

Characteristics of Libyan patients with congestive heart failure and physician adherence to management guidelines at a teaching hospital in Benghazi

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Abbreviations

| | |
|---------------|---|
| AF | Atrial Fibrillation |
| CHF | Congestive Heart Failure |
| CRT | Cardiac Resynchronization Therapy |
| CCBs | Calcium Channel Blockers |
| EF | Ejection Fraction |
| ESC | European Society Of Cardiology |
| GFR | Glomerular Filtration Rate |
| HF | Heart Failure |
| HF_REF | Heart Failure With Reduced Ejection Fraction |
| HF_PEF | Heart Failure With Preserved Ejection Fraction |
| HTN | Hypertension |
| ICD | Intra Cardiac Defibrillator |
| MRA | Mineralocorticoid/Aldosterone Receptor Antagonist |
| LV | Left Ventricle |
| SPSS | Statistical Package of Social Science |
| VHD | Valvular Heart Disease |

Abstract:

Background: Chronic heart failure (CHF) is a serious public health problem globally, with a progressive and lethal course.

Aim: To study the characteristics of Libyan patients with congestive heart failure admitted to (Hawari General Hospital) and to study the adherence of physicians to guideline management of patients with congestive heart failure that recommended by European Society Of Cardiology guidelines on 2012 which should be followed to improve the outcome of these patients.

Methodology: Descriptive retrospective study included all files of patients admitted to Hawari General Hospital diagnosed as congestive heart failure with ejection fraction $\leq 45\%$ by Echocardiography.

Results: Of 122 CHF patients, Majority were males 73.8%, the mean age was 61.2 ± 14 years. Ischemic heart disease, was the predominant comorbid illness, followed by hypertension and diabetes. Comorbid illness were distributed similarly in male and female in most of illness. 52.2% of male patients were smokers. Mean EF% was $34.6\% \pm 8\%$, serum Creatinine level above 1.2mg/dl was accounted in 49.2% . There was difference between mean hemoglobin level of male and female. ACEI & ARB, Diuretic & Aspirin were the highest adhered to recommendations in Hospital, while the least adhered to recommendations were Hydralazine, Digoxin and Warfarin. ACEI & ARB, Aspirin & β -Blocker were the highest adhered to recommendations at discharge from Hospital, while the least adhered to recommendations were Hydralazine, Digoxin and Amiodarone. Of all drugs there were no significance difference between male and female in adherence to recommendations in hospital or in discharge from hospital.

Conclusion: ACEI & ARB, aspirin & β -blocker were the highest adhered to recommendations at discharge from hospital, while the least adhered to recommendations were hydralazine, digoxin and amidarone. Drug adherence did not exceeding 82% in both hospital and hospital discharge, while many of recommended drugs not reaching even 50%, and some of them not used at all.

Introduction:

Heart failure is a major cause of serious morbidity and mortality in the population and one of the leading medical causes of hospitalisation among people aged greater than 60 years⁽¹⁻⁴⁾. The burden of the disease and the resources required to manage it are likely to escalate over the coming decades for several reasons^(4,5). Probably, the most important reason is the increasing number of older people in the population, a group at high risk of developing heart failure. Clinical trials provide important, detailed information on the natural history of highly selected groups of patients with heart failure. Epidemiological studies often provide detailed information, however, on a relatively small number of patients⁽⁶⁻⁸⁾. Hospital discharge and health service statistics provide data on large numbers of patients but limited data on the accuracy of the diagnosis of heart failure or on conditions other than the principle diagnosis^(3,9,10). The majority of first presentations of heart failure occur in hospital and over 40% of patients in the community with heart failure have been hospitalised within the previous year^(11,12). Hospitalisation is a key event that provides an opportunity to clarify the diagnosis and optimise therapy. Accordingly, the EuroHeart Failure survey was devised and

conducted, as part of the EuroHeart Survey programme in order to determine whether consecutive patients with known or suspected heart failure during a hospital admission were being investigated and treated in accordance with ESC guidelines⁽¹³⁾.

