic dysfunction with cutoff value=1166 , with sensitivity=87% and specificity=62%.

The multivariate analysis revealed that the independent variables for predicting post operative systolic dysfunction were preoperative GLS and dp/dt.

Table(1): Differentiation between group1A(20 patients) and group 1B(21 patients) according to baseline and clinical characteristics.

Variable	Group 1A (n = 20)	Group 1B (n = 21)	P-value
Age (mean±SD)	34±8.51	53±8.06	<0.001
Sex Male No (%) Female No (%)	 10 (50%) 10 (50%)	 9 (43%) 12 (57%)	0.38
HTN No (%)	0 (0.0%)	5 (24%)	
DM No (%)	0 (0%)	6 (28%)	
MR etiology Rheumatic No (%) Degenerative No (%)	 10 (50%) 10 (50%)	 5 (24%) 16 (76%)	<0.05

Table(2): Differentiation between the two sub groups in different echo parameters

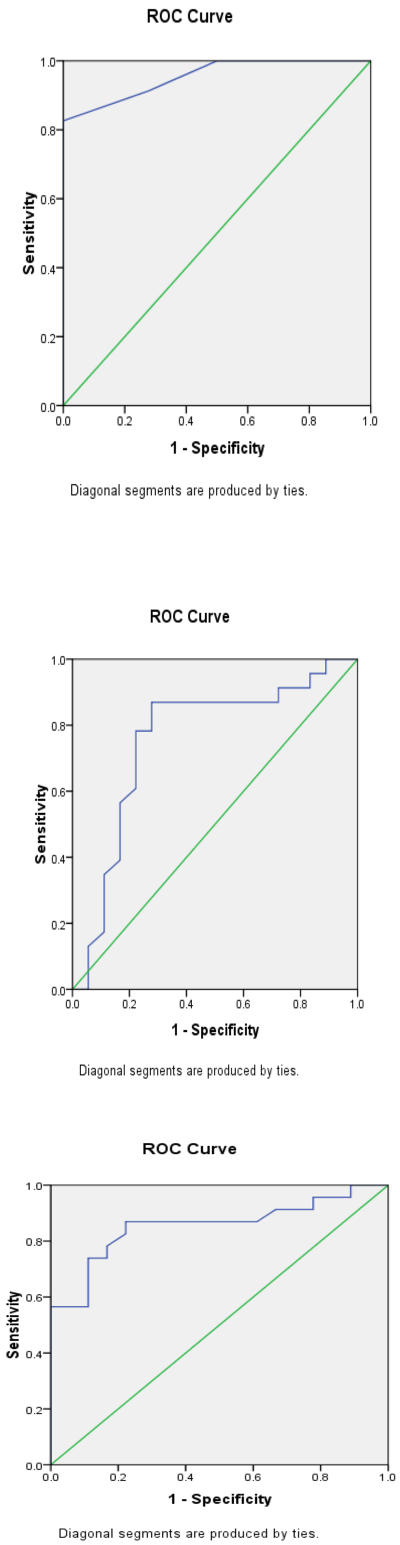
Variable	Group 1A Mean±SD	Group 1B Mean±SD	P-value
Preoperative EF by Teicholz (%)	63±3.9	59±3.8	<0.05
Postoperative EF by Teicholz (%)	57±3.04	52±3.09	<0.001
Δ EF by Teicholz(%)	5.6±3.6	7.2±2.4	0.06
Preoperative Mod. Simpson (%)	55±1.6	52±1.5	<0.001
Postoperative Mod. Simpson (%)	53±2.5	44±2.6	<0.001
Δ Mod. Simpson (%)	2.5±1.5	7.5±3.2	<0.001
Maximum dP/dt (mmHg/sec)	1259±258	1025±194	<0.05
Preoperative driving force (Newton)	1.4±0.46	0.4±0.08	0.31
Preoperative e' wave velocity(TDI) (cm/s)	9.2±1.26	9.1±1.1	0.89
Preoperative S wave velocity (TDI)(cm/s)	6.8±0.9	6.2±1.1	0.38
Preoperative GLS	-19.1±1.6	-15.6±2.8	<0.001
Postoperative GLS	-18±1.9	-11.6±1.6	<0.001
Δ GLS	1.1±0.17	3.9±1.7	<0.05

Table(3): The ROC curve result of pre operative modified Simpson, dP/dt and GLS for prediction of post operative systolic dysfunction

Variables	Cut off	AUC	P-value	95% CI	Sensitivity	Specificity
Preoperative Mod. Simpson %	54.5	0.95	<0.001	0.89-1.01	91	77
Maximum dP/dt mmHg/sec	1166	0.75	<0.05	0.59-0.92	87	62
Preoperative GLS	-18.55	0.85	<0.001	0.73-0.97	87	78

Table(4): Multivariate analysis of pre operative modified Simpson, dP/dt, GLS and degenerative MR etiology for prediction of post operative systolic dysfunction .

