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COST SAVINGS ASCHIEVED BY REDUCING NEED FOR CARDIAC DEVICES IN PATIENTS WITH SEVERE HEART FAILURE USING LCZ696(SACUBITRIL / VALSARTAN)

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) with and without automatic implantable cardioverter-defibrillators (AICDs), AICDs have been recommended as class1A recommendation for a certain subset of patients with Congestive heart failure with reduced ejection fraction (CHFrEF) based on multiple major trials that showed improved mortality and morbidity with these devices, however this comes at great cost which might be unaffordable in some health systems, LCZ696 in previous publication showed improvement in ejection fraction, in this study we for the first time showed some of the cost savings this medication had contributed to by reducing the need for such devices. **Materials & Methods:** A chart review of patients placed on LCZ696 for clinical purposes over 36 months between 2016 and 2018. All follow-up visits were analyzed. Quality of life-based on New York Heart Association (NYHA) classification was recorded. All hospital admissions, deaths, labs, echocardiograms were recorded. Length of the study was 3months- 36 months (mean of 16 months), all patients whose charts were reviewed, signed an informed consent form allowing for this charts review. **Results:** 180 charts were reviewed; mean follow-up was 16 months, 14 patients (8%) died during follow-up. 29 patients(16%)stopped the medication, patients receiving LCZ 696 showed 43% improvement in EF and 41% improvement in NYHA class.(125) patients had an ejection fraction of less than 35%on initial presentations, of those (73) patients (64%) improved their ejection fraction to above 35%, and 12 patients (10%) did not have a follow-up echocardiogram, 5 patients (3%) lost follow-up. **Conclusion:** use of LCZ696 did improve not only quality of life but also ejection fraction resulting in a reduction in the need of devices with subsequent major health cost savings, based on our knowledge this result is the first time to be measured statistically and reported.

KEYWORDS: Sacubitril / valsartan, heart failure, angiotensin receptor-neprilysin inhibitors (ARNIs), NOTE: the guidelines of the STROBE Statement have been adopted in this study.

INTRODUCTION

Congestive heart failure with reduced ejection fraction (CHFrEF) is becoming the nightmare of any health system across the globe, millions of patients are suffering from such illness with all the subsequent costs incurred from the high mortality, high morbidity, increasing number of emergency room visits, and hospitalizations, in addition to loss of productivity of these patients in the community due to the disabling lifestyle. Through our history dealing with this illness many milestones have been achieved from the coronary care units foundations to innovations in management of acute myocardial infarctions with thrombolytics and subsequent primary percutaneous interventions, allowing for better preservation of myocardial muscle hence reducing incidence of ischemic cardiomyopathy, to the medical innovations in the form of B blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists. Despite all of these milestones still, this illness has high mortality and morbidity making us health caregivers feels desperate for extra help.

In addition to this grave outlook on this illness, it also consumes a great portion of any health care budget through the loss of productivity of these patients to the high costs of recurrent emergency room visits and hospitalizations, and finally through the need for cardiac devices, which was acknowledged as class 1A in most of the guidelines for many of such patients.

Since 2014/2015 a new add on came to the medicine cabinet of health caregivers named LCZ696 (trade name Entresto) which is a unique combinations of an angiotensin receptor blocker ARB (valsartan) and a neprilysin inhibitor (inhibits breakdown of natriuretic peptides ANP, CNP, BNP) which has been proven to be superior to angiotensin-converting enzyme inhibitors (ACE inhibitors) in a major clinical trial (the Paradigm heart failure trial) that was ended prematurely secondary to great improvement noted in the treatment group versus the ACE inhibitor arm, that was published in NEJM 2014 (1), in this trial there was 20% improvement in primary endpoints of mortality and heart failure hospitalizations, while maintaining a good safety profile. Here in the middle east namely Palestine we are not any luckier, in fact we think the prevalence of congestive heart failure with reduced ejection fraction (CHFrEF) is higher than average due to the preponderance of risk factors such as smoking, unhealthy diets, limited health resources, and limited insurance coverage. (2.3) Our country limited health care budget made following the guidelines in terms of applying heart devices to candidates extremely demanding and illogic.

METHODS

All charts of patients who are followed at al-Dalia medical clinic with the diagnosis of CHFrEF who were placed on LCZ-696 due to clinical purposes based on the discretion of their treating physicians were included in the study. All medications adjustments were left to the discretion of treating physicians.

All patients signed an informed consent allowing for chart review, all patients were blinded to the results.
Study patients are followed monthly at the clinic for three months then every three months thereafter. Lab tests were performed every 3 months.

Echocardiograms were performed by multiple operators with ejection fraction and left ventricular dimensions being measured according to standard protocol.

All adverse events, deaths, hospitalizations and emergency room visits were captured and included in the analysis.