Importance Of Guidelines:⁽¹⁴⁾

In general guidelines aim to present management recommendations based on all of the relevant evidence on a particular subject. This is done in order to help physicians select the best possible management strategies for the individual patient suffering from a specific condition, taking into account the impact on outcome and also the risk:benefit ratio of a particular diagnostic or therapeutic procedure. Numerous studies have demonstrated that patient outcome improve when guideline recommendations, based on the rigorous assessment of evidence based research, are applied in clinical practice.

Definition Of Heart Failure:

Heart failure can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures (or only at

the expense of increased filling pressures)⁽¹⁵⁾. For the purposes of these guidelines, HF is defined, clinically, as a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function. The diagnosis of HF can be difficult. Many of the symptoms of HF are non discriminating and, therefore, of limited diagnostic value^(16–20).

Many of the signs of HF result from sodium and water retention and resolve quickly with diuretic therapy, i.e. may be absent in patients receiving such treatment. Demonstration of an underlying cardiac cause is therefore central to the diagnosis of HF. This is usually myocardial disease causing systolic ventricular dysfunction. However, abnormalities of ventricular diastolic function or of the valves, pericardium, endocardium, heart rhythm, and conduction can also cause HF (and more than one abnormality can be present). Identification of the underlying cardiac problem is also crucial for therapeutic reasons, as the precise pathology determines the specific treatment used (e.g. valve surgery for valvular disease, specific pharmacological therapy for LV systolic dysfunction, etc).

Terminology related to left ventricular ejection fraction:

The main terminology used to describe HF is historical and is based on measurement of LV ejection fraction (EF).

Mathematically, EF is the stroke volume (which is the end-diastolic volume minus the end-systolic volume) divided by the end-diastolic volume. In patients with reduced contraction and emptying of the left ventricle (i.e. systolic dysfunction), stroke volume is maintained by an increase in end-diastolic volume (because the left ventricle dilates), i.e. the heart ejects a smaller fraction of a larger volume.

The more severe the systolic dysfunction, the more the EF is reduced from normal and, generally, the greater the end-diastolic and end-systolic volumes. The EF is considered important in HF, not only because of its prognostic importance (the lower the EF the poorer the survival) but also because most clinical trials selected patients on the bases of their EF (usually measured using a radionuclide technique or (echocardiography).

Patient with HF and $EF \leq 45\%$ is called heart failure with reduced EF (HF-REF), while patient with HF and EF more than 45% is called heart failure with preserved EF (HF-PEF).

Terminology related to the symptomatic severity of heart Failure:

The NYHA functional classification (Table 1) has been used to select patients in almost all randomized treatment trials in HF and, therefore, to describe which patients benefit from effective therapies. Patients in NYHA class I have no symptoms attributable to heart disease; those in NYHA classes II, III or IV are sometimes said to have mild, moderate or severe symptoms, respectively. It is important to note, however, that symptom severity correlates poorly with ventricular function, and that although there is a clear relationship between severity of symptoms and survival, patients with mild symptoms may still have a relatively high absolute risk of hospitalization and death^(21 – 23). Symptoms can also change rapidly; for example, a stable patient with mild symptoms can become suddenly breathless at rest with the onset of an arrhythmia, and an acutely unwell patient with pulmonary oedema and NYHA class IV symptoms may improve rapidly with the administration of a diuretic. Deterioration in symptoms indicates heightened risk of hospitalization and death, and is an indication to seek prompt medical attention and treatment. Obviously, improvement in symptoms (preferably to the point of the patient becoming

asymptomatic) is one of the two major goals of treatment of HF (the other being to reduce morbidity, including hospital admissions, and mortality).

Table1: New York Heart Association functional classification

It is based on severity of symptoms and physical activity

Class I

No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.

Class II

Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitation.

Class III

Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue dyspnea, fatigue, or palpitation.

