Outcome of Ischemic Stroke with or without Left Ventricular Systolic Dysfunction

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Abstract

Background: *Patients experiencing stroke with Left Ventricular Systolic Dysfunction (LVSD) face elevated mortality rates, heightened dependency, prolonged hospitalization, increased ICU referrals, and greater complication risks compared to those without LVSD.*

Objective*: This study aims to evaluate the outcomes differences of ischemic stroke patients with and without LVSD, as well as within subgroups of LVSD severity.*

Materials and Methods: *The study was Conducted in the Department of Neurology, Dhaka Medical College and Hospital (DMCH) from January 2022 to December 2023. In this prospective cohort study we enrolled 117 acute ischemic stroke patients meeting predetermined inclusion and exclusion criteria. LVSD diagnosis was established through echocardiography. Patient outcomes, including hospital duration, ICU necessity, mortality, and modified Ranking Scale (mRS) scores, were assessed and compared.*

Results: *Among the 117 patients, 61 were classified under stroke with LVSD, while 56 were without LVSD. The mean(SD) age was 65.50(9.94) years for LVSD and 63.78(10.85) years for non-LVSD patients. Male predominance was observed in both groups, with 83.6% males in the LVSD group and 67.9% in the non-LVSD group.*

Mortality rates at hospital and the first month were 5.4 times higher in LVSD patients compared to non-LVSD patients (9.8% vs. 1.8%, p- value 0.029). Total 3-month mortality was nearly three times higher in LVSD patients (27.9% vs. 10.7%, p <0.05). mRS scores indicated significantly poorer functional outcomes at 1 and 3 months for LVSD patients compared to non-LVSD patients. (mRS >2 in 95.1% vs 83.9%) at 1 month and mRS >2 in 68.9% vs 39.3% at 3 months). Length of hospital stay was longer for LVSD patients (median [IQR] 10 [8-15] days) compared to non-LVSD patients (median [IQR] 7 [4-11] days). Need for ICU referral of the ischemic stroke patients with LVSD was 2.3 times more than non-LVSD patients (32.8% vs 14.3%, p- value 0.029).

Conclusion: *Ischemic Stroke patients with LVSD exhibit poorer clinical outcomes, higher mortality rates, increased dependency, prolonged hospital stay and greater need for ICU referral compared to those without LVSD.*

Key words: *Ischemic stroke, left ventricular dysfunction, outcome.*

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Introduction:

Globally, stroke is a significant health issue and the second leading cause of mortality and the third leading cause of morbidity.[1] The prevalence of stroke is also high in Bangladesh, about 11.4 per thousand population.[2] Asymptomatic and even milder degrees of left ventricular dysfunction also increase the risk of stroke.[3] Left ventricular dysfunction is also a predictor of poorer clinical outcomes, even in patients with thrombolysis.[4] Wei, N et al. found that, he presence of left ventricular dysfunction in patients with stroke increases risk of death.[5] Other studies with short-term outcomes also

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revealed similar outcomes.[6-8] Stroke severity is also associated with left ventricular dysfunction.[9] The pathophysiology of adverse outcomes involves increased stroke severity, dysregulated cerebral autoregulation, and increased risk of recurrent stroke due to cardioembolic phenomenon.[10,11] Left ventricular dysfunction also increases the healthcare cost and hospital stay.[12]

There is a paucity of research in Bangladesh about the impact of left ventricular dysfunction on the outcome of stroke. In this study, we aimed to compare mortality, hospital stay, and morbidity outcomes.

Materials and methods:

Study Design and patient demographics

Prospective cohort study conducted from January 2022 to December 2023 at Dhaka Medical College Hospital (DMCH), focusing on patients with ischemic stroke, both with and without left ventricular systolic dysfunction (LVSD), admitted to the Neurology ward. Ethical approval was obtained from the DMCH ethical review board prior to the study. Patients were selected based on specific inclusion and exclusion criteria, including age (≥45 years) and diagnostic criteria for exposure (EF<50%) and control (EF >50%) cohorts. After subject selection, detailed explanations of the study's nature, purpose, and benefits were provided to each participant, encouraging voluntary participation. Informed written consent was obtained from all participants. Detailed personal, family, and medical histories were collected, and routine neurological and cardiovascular assessments were conducted for all patients. Diagnosis of ischemic stroke was initially based on positive lesions observed on brain CT scans or diffusion-weighted imaging (DWI) with corresponding ADC sequences on brain MRI.