Variables	Odds ratio	P-value
Preoperative Mod. Simpson	18.69	0.08
Maximum dP/dt	27.65	<0.05
Preoperative GLS	48.97	<0.05
MR etiology	13.84	0.07



ROC curve of pre operative modified simpson in the upper left panel, dp/dt in upper right panel and GLS in the lower panel for prediction of post operative systolic dysfunction.

In group 2 there there were stastistically high significant difference between ages of the two sub groups (group2A and group 2B) with higher ages in Group 2B . Also there were signifinant difference in risk factors between the two groups(HTN and DM) , these risk factors were found only in Group 2B. Also there were signifinant difference in etiology of MR between the two groups with more degenerative MR in Group 2B.

In group 2 there was statistically significant difference between the two subgroups (group 2A and group 2B) as regard pre and post operative IVRT/T(E-è) and its change and pre and post operative GLS and its change

ROC curve analysis revealed high significant value of pre operative GLS in predicting post operative diastolic dysfunction with cutoff value=-18.5 , with sensitivity=89% and specificity=69%. Also the test revealed significant value of pre operative IVRT/T(E-e\) in predicting post operative diastolic dysfunction with cutoff value=2.95 ,with sensitivity=73% and specificity=73%.

The multivariate analysis revealed that the independent variables for predicting post operative diastolic dysfunction were pre operative GLS and preoperative IVRT/T (E-e\).

Table(5): Differentiation between group2A(18 patients) and group 2B(23 patients) according to baseline and clinical characteristics.

Variable	Group 2A (n = 18)	Group 2B (n = 23)	P-value
Age (mean±SD)	35±7.7	56±6	<0.001
Sex Male No (%) Female No (%)	 8 (44%) 10 (56%)	 10 (43%) 13 (57%)	0.2
HTN No (%)	0 (0.0%)	5 (22%)	
DM No (%)	0 (0.0%)	6 (26%)	
MR etiology Rheumatic No (%) Degenerative No (%)	 10 (56%) 8 (44%)	 5 (22%) 18 (78%)	<0.05

Table(6): Differentiation between the two sub groups in different echo parameters

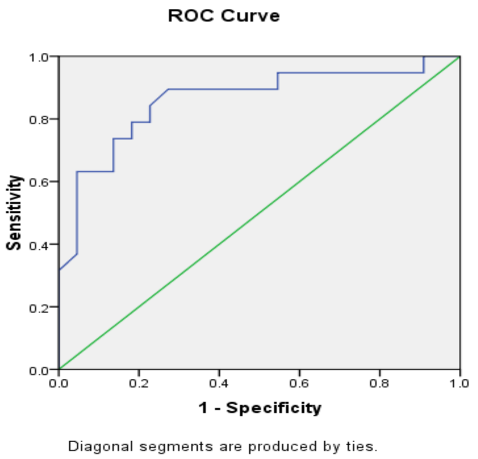
Variable	Group 2A Mean±SD	Group 2B Mean±SD	P-value
Preoperative IVRT/T (E-e\) ratio	3.5±0.6	2.8±0.7	<0.05
Postoperative IVRT/T (E-e\) ratio	3.9±0.36	2.1±0.6	<0.001
Δ IVRT/T (E-e\) ratio	-0.45±0.8	0.87±0.8	<0.001
Preoperative DF (Newton)	1.2±0.41	0.4±0.12	0.39
Preoperative GLS	-18.8±1.9	-15.2±2.7	<0.001
Postoperative GLS	-17.4±2.5	-11.6±1.7	<0.001
Δ GLS	1.5±1.2	3.6±1.5	<0.05
Preoperative e\ velocity (cm/s)	9.2±1.15	9.1±1.25	0.85
Preoperative S wave velocity (cm/s)	8.2±0.82	8.3±0.82	0.86