Class IV

Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Epidemiology, aetiology, pathophysiology, and natural history of heart failure:

Approximately 1–2% of the adult population in developed countries has HF, with the prevalence rising to $\geq 10\%$ among persons 70 years of age or older⁽²⁴⁾. At least half of patients with HF have a low EF (i.e. HF-REF). HF-REF is the best understood type of HF in terms of pathophysiology and treatment, and is the focus of ESC guidelines. Coronary artery disease (CAD) is the cause of approximately two-thirds of cases of systolic HF, although hypertension and diabetes are probable contributing factors in many cases. There are many other causes of systolic HF, which include previous viral infection (recognized or unrecognized), alcohol abuse, chemotherapy (e.g. doxorubicin or trastuzumab), and ‘idiopathic’ dilated cardiomyopathy (although the cause is thought to be unknown, some of these cases may have a genetic basis)⁽²⁵⁾. The common risk factors of heart failure are high blood pressure, diabetes, coronary heart disease, smoking, obesity, alcohol use, valvular heart disease, sleep apnea, arrhythmia, and congenital heart defects.

HF-PEF seems to have a different epidemiological and aetiological profile from HF-REF^(26,27). Patients with HF-PEF

are older and more often female and obese than those with HF-REF. They are less likely to have coronary heart disease and more likely to have hypertension and atrial fibrillation (AF).

Patients with HF-PEF have a better prognosis than those with HF-REF⁽²⁸⁾. In patients with LV systolic dysfunction, the maladaptive changes occurring in surviving myocytes and extracellular matrix after myocardial injury (e.g. myocardial infarction) lead to pathological ‘remodelling’ of the ventricle with dilatation and impaired contractility, one measure of which is a reduced EF⁽²⁹⁾. What characterizes untreated systolic dysfunction is progressive worsening of these changes over time, with increasing enlargement of the left ventricle and decline in EF, even though the patient may be symptomless initially. Two mechanisms are thought to account for this progression. The first is occurrence of further events leading to additional myocyte death (e.g. recurrent myocardial infarction). The other is the systemic responses induced by the decline in systolic function, particularly neurohumoral activation.

Two key neurohumoral systems activated in HF are the renin–angiotensin–aldosterone system and sympathetic nervous system. In addition to causing further myocardial injury, these systemic responses have detrimental effects on the blood

vessels, kidneys, muscles, bone marrow, lungs, and liver, and create a pathophysiological ‘vicious cycle’, accounting for many of the clinical features of the HF syndrome, including myocardial electrical instability. Interruption of these two key processes is the basis of much of the effective treatment of HF⁽²⁹⁾.

Clinically, the aforementioned changes are associated with the development of symptoms and worsening of these over time, leading to diminished quality of life, declining functional capacity, episodes of frank decompensation leading to hospital admission (which is often recurrent and costly to health services), and premature death, usually due to pump failure or a ventricular arrhythmia. The limited cardiac reserve of such patients is also dependent on atrial contraction, synchronized contraction of the left ventricle, and a normal interaction between the right and left ventricles. Intercurrent events affecting any of these [e.g. the development of AF or conduction abnormalities, such as left bundle branch block (LBBB)] or imposing an additional haemodynamic load on the failing heart (e.g. anaemia) can lead to acute decompensation. Before 1990, the modern era of treatment, 60–70% of patients died within 5 years of diagnosis, and admission to hospital

with worsening symptoms was frequent and recurrent, leading to an epidemic of hospitalization for HF in many countries^(30–32).

Effective treatment has improved both of these outcomes, with a relative reduction in hospitalization in recent years of 30–50% and smaller but significant decreases in mortality^(30–32).

Diagnosis Of Heart Failure:

Symptoms and signs:

The diagnosis of HF can be difficult, especially in the early stages. Although symptoms bring patients to medical attention, many of the symptoms of HF (Table 2) are non-specific and do not, therefore, help discriminate between HF and other problems. Symptoms that are more specific (i.e. orthopnoea and paroxysmal nocturnal dyspnoea) are less common, especially in patients with milder symptoms, and are, therefore, insensitive^(16–20). Many of the signs of HF result from sodium and water retention, and are, therefore, also not specific. Peripheral oedema has other causes as well, and is particularly non-specific. Signs resulting from sodium and water retention (e.g. peripheral oedema) resolve quickly with diuretic therapy (i.e. may be absent in patients receiving such treatment, making it more difficult to assess patients already treated in this way).