Echocardiographic data acquisition and analysis

The presence and severity of LVSD were determined using 2D echocardiography with the Philips EPIQ 7 cardiac ultrasound machine, and LV ejection fraction (EF) was calculated using the Modified Simpson's method. Patients were divided into two categories: those with and those without LVSD. LVSD was defined as LVEF < 50%. An LVEF of 50% was chosen, as this value is still clinically relevant according to the American College of Cardiology guidelines. Additionally, routine electrocardiography (ECG) was performed to diagnose atrial fibrillation (AF) and ischemic heart disease (IHD).

Data collection and evaluation

Data collection involved face-to-face interviews, physical examinations, and investigations using a pre-designed data collection sheet. For patients unable to provide informed consent, consent was obtained from their families. Demographic, clinical, and biochemical variables were noted, and necessary blood workups were performed. Patients were followed up at the hospital, stroke clinic at one month and three months' post-admission

Evaluation of outcomes

Outcome determinants included mortality and morbidity measured using the modified Rankin Scale (mRS), with scores of 3, 4, and 5 considered poor outcomes and scores of 0-2 considered good outcomes. The primary concern of this study was to find the difference in mortality, disability, length of hospital stay, and need for ICU referral in an ischemic stroke patient with or without left ventricular systolic dysfunction and according to the severity of LVSD among the Bangladeshi population.

Statistical analysis

All collected information was stored in separate data record forms, checked for accuracy, inputted into Microsoft Excel, and transcribed into statistical software. Statistical analyses were performed using SPSS version 26.0, including means, standard deviations, and percentage frequencies. Significance was determined by a p-value of less than 0.05. Various statistical tests such as unpaired t-test, Mann–Whitney U test, Kruskal-Wallis test, Chi-square test, Fisher's exact test, and multivariable logistic regression analysis were conducted as applicable. Survival analysis using Kaplan-Meier graphs and log-rank tests measured significance, and Hazard ratios with 95% confidence intervals were calculated.

Results

The present study was undertaken to compare the outcome of ischemic stroke with or without LVSD. For this study 61 patients with ischemic stroke with LVSD and 56 ischemic stroke without LVSD patients admitted in the Neurology Department of Dhaka Medical College and Hospital, Dhaka were included. Flowchart of patient selection in Figure-1.