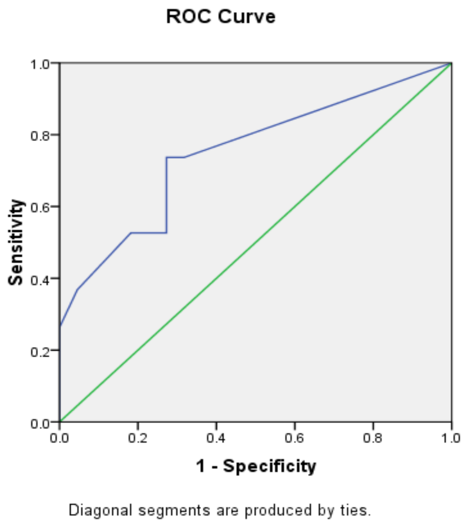
Table(7): The ROC curve result of pre operative GLS and IVRT/T(E-e\) ratio for prediction of post operative diastolic dysfunction

Variables	Cut off	AUC	P-value	95% CI	Sensitivity	Specificity
Preoperative GLS	-18.5	0.86	<0.001	0.74-0.98	89	69
Preoperative IVRT/T(E-e\) ratio	2.95	0.74	<0.05	0.59-0.9	73	73

Table(8): Multivariate analysis of pre operative GLS, IVRT/T(E-e\) and MR etiology for prediction of post operative diastolic dysfunction .

Variables	Odds ratio	P-value
Preoperative GLS	35.08	<0.05
Preoperative IVRT/T (E-e\)	13.28	<0.05
MR etiology(degenerative)	14.64	0.08





ROC curve of pre operative GLS in the upper panel and pre operative IVRT/T(E--e\) in lower one for prediction of post operative diastolic dysfunction

DISCUSSION

The mean age of our study was 45 ys± 7.5 , the study age was concordant with **Kim et al(2008)** [(11)] who studied early systolic mitral annular velocity as a marker of systolic function in patients with significant MR with mean age 47 ys± 15, but this was discordant with[(3)] **Witkowski et al,2013**[(18)] who studied the global longitudinal strain as apredictor of systolic dysfunction after mitral valve surgery with mean age 61 ys± 15

According to risk factors 5 (12%) patients were hypertensive and 6(15%) patients were diabetic . This was concordant with **Tribouilloy et al(2011)** [(16)] study who studied end systolic dimension to ejection fraction as a predictor of post operative systolic dysfunction after valve surgery where 7% of patients were diabetic , while our result were discordant with **Suehiro et al(2014)** [(15)] study who tested the early diastolic mitral annular velocity as a predictor of post operative LV dysfunction after mitral valve surgery where large number of patients (54%) were hypertensive.

According to MR etiology 15(37%) patients had rheumatic MR and more patients 26(63%) had degenerative MR. This was concordant with **Kim et al(2008)** [11] where 89% of patients had degenerative MR and 11% of patients had rheumatic MR. While this was discordant with **Agustin et al(2010)** [2] who compare the value of the preoperative strain and strain rate derived by either speckle-tracking echocardiography or tissue Doppler imaging (TDI) for predicting the medium-term decrease in left ventricular ejection fraction following surgery, where more patients had rheumatic MR.

In our study in group 1 there were significant difference between the two subgroups 1A(normal post operative systolic function) and 1B(post operative systolic dysfunction) in relation to the change in systolic function by modified simpson , preoperative GLS and dp/dt . This was concordant with **Agustin et al(2010)** [2] who compare the value of the preoperative strain and strain rate derived by either speckle-tracking echocardiography or tissue Doppler imaging (TDI) for predicting left ventricular dysfunction following mitral valve surgery. And also concordant with **Isla et al (2009)** [10] results who assess preoperative LV function using speckle tracking Echocardiography in patients with chronic MR.

In our study in group 1 there were no significant difference between the two subgroups 1A(normal post operative systolic function) and 1B(post operative systolic dysfunction) in relation to pre operative , post operative or the change in early systolic mitral annular velocity by tissue Doppler imaging (S wave), this was concordant with **Donal et al(2012)** [8] who study the prediction of LV EF 6 months after mitral surgery ,but was discordant with **Agricola et al (2004)** [1] who found that Sm velocity 10 cm/s (sensitivity 90% and specificity 85%) were the best discriminant cut off values of postoperative EF reduction > 10% after mitral valve surgery.

Also no significant difference between the two subgroups 1A(normal post operative systolic function) and 1B(post operative systolic dysfunction) in relation to pre operative , post operative or the change in early diastolic Driving Force , this was discordant with **Ammar et al (2015)** [5] who study prediction of LV function 6 months after aortic valve replacement , **Ammar et al(2015)** [5] found a significant difference between the two groups in relation to pre operative early diastolic Driving Force with cut off value o.5 (sensitivity 80% and specificity 100%) can predict post operative systolic dysfunction. This may be related to inaccurate assessment of Driving Force due to high E wave velocity with MR , difficulties in post operative accurate assessment of deceleration time with prothetic valve and irregular heart beats with atrial fibrillation.