More specific signs, such as elevated jugular venous pressure and displacement of the apical impulse, are harder to detect and, therefore, less reproducible (i.e. agreement between different doctors examining the same patient may be poor)^(16–20).

Symptoms and signs may be particularly difficult to identify and interpret in obese individuals, in the elderly, and in patients with chronic lung disease^(33–35). The patient's medical history is also important. HF is unusual in an individual with no relevant medical history (e.g. a potential cause of cardiac damage), whereas certain features, particularly previous myocardial infarction, greatly increase the likelihood of HF in a patient with appropriate symptoms and signs^(16–19). These points highlight the need to obtain objective evidence of a structural or functional cardiac abnormality that is thought to account for the patient's symptoms and signs, to secure the diagnosis of HF. Once the diagnosis of HF has been made, it is important to establish the cause, particularly specific correctable causes. Symptoms and signs are important in monitoring a patient's response to treatment and stability over time. Persistence of symptoms despite treatment usually indicates the need for additional therapy, and worsening of symptoms is a serious development (placing the patient at risk of urgent hospital

admission and death) and merits prompt medical attention.

Table 2 Symptoms and signs typical of heart failure

| Symptoms | Signs |
|---|--|
| Typical | More specific |
| Breathlessness | Elevated jugular venous pressure |
| Orthopnoea | Hepatojugular reflux |
| Paroxysmal nocturnal dyspnea | Third heart sound (gallop rhythm) |
| Reduced exercise tolerance | Laterally displaced apical impulse |
| Fatigue, tiredness, increased time to recover after exercise | Cardiac murmur |
| Ankle swelling | |
| Less typical | Less specific |
| Nocturnal cough | Peripheral oedema (ankle,sacral,scrotal) |
| Wheezing | Pulmonary crepitations |
| Weight gain (>2 kg/week) | pleural effusion |
| Weight loss (in advanced heart fa | Tachycardia |
| Bloated feeling | Irregular pulse |
| Loss of appetite | Tachypnoea (>16 breaths/min) |
| Confusion (especially in the elderly) | Hepatomegaly |
| Depression | Ascites |
| Palpitation | Tissue wasting (cachexia) |
| Syncope | |

Pharmacological treatment of heart failure with reduced ejection fraction (systolic heart failure) according to ESC guidelines on 2012:

1.1 Objectives in the management of heart failure

The goals of treatment in patients with established HF are to relieve symptoms and signs (e.g. oedema), prevent hospital admission, and improve survival. It is now recognized that preventing HF hospitalization is important for patients and healthcare systems⁽³⁶⁾. Reductions in mortality and hospital admission rates both reflect the ability of effective treatments to slow or prevent progressive worsening of HF. This is often accompanied by reverse LV remodeling and a reduction in circulating natriuretic peptide concentrations^(37,38). The relief of symptoms, improvement in quality of life, and increase in functional capacity are also of the most importance to patients, but they have not been the primary outcome in most trials⁽³⁹⁾. This is in part because they are difficult to measure and partly because some treatments previously shown to improve these outcomes also decreased survival^(40,41). However, effective pharmacological therapies and CRT improve these outcomes, as well as mortality and hospitalization.

1.2 Treatments recommended in potentially all patients with systolic heart failure (NYHA class II–IV):

a. Angiotensin-converting enzyme inhibitors

Angiotensin converting enzyme inhibitors should be considered in patients with NYHA functional classes (II–IV) of heart failure due to left ventricular systolic dysfunction with an $EF \leq 40\%$ ⁽⁴²⁻⁴⁶⁾. (**class I level of Evidence=A**).

This is in part because ACE inhibitors have a modest effect on LV remodeling^(42,43).

ACE inhibitors occasionally cause worsening of renal function, hyperkalaemia, symptomatic hypotension, cough, and, rarely, angioedema. An ACE inhibitor should only be used in patients with adequate renal function (creatinine ≤ 221 mmol/L or ≤ 2.5 mg/dL or $eGFR \geq 30$ mL/min/1.73 m²) and a normal serum potassium level⁽⁴⁷⁾.

b. Beta Blockers

All patients with heart failure due to left ventricular systolic dysfunction of NYHA functional classes (II–IV) should be started on beta blocker therapy as soon as their condition is stable (unless contraindicated by a history of asthma, heart block or symptomatic hypotension)⁽⁴⁸⁻⁵⁴⁾.