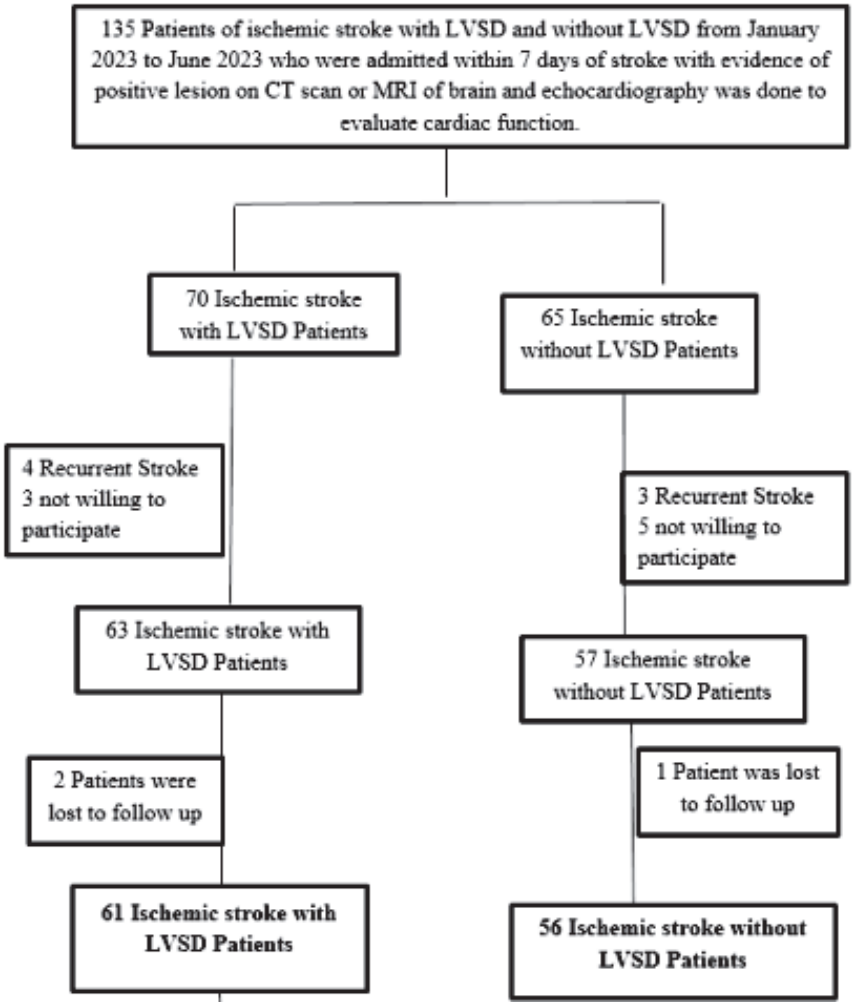

Figure 1. *Flowchart of patient selection.*

Baseline characteristics: In patients with LVSD, the mean age was 65.50 years (± 9.94 years), while among those without LVSD, the mean age was 63.78 years (± 10.85 years). In terms of gender distribution, 51 (83.6%) individuals with LVSD were male, whereas among those without LVSD, 38 (67.9%) were male. The relationship between comorbidities and stroke among patients with and without LVSD. For diabetes mellitus (DM), 23 (37.7%) stroke patients with LVSD had DM, compared to 21 (37.5%) stroke patients without LVSD. Hypertension (HTN) was present in 38 (62.3%) patients with LVSD and 28 (50%) patients without LVSD. Ischemic heart disease (IHD) was present in 23 (37.7%) patients with LVSD and 6 (10.7%) patients without LVSD. Dyslipidemia was present in 12 (19.7%) patients with LVSD and 8 (14.3%) patients without LVSD. Additionally, smoking prevalence was 44.25% in LVSD patients and 37.5% in non-LVSD patients.

Demographic characteristics, co-morbidities, Baselines information and Investigations profile of the patients appear in Table 1

In LVSD, the median (IQR) pulse rate was 86 (83-94), and the systolic and diastolic blood pressures were 150 (132-160) mmHg and 90 (80-100) mmHg, respectively. In the non-LVSD group, the median (IQR) pulse rate was 80 (72-88), with systolic and diastolic blood pressures of 140 (120-150) mmHg and 80 (77-90) mmHg, respectively.

Table I

Demographics, Co-Morbidities, Investigations profiles and Baseline information of Acute Ischemic Stroke patients with or without Left Ventricular Systolic Dysfunction.

Variables	LVSD (N=61)	No LVSD (N=56)	p Value
Age Mean±SD (years)	65.50 ± 9.94	63.78 ± 10.85	0.372
Gender (n,%)			
Male	51 (83.6)	38 (67.9)	0.053
Comorbidities			
Diabetes Mellitus (DM)	23 (37.7%)	21 (37.5%)	0.459
Hypertension (HTN)	38 (62.3%)	28 (50%)	0.017
Dyslipidemia	12 (19.7%)	8 (14.3%)	0.439
Ischemic Heart Disease (IHD)	23 (37.7%)	6 (10.7%)	0.001
Smoking status			
Current smoker	11(18%)	4(7.14%)	0.221
Former-smoker	16(26.25%)	17(30.36%)	
Non-smoker	34(55.75%)	35(62.5%)	
Admission GCS			
Total (Median, IQR)	11(9-14)	13(10-14)	0.069
Initial NIHSS			
Total (Median, IQR)	15(12-20)	14(13-16)	0.186
Investigation biomarker Profile			
Hb%	12(10-13)	12(11-12)	0.261
Total count	9.8(8.18-12)	8.7(7.25-11.66)	0.450
Neutrophil	79(70-84)	77.5(70-82)	0.452
Platelet count	241(205-317)	241.5(240-280)	0.959
RBS	6.9(5.8-8.8)	7.9(6.23-9.48)	0.118
S. Creatinine	1.08(0.9-1.2)	1.02(0.88-1.2)	0.937
Sodium	138(135-145)	138(136-142.8)	0.539
Potassium	4.1(3.8-4.5)	4.1(3.7-4.2)	0.243
LDL (mg/dl)	108(86-152)	85(79-122)	0.019
HDL (mg/dl)	38(31-42)	38(35-42)	0.622
TG (mg/dl)	128(105-177)	152(109-135)	0.182
Total cholesterol (mg/dl)	197(157-219)	178(144-191)	0.010
NT pro BNP	848.5(540-1755)	32(23-56)	<0.001
EF%	38(33-42)	63(60-65)	<0.001

For the GCS, 44.3% of the LVSD group had a score of 9-12, while 53.6% of the Non LVSD group had 13-15(Moderate). NIHSS score on admission was higher for participants with LVSD (Median, IQR; 15(12-20)) compared to those without LVSD (Median, IQR; 14(13-16)). The baseline mRS at admission, the table shows that both LVSD and without LVSD group had mRS >2 in majority patient, 98.3% of LVSD and 98.2% of the non-LVSD group.