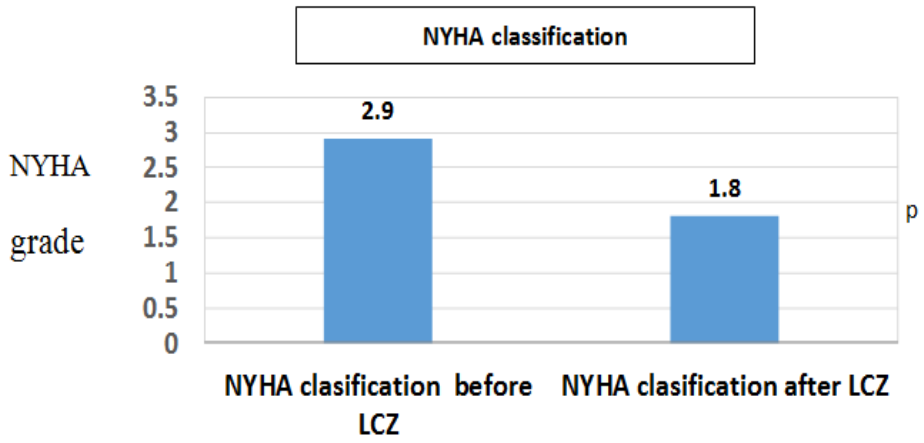
RESULTS

A total of 180 consecutive patients were included in the analysis between 2016 and 2018, Patients demographics were tabulated see table 1,2,3 Of 180 patient charts analyzed 125 patients fulfill the criteria for the study, their pretreatment ejection fraction was less than 35%,of those 12 patients (10%) were not included in the analysis secondary to second echocardiogram was not obtained at the time of data analysis.

Of those 125 patients, 73 patients (64%) of the study sample improved their ejection fraction to above 35%. See table 4
NYHA functional classification class for the whole group improved by 1.3 points (41%) P<005 over the study period. See graph A.

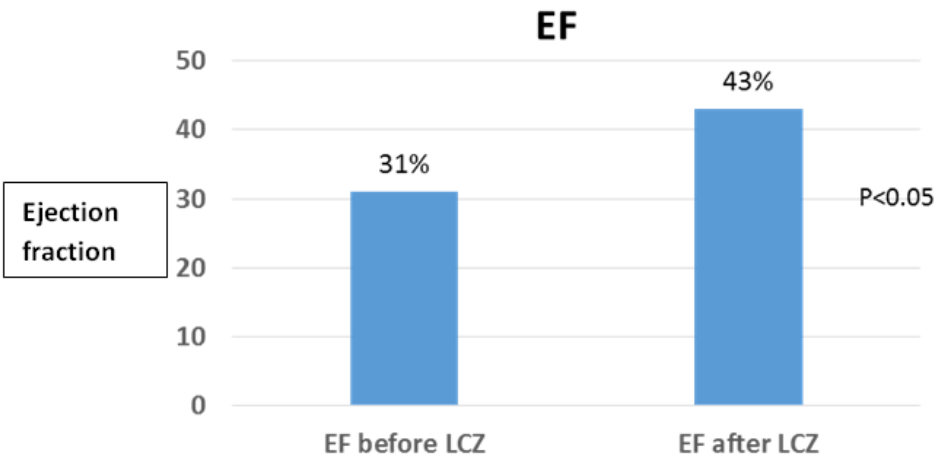
Heart failure in terms of quality of life was classified based on New York Heart Association functional classification.
Class I - No symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc.
Class II - Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
Class III - Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20-100 m).Comfortable only at rest.
Class IV - Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

Graph A



Ejection fraction improved by an absolute 12 points (43%) P<0.05 over the study period. See graph B.

NYHA; New York heart association functional classification, LCZ; LCZ696 (sacubutril/Valsartan)



Graph B: Left ventricular Ejection fraction.

29 patients of the 180 patients (16%) needed to stop the medication for various reasons.14 patients (7%) of the whole group died during the study period due to different causes related to heart failure. Four patients (2%) needed hospitalizations for heart failure exacerbation. Six other patients needed hospitalizations but preferred not to secondary to financial reasons.34 patients (19%) out of the (n=180) and 12 patients (10%) out of the 125 (study group) did not have follow-up echocardiography and were excluded from the analysis.

The statistical analysis was performed using SPSS, all results mentioned were matching the results obtained from SPSS, all results scientifically significant to relies, and all analysis was done by p-value < or = 0.05.

DISCUSSION

Around 10 million people with CHFrEF in Europe, 2% of USA population suffer from CHFrEF, similar rates are noted through the whole globe making heart failure the epidemic of the century, despite of the national and international guidelines strongly recommending cardiac devices like (CRT-P,CRT-D, or AICD) to a subset of patients with heart failure, namely those with ejection fraction of less than 35% with or without LBBB as class 1A indication (4,5,6), unfortunately not all health care systems can afford the huge cost, after the introduction of LCZ696 -post the Paradigm heart failure trial with its great impact on mortality improved by 20% and rate of hospitalizations improved by 21% and despite of the cost limitations of this medicine we showed in a previous publication(8) improvement in ejection fraction by 39% which rendered some of the patients with CHFrEF who were candidates to receive devices not needing them based on current recommendations. In our community we believe with the limited health care budget we have, that the use of this medication LCZ696 will result not only in improving mortality and morbidity of CHFrEF but also in major reduction of cost related to decreasing rate hospitalizations and emergency room visits as well as the need for different kinds of cardiac devices which - as far as we know -has not been shown before.