Also no significant difference between the two subgroups 1A(normal post operative systolic function) and 1B(post operative systolic dysfunction) in relation to pre operative , post operative or the change in early diastolic mitral annular velocity measured by tissue Doppler(è) , this was discordant with **Suehiro et al (2014)** [15] who found that patients with lower preoperative **è** value had greater decrease in ejection fraction after surgery and clinician can predict postoperative LV dysfunction with sensitivity of 80% in patients with preoperative è value less than 6.5 cm/sec.

In our study ROC curve analysis showed that the cutoff value of GLS in predicting post operative systolic dysfunction was -18.5 , which is concordant with **Donal et al(2012)** [8] study which revealed cutoff value equal -18 in prediction of LV EF deterioration 6 months after mitral surgery ,while **Witkowski et al(2013)** [18] study revealed higher cutoff value of GLS(-20) in prediction of systolic dysfunction .

The cutoff value of LVEF as apredictor of post operative systolic dysfunction was 54% in our study , this was concordant with **Isla et al (2009)** [10] study who revealed the same EF(54%) as apredictor of post operative systolic dysfunction , while higher cutoff value of EF(60%) was in **Witkowski et al(2013)** [18] .

The cutoff value of dp/dt as a predictor of post operative systolic dysfunction was 1166 mmHg/sec in our study , this was concordant with **Agustin et al(2010)** [2] study who revealed dp/dt of 1150 mmHg/sec as a predictor of post operative systolic dysfunction. While in **Nazli et al (2003)** [13] study lower level of dp/dt cutoff value(1130 mmHg/sec) was used as a predictor of post operative systolic dysfunction .

Multivariate analysis of our study revealed that the most independable variables for predicting post operative systolic dysfunction were GLs and dp/dt. This was concordant with **Isla et al (2009)** [10] study who revealed that the most independable variable for predicting post operative systolic dysfunction was the GLS.

In our study in group 2 there were significant difference between the two subgroups 2A(normal post operative diastolic function) and 2B(post operative diastolic dysfunction) in relation to IVRT/T(E-è) and post operative E/è . This was concordant with **Suehiro et al (2014)** [15] study in which there was significant difference between the two groups in relation to perioperative E/è.

In our study in group 2 there were significant difference between the two subgroups 2A(normal post operative diastolic function) and 2B(post operative diastolic dysfunction) in relation to pre operative GLS. This was concordant with **Agustin et al(2010)** [2] who compare the value of the preoperative strain and strain rate derived by either speckle-tracking echocardiography or tissue Doppler imaging (TDI) for predicting left ventricular dysfunction following mitral valve surgery. And also concordant with **Isla et al (2009)** [10] results who assess preoperative LV function using speckle tracking Echocardiography in patients with chronic MR.

Also no significant difference between the two subgroups 2A(normal post operative diastolic function) and 2B(post operative diastolic dysfunction) in relation to pre operative , post operative or the change in early systolic mitral annular velocity by tissue Doppler imaging (S wave) , early diastolic Driving Force and early diastolic mitral annular velocity measured by tissue Doppler(è) as discussed before.

In our study ROC curve analysis showed that the cutoff value of GLS in predicting post operative diastolic dysfunction was -18.5 , which is concordant with **Buggey et al(2017)** [6] study which revealed cutoff value equal -16 to predict worse outcomes in patients with heart failure with preserved systolic function .

The cutoff value of IVRT/T(E-è) in our study for predicting post operative diastolic dysfunction was 2.95 , this was concordant with **Diwan et al(2005)** [7] who revealed that IVRT/T(E-è) less than 3 is apredictor of mean PCWP more than 15 in patients with chronic MR and normal EF.

Multivariate analysis of our study revealed that the most independable variables for predicting post operative diastolic dysfunction were GLS and IVRT/T(E-è), which is first reported according to our knowledge.

CONCLUSIONS

We can depend on pre operative Global Longitudinal Strain (GLS) and dp/dt in predicting post operative systolic dysfunction with cut off value=-18.5 and 1166 mmHg/sec respectively. We can also can depend on preoperative GLS and IVRT/T (E-e\) in predicting post operative diastolic dysfunction with cutoff value=-18.5 and 2.95 respectively.

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