In investigation profile the individuals with Left Ventricular Systolic Dysfunction (LVSD) and those without LVSD across various clinical variables. The variables include hemoglobin (Hb%), total count, neutrophil count, platelet count, random blood sugar (RBS), serum creatinine, sodium, potassium, LDL cholesterol, HDL cholesterol, triglycerides (TG), total cholesterol, NT pro BNP levels, and ejection

fraction (EF%). P-values indicate the statistical significance of the differences observed between the two groups. Notable differences include significantly lower EF% and higher NT pro BNP levels in the LVSD group compared to the non-LVSD group, suggesting impaired cardiac function. Additionally, differences in LDL cholesterol, total cholesterol, and Hb% are statistically significant, indicating potential differences in lipid metabolism and hemoglobin levels between the two groups.

Clinical outcomesTop of Form:

Early mortality (up to one month) was significant in LVSD than non-LVSD (p 0.029) and at 3 month follow up the mortality is almost equal (p= >0.99).

The mean survival times of each group were presented based on the Kaplan–Meier estimates. The cumulative incidence of death was significantly different among LVSD groups and Non-LVSD group (log-rank P =0.016; Figure 2)

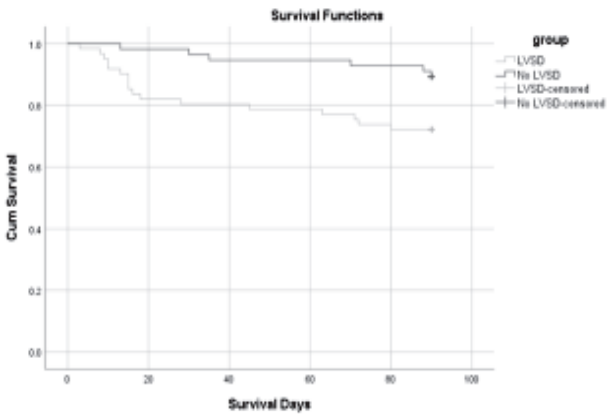

Figure 2: *Kaplan–Meier curves of with or without LVSD level on mortality. LVSD, left ventricular systolic dysfunction.*

Table III shows Total mortality 3.314 times more mortality in LVSD group than in non LVSD group.

Table II

Total Mortality in AIS Patients with or without LVSD

	No of patients in the analysis					
Group	Day 1	Day 20	Day 40	Day 60	Day 80	Day 90
LVSD (censored)	61	53	51	49	45	44
No-LVSD (censored)	56	56	54	53	52	50
LVSD (Death)	00	8	2	2	4	1
No-LVSD (Death)	00	01	2	00	1	2

Table III

Total Mortality in AIS Patients with or without LVSD

Events	Total study subjects (n=117)	LVSD (n=61)	Non- LVSD (n=56)	HR (95%CI)	p Value
Death	23 (19.7%)	17 (27.9%)	6 (10.7%)	3.134 (1.036 to 9.475)	0.016

Table IV shows at 1 month, 95.1% of the LVSD group scored >2 on the mRS, while 83.9% of the non-LVSD group shared this score. For an mRS score of 0-2 (indicating good functional outcome), 4.9% of the LVSD group achieved this score, compared to only 16.9% of the non-LVSD group. At 3 months at 31.1% of the LVSD group achieved an mRS score of 0-2 (indicating good functional outcome), whereas 60.7% of the non-LVSD group obtained the same score. Conversely, for an mRS score >2 (indicating poor functional outcome), 68.9% of the LVSD group scored this, compared to only 39.3% of the non-LVSD group. Stroke-related disability (as described by mRS) at discharge and at 3 months worsened significantly among the LVSD groups (Figure 2)