The main clinical indication for ICD implantation here in Palestine depending on the American heart association recommendation is left ventricular dysfunction (EF ≤35%). While CRT-D therapy primarily indicated for patients with a low ejection fraction of less than 35% and QRS duration equal to or greater than 130 ms, (4)(5)(6)(7).

It is estimated that an AICD will cost on average 15800 Jordanian dinars in Palestine and around 9000 dinars in Jordan while a CRT-D will cost close to 17800 JD in Palestine and 13500 JD in Jordan. In our sample, the total savings will be estimated from reducing the need for cardiac devices to close to 1.2 million dinars (1.7 million dollars) per patient sample(113 patients). See table 5.

Table 1: demographic description based on gender.

Table 1: Number of participants	
Male	114 (63%)
Female	66 (37%)
Total	180
Mean of age	61

Table 2: concurrent medications of patients (who entered in the analysis) excluding ACEi/ARBs.

Medications of participants	
Diuretics	(89%)
Beta blockers	(85%)
Aldactone	(66%)
Digoxin	(36%)
Aspirin	(85%)
Statins	(66%)

Table 3: medical history of patient sample. HFrEF; heart failure with reduced ejection fraction, ischemic; ischemic heart disease with previous myocardial infarction, CRDT; cardiac resynchronization therapy device, AICD; Automatic implantable cardioverter defibrillator.

Patient Medical history		
Medical problem	**No. of patients**	**Percentage**
Hypertension	109	61%
Diabetes mellitus	79	44%
HFrEF*	180	100%
Ischemic(CAD)*	113	63%
CRTD*	7	4%
AICD*	11	6%
Atrial fibrillation	32	18%

Table 4.

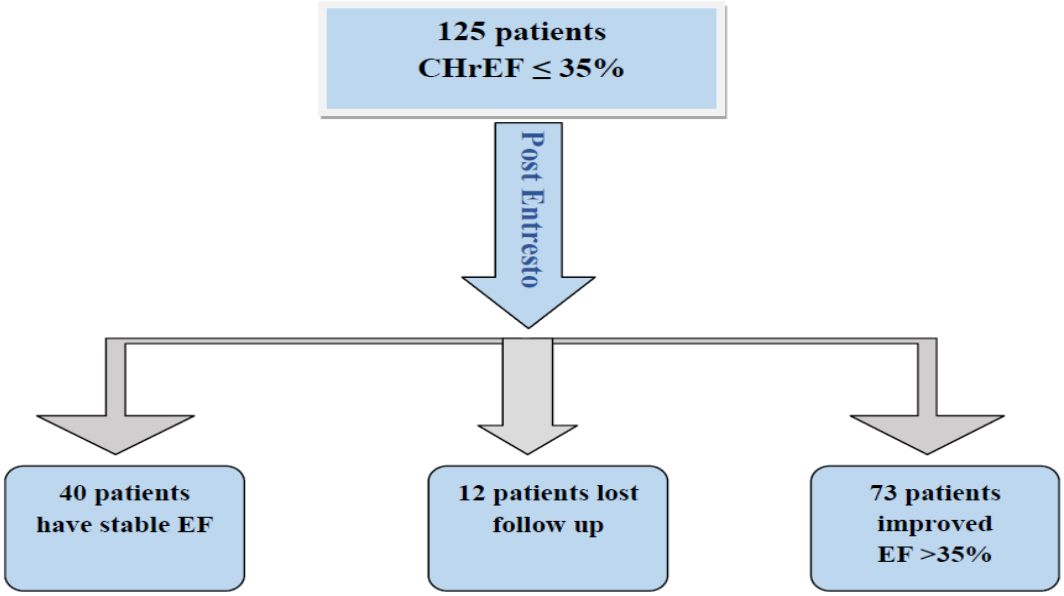


Table 5.

73 patients with improved EF		Cost of device (if EF did not improve) AICD/CRTD
Normal QRS	47 (64%)	742600 JD (AICD cost)
WIDE QRS	26 (36%)	462800 JD (CRTD cost)

CONCLUSION

In this study despite its limitations, we think that LCZ696 (sacubitril/valsartan) has a very promising outcome on quality of life and ejection fraction in a group of patients with congestive heart failure and reduced ejection fraction. There were statistical improvements in quality of life as well as on ejection fraction with an acceptable safety margin. These results we think will result in major health cost savings mainly from reducing hospitalizations ,emergency room visits and more so from decreasing the numbers of patients candidates needing various cardiac devices. However such results need to be replicated in other prospective and retrospective studies.

Limitation of the study

- Retrospective chart analysis
- Small number of patients.
- No core lab for echocardiography

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