Bisoprolol, Carvedilol, Metoprolol or Nebivolol should be the

beta blocker of first choice for the treatment of patients with chronic heart failure due to left ventricular systolic dysfunction⁽⁴⁸⁻⁵⁴⁾. **(class I level of Evidence = A)**.

c. Aldosterone Antagonists

An MRA is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF \leq 35%, despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death⁽⁵⁵⁻⁵⁶⁾. **(class I level of Evidence=A)**.

1.3 Other treatments recommended in selected patients with systolic heart failure (NYHA class II–IV):

Most of these drugs have shown convincing benefits in terms of symptom reduction, HF hospitalization, or both, and are useful alternative or additional treatments in patients with HF.

a. Angiotensin Receptor Blockers

Recommended to reduce the risk of HF hospitalization and the risk of premature death in patients with an EF \leq 40% and unable to tolerate an ACE inhibitor because of cough (patients should also receive a beta-blocker and an MRA)^(57,58). **(class I level of Evidence = A)**.

Recommended to reduce the risk of HF hospitalization in

patients with an EF \leq 40% and persisting symptoms (NYHA class II–IV) despite treatment with an ACE inhibitor and a beta-blocker who are unable to tolerate an MRA^(59,60). **(class I level of Evidence=A).**

b. Digoxin

Digoxin should be considered as a second drug in addition to beta blocker for achieving adequate control of the ventricular response to atrial fibrillation in patients with heart failure⁽⁶¹⁾.

(class IIa level of Evidence=B).

May be considered to reduce the risk of HF hospitalization in patients with an EF \leq 45% and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA⁽⁶¹⁾. **(class IIb level of Evidence=B).**

May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF \leq 45% who are unable to tolerate a beta-blocker (ivabradine is an alternative in patients with a heart rate \geq 70 b.p.m). Patients should also receive an ACE inhibitor (or ARB) and an MRA⁽⁶¹⁾. **(class IIb level Evidence=B)**

c. Ivabradine

Ivabradine is a drug that inhibits the **If channel** in the sinus

node. Its only known pharmacological effect is to slow the heart rate in patients in sinus rhythm (it does not slow the ventricular rate in AF) Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF $\leq 35\%$, a heart rate remaining ≥ 70 b.p.m, and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB)⁽⁶²⁾. **(class IIa level of Evidence=B).**

May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF $\leq 35\%$ and a heart rate ≥ 70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA⁽⁶²⁾. **(class IIb level of Evidence=C).**

d. Hydralazine and Isosorbide Dinitrate

May be considered as an alternative to an ACE inhibitor or ARB, if neither is tolerated due to renal dysfunction or hyperkalaemia, to reduce the risk of HF hospitalization and risk of premature death in patients with an EF $\leq 45\%$ and dilated LV (or EF $\leq 35\%$). Patients should also receive a beta blocker and an MRA^(63,64). **(class IIb level of Evidence=B).**

May be considered to reduce the risk of HF hospitalization and

risk of premature death in patients in patients with an EF \leq 45% and dilated LV (or EF \leq 35%) and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA⁽⁶⁵⁾. **(class IIb level of Evidence=B).**

1.4 Treatments not recommended (unproven benefit):

a. 3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors ('statins')

Although there is a wealth of robust evidence supporting the value of statins in patients with atherosclerotic (arterial) disease, most trials excluded patients with HF (because it was uncertain that they would benefit)⁽⁶⁶⁾. Two recent trials studied statin treatment specifically in patients with chronic HF and did not demonstrate convincing evidence of benefit (although there was little evidence of harm)^(67,68). Despite the evidence in other areas of cardiovascular medicine, the evidence does not therefore support the initiation of statins in most patients with chronic HF.

b. Oral Anticoagulants(Warfarin)

Other than in patients with AF (both HF-REF and HF-PEF), there is no evidence that an oral anticoagulant reduces mortality–morbidity compared with placebo or

aspirin⁽⁶⁹⁾. Treatment with warfarin (goal international normalized ratio [INR] 2.0-3.0) is recommended for all patients with HF and chronic or documented paroxysmal, persistent, or long standing atrial fibrillation or a history of systemic or pulmonary emboli, including stroke or transient ischemic attack unless contraindicated⁽⁶⁹⁾.