Table IV

Disability(mRS) in Stroke Patients with or without LVSD

Outcome scales	LVSD (n=61)	No LVSD(n=56)	p value
At 1 month			
Good functional outcome (mRS 0-2)	3 (4.9%)	9 (16.1%)	0.067
Poor functional outcome (mRS >2)	58 (95.1%)	47 (83.9%)	
At 3 month			
Good functional outcome (mRS 0-2)	19 (31.1%)	34 (60.7%)	**<0.001**
Poor functional outcome (mRS >2)	42 (68.9%)	22 (39.3%)	

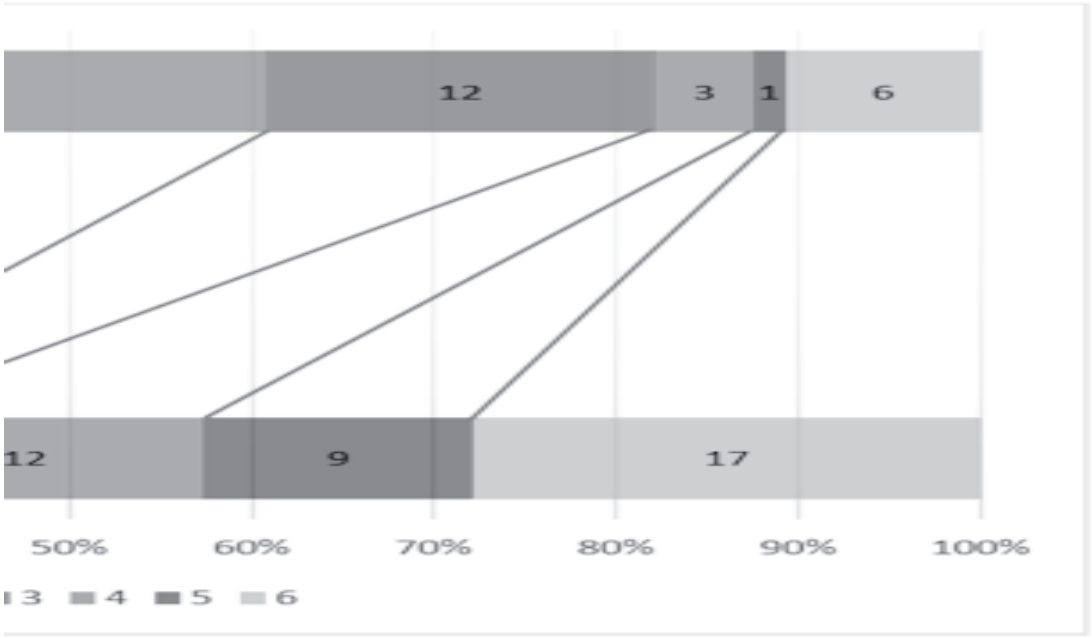

Figure 2. *Distributions of modified Rankin Scale at 3 month*

Table V shows Length of hospital stay of the stroke patients with the LVSD was 10 days with a IQR of 8-15 and without the LVSD was 7 days with a IQR of 4-11. Need for ICU referral of the ischemic stroke patients with the LVSD was 32.8% while and without the LVSD was 14.3%. also in Table V.

Table V

Length of hospital stay and Need for ICU Referral in AIS Patients with or without LVSD

Outcome scales	LVSD (n=61)	No LVSD(n=56)	p value
Length of hospital stay			
Median (IQR)	10 (8-15)	7 (4-11)	<0.001
Need for ICU Referral			
Yes	20 (32.8%)	8 (14.3%)	0.029

Table VI

Multivariable logistic regression model for poor functional outcome at 3 months

	p-value	OR	95% CI for OR	
			Lower	Upper
Diabetes Mellitus	0.606	0.670	0.146	3.064
Hypertension	0.751	0.770	0.153	3.867
Ischemic Heart Disease (IHD)	0.004	4.781	1.668	13.698
Dyslipidemia	0.719	1.395	0.227	8.566
Smoking	0.452	0.536	0.106	2.720
Gender (male)	0.031	2.833	1.098	7.310
Initial NIHSS	0.116	3.383	0.739	15.479
Duration of Hospital stay	0.201	2.804	0.577	13.619

Table VI shows Multivariable logistic analysis showed that male gender (OR:2.833; 95%CI: 1.0988 to 7.310), IHD (OR:4.781, 95%CI: 1.668 to 13.698), in the LVSD group were independently associated ($p<0.05$) unfavorable outcome.