1.5 Antiplatelet

Long-term treatment with an antiplatelet agent, generally aspirin in doses of 75 to 81 mg, is recommended for patients with HF due to ischemic cardiomyopathy, whether or not they are receiving ACE inhibitors⁽⁷⁰⁾. (Strength of Evidence = B).

Clopidogrel (75 mg) may be considered as alternatives to aspirin⁽⁷⁰⁾. **(Strength of Evidence = B).**

Routine use of aspirin is not recommended in patients with HF without atherosclerotic vascular disease⁽⁷⁰⁾. **(Strength of Evidence = C).**

1.6 Diuretics

Diuretic therapy should be considered for heart failure patients with dyspnoea or oedema (ankle or pulmonary)⁽¹⁴⁾. The effects of diuretics on mortality and morbidity have not been studied in patients with HF, unlike ACE inhibitors, beta blockers, and MRAs (and other treatments). However, diuretics

relieve dyspnoea and oedema and are recommended for this reason in patients with signs and symptoms of congestion, irrespective of EF⁽¹⁴⁾.

Loop diuretics produce a more intense and shorter diuresis than thiazides, which cause a more gentle and prolonged diuresis.

Thiazides may be less effective in patients with reduced kidney function. Loop diuretics are usually preferred to thiazides in HF-REF although they act synergistically and the combination may be used (usually on a temporary basis) to treat resistant oedema. The aim of using diuretics is to achieve and maintain euvolaemia (the patient's 'dry weight') with the lowest achievable dose. This means that the dose must be adjusted, particularly after restoration of dry body weight, to avoid the risk of dehydration leading to hypotension and renal dysfunction⁽¹⁴⁾.

1.7 Amiodarone

Amiodarone is recommended in patients with an ICD, who continue to have symptomatic ventricular arrhythmias or recurrent shocks despite optimal treatment and device re-programming⁽¹⁴⁾.

Amiodarone may be considered as a treatment to prevent recurrence of sustained symptomatic ventricular arrhythmias in

otherwise optimally treated patients in whom an ICD is not considered appropriate⁽¹⁴⁾.

Routine use of amiodarone is not recommended in patients with non-sustained ventricular arrhythmias or for primary prevention of sudden death in patients with HF because of lack of benefit and potential drug toxicity^(71,72).

Amiodarone may be considered in patients unable to tolerate a beta-blocker or digoxin for controlling heart rate in patient with HF (NYHA functional class II–IV) and persistent/permanent AF⁽¹⁴⁾.

Amiodarone may be considered in addition to either a beta-blocker or digoxin (but not both) to control the ventricular rate in patients with an inadequate response⁽¹⁴⁾.

pharmacological cardioversion with amiodarone may be considered in patients with AF and persisting symptoms and/or signs of HF, despite optimum pharmacological treatment and adequate control of the ventricular rate, to improve clinical/symptomatic status⁽¹⁴⁾.

1.8 Treatments not recommended (believed to cause harm):

a. glitazones should not be used as they cause worsening HF and increase the risk of HF hospitalization⁽⁷³⁻⁷⁵⁾. **(class III level of Evidence = A).**

- b.** Most CCBs (with the exception of amlodipine and felodipine) should not be used as they have a negative inotropic effect and can cause worsening HF⁽⁷⁶⁾. **(class III level of Evidence = B).**
- c.** NSAIDs and COX-2 inhibitors should be avoided if possible as they may cause sodium and water retention, worsening renal function and worsening HF^(77,78). **(class III level of Evidence=B).**
- d.** The addition of an ARB (or renin inhibitor) to the combination of an ACE inhibitor and a mineralocorticoid antagonist is not recommended because of the risk of renal dysfunction and hyperkalaemia⁽¹⁴⁾. **(class III level of Evidence = C).**

Aim of The study:

- 1.To study the characteristics of Libyan patients with congestive heart failure admitted to **(Hawari General Hospital)**.
2. To study the adherence of physicians to guideline management of patients with congestive heart failure that recommended by European Society Of Cardiology on 2012 which should be followed to improve the outcome of these patients.