Discussion:

In terms of financial, social, and health costs, stroke is one of the most common diseases in Bangladesh. This is the first-ever study in this institute to demonstrate the outcome of stroke patients with or without LVSD. This study provides essential information about the disability and mortality of stroke in the LVSD, non-LVSD groups and sub-group of LVSD. Stroke patients who were enrolled in this study were examined on admission and followed-up at hospital, after one month and 3 months to see the outcomes.

During the study period, 117 patients admitted to this institute with Ischemic stroke were enrolled for this study. Among them, 61 patients had strokes with LVSD, and 56 had strokes without LVSD. In our study, the incidence of stroke was higher in male patients in both the LVSD and non-LVSD groups, which is 51 (83.6%) and 38 (67.9%), respectively. The mean age of stroke in the LVSD group was 65.50 ± 9.94 years, and stroke without LVSD was 63.78 ± 10.85 years. According to this study, older male patients; either LVSD or non-LVSD; had a higher risk of stroke, similar to previous studies done by some Bangladeshi researchers.[4] Another stroke registry gathered data from 679 stroke patients in BIRDEM General Hospital, Dhaka, Bangladesh. Mean age of the stroke patients was 60.6 years; the majority of patients (67.7%) were male.[13] Consistent with earlier research, this study indicated that patients with a prior history of coronary heart disease had a higher risk of developing stroke among LVSD patients (37.7%) compared with non-LVSD patients (10.7%). A prior study found that the incidence of IHD in stroke with LVSD was 32.11%, and stroke without LVSD was 7.9%, which supports this study.[11] The LVSD group comprised 62.3% hypertensive patients. In contrast, 50% non-LVSD patients had hypertension, indicating a higher prevalence in LVSD group. this study shows hypertensive is more common risk factor in both LVSD and non-LVSD group. a Study in Bangladesh informed that hypertension was the most common risk factor observed among the stroke patients 79.2%.[4] Another previous study found that hypertension in the LVSD stroke group was more 93.3% than in the non-LVSD group 74.1%, similar to this study.[14] The incidence of diabetes more in the LVSD group 37.7% than in the non-LVSD group 37.5%, which was comparable to a previous study 39.4% in LVSD group and 29.7% in non-LVSD group.[11] In our study, 44.25% in LVSD and 37.5% in non-LVSD stroke patients were smoker, this result was supported by a study where smoker in LVSD group was 56.3% and in non-LVSD group was 37.4%.[15] Pulse rate was considerably higher in

LVSD groups during examinations of stroke patients 86(83-94) vs 80(72-88), p-0.161). a previous study showed that pulse rate in LVSD 87.38 (67.06-98.32) and in non-LVSD 80.32 (62-89) group[15] However, systolic blood pressure was higher in LVSD group patients 150(132-160) vs 140(120-150),p 0.007), (median, IQR) which was supported by a study where SBP in LVSD group was 140.9± 16.7 vs non-LVSD group 134.2±16.4.[14] The stroke patients were assessed by the Glasgow Coma Scale, National Institutes of Health Stroke Scale (NIHSS), and Modified Rankin Scale (mRS) on admission. According to the GCS scale, patients who had LVSD had a higher severe score (GCS 3-8, 14.8%,)) than patients who did not have LVSD (GCS 3-8, 7.1%)) which is statistically significant (p=0.037). But GCS 13-15 more frequent in non-LVSD patients about 53.6% whereas LVSD patients had 41% which is also statistically significant (p=0.042). Baseline NIHSS on arrival was not significant between LVSD and non-LVSD patient group (5-15 NIHSS, 52.5%% vs 66.1%, p =0.188; 16-20 NIHSS 26.2% vs 17.9%, p=0.374; and NIHSS 21-42, 21.3% vs 16.1%, p=0.489). This study shows that NIHSS score on admission was higher for participants with LVSD (Median, IQR; 15(12-20)) compared to those without LVSD (Median, IQR; 14(13-16)), and this difference was not statistically significant (p=0.293). a retrospective study on 937 stroke patient with or without LVSD found that LVSD patients had NIHSS Median, IQR; 18 (11-22) and on non-LVSD patients had Median, IQR; 15 (08-21) [16]. This study shows that at hospital mortality and 1st month mortality, both are 5.4 times higher in LVSD than non-LVSD, 9.8% vs 1.8% (p=0.029). another study found that early mortality was 3 times higher in the LVSD group than Non-LVSD.[15] A prior shudy showed that in hospital mortality for stroke patients with LVSD were 2 times higher than those without LVSD.[12] This result was remarkably comparable to our findings. At 3rd month follow up the mortality is slightly higher in LVSD group than non-LVSD group (8.2% vs 7.14%) which is not statistically significant (p >0.99). Total mortality at 3 months is almost 3 times greater in LVSD than non-LVSD patients (27.9%vs 10.7%, p<0.05). another study showed that total mortality at 3 months is more in LVSD than non-LVSD group (26.10% vs 12.40%) which was also similar to our findings.[17] Modified Rankin Scale (mRS) assessed the outcome. at 1 month follow up mRS was ≤2 in 4.9% vs 16.1%), mRS was >2 in 95.1% vs 83.9%) in LVSD group vs non-LVSD group. its showed that unfavorable outcome has identified in both group but more unfavorable in LVSD group than non-LVSD group. No study was found to compare our 1 month findings due to different methodology. Functional outcome at 3 months follow up mRS was ≤2 in 31.1% vs 60.7%)), mRS was >2 in 68.9% vs 39.3%) in LVSD group vs non-LVSD group. its showed that favorable outcome has identified in non-LVSD group than LVSD group. So, at 3 months 68.9% of LVSD patients and 39.3% of non-LVSD patients showed unfavorable outcome. The difference was statistically significant with a p-value of <0.001. From the study of Acute Stroke Registry and Analysis of Lausanne (ASTRAL) registry, stroke-related disability was worse in the LVSD group. another previous study found that dependency/ poor functional outcome at 3 months was 60% in the LVSD group, but 37.7% in the non-LVSD group. that supports this study's findings.[17]

Length of hospital stay of the stroke patients with the LVSD was 10 days with a IQR of 8-15 and without the LVSD was 7 days with a IQR of 4-11. That results show that stroke patients with LVSD had a longer in-hospital Length of hospital stay (LOS) compared to those without LVSD. a earlier work showed that stroke patients with LVSD had a longer in-hospital stay (LOS) compared to those without LVSD about 5.9 days (95% CI: 5.8-6.1) with LVSD and 4.6 (95% CI:4.6-4.7) days without LVSD.[12]

Need for ICU referral of the ischemic stroke patients with LVSD was 2.3 times more than non-LVSD patients (32.8% vs 14.3%, p 0.029**)** hospital stay was statistically significant in both group.

In the multivariable logistic regression analysis in LVSD group Patients shows that IHD (OR: 4.781, 95% CI: 1.668 to 13.698), and male gender (OR: 2.833; 95%CI: 1.0988 to 7.310), in the LVSD group were independent predictors

of poor functional outcomes (mRS >2) at 3 months. an existing literature showed that in the multivariable analysis, poor functional outcomes at 3 months were significantly associated with IHD (OR:3.25, 95% CI: 1.82–5.81; P-value <0.001) [18]. Wei *et al*,.2023 a prior research found that male gender in low EF was significantly associated with poor functional outcome (OR: 1.64; 95%CI: 1.28 to 2.10, P-value <0.001).[19]

Patient with declining ejection fraction (LVSD) had high left ventricular filling pressure that led to decrease in the stroke volume. Reduced ejection fraction has shown to have a role in causing decreased of brain blood vessels reactivity which subsequently leads to cerebral hypoperfusion. Left ventricular ejection fraction was a determinant factor for clinical outcomes in ischemic stroke patients.[20]

Moreover, this study leads us to the conclusion that stroke patients with LVSD have worse clinical outcomes, severe strokes, higher mortality rates, Longer hospital stay. A greater need for ICU referral and more stroke-related complications. The findings of the thesis warrant further research into the management and prevention of ischemic strokes in patients with LVSD to improve their long-term outcomes. The study also highlights the importance of early diagnosis and intervention of LVSD to minimize the risk of ischemic stroke and reduce the associated morbidity and mortality.

Conclusion:

Our study demonstrated that Ischemic Stroke patients with LVSD have worse clinical outcomes, higher mortality rates, excessive dependency, longer hospital stay time and greater need for ICU referral than patients without LVSD. The outcome was measured by mRS score which was significantly higher in LVSD group than non-LVSD group, after the end of 1st month and 3rd month follow up.

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