Methodology:

Sitting: Hawari General Hospital _ Benghazi.

Study population:

All files of patients admitted to Hawari General Hospital (cardiology unit) diagnosed as congestive heart failure with ejection fraction $\leq 45\%$ by Echocardiography were included.

Data like age, sex, history of medical disease, type of treatment in hospital and at discharge were included in (appendix I).

Duration of the study: From (1st Jan to 31st of Dec 2013).

Type of the study : Descriptive retrospective study.

Data analysis: All data were entered and analyzed using SPSS software, version 18.

Descriptive statistics : as mean , median, mode were calculated for quantitative variables.

Analytic statistics: t-test was used to find if there is difference between two means. Chi- square test was used to find the difference between the distribution of variables in different groups. A p value of less than 0.05 was considered statistically significant.

Results:

Table 1 : Distribution of patients according to age.

| Age /year | No. | % |
|--------------|------------|------------|
| < 30 | 2 | 1.6 |
| 31- 40 | 8 | 6.6 |
| 41 - 50 | 14 | 11.5 |
| 51 - 60 | 33 | 27 |
| 61-70 | 36 | 29.5 |
| 71-80 | 21 | 17.2 |
| >80 | 8 | 6.6 |
| Total | 122 | 100 |

Mean age = 61.2years \pm 14. Median= 62years. Minimum age=17 years. Maximum =95 Years.

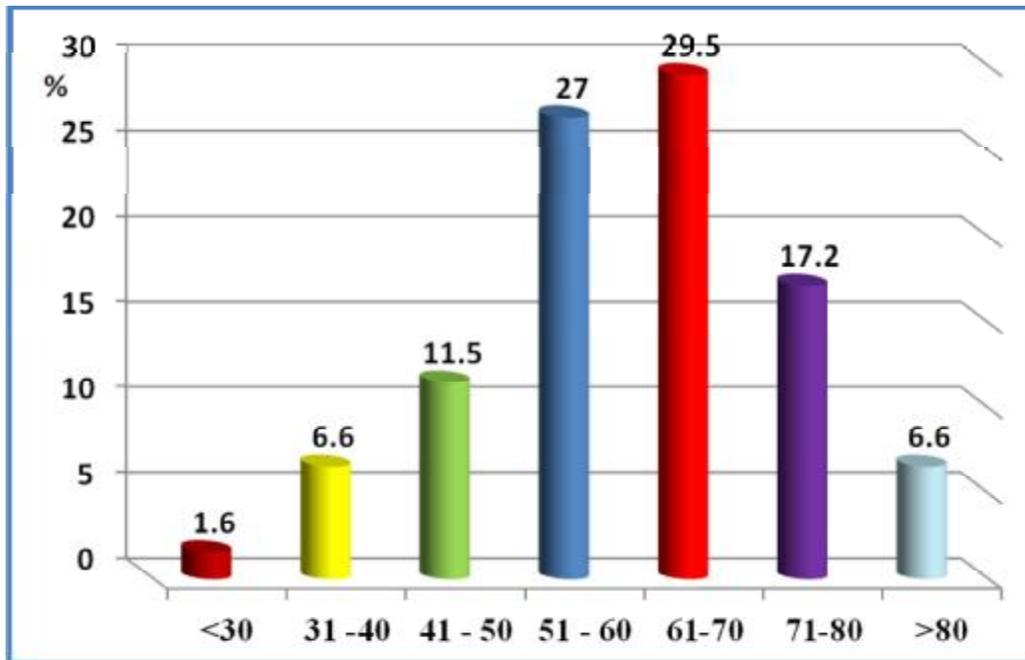


Fig. 1: Distribution of patients according to age.

Table 2 :Distribution of patients according to the sex.

| Sex | No. | % |
|--------|-----|------|
| Male | 90 | 73.8 |
| Female | 32 | 26.2 |
| Total | 122 | 100 |

M:F = 2.8 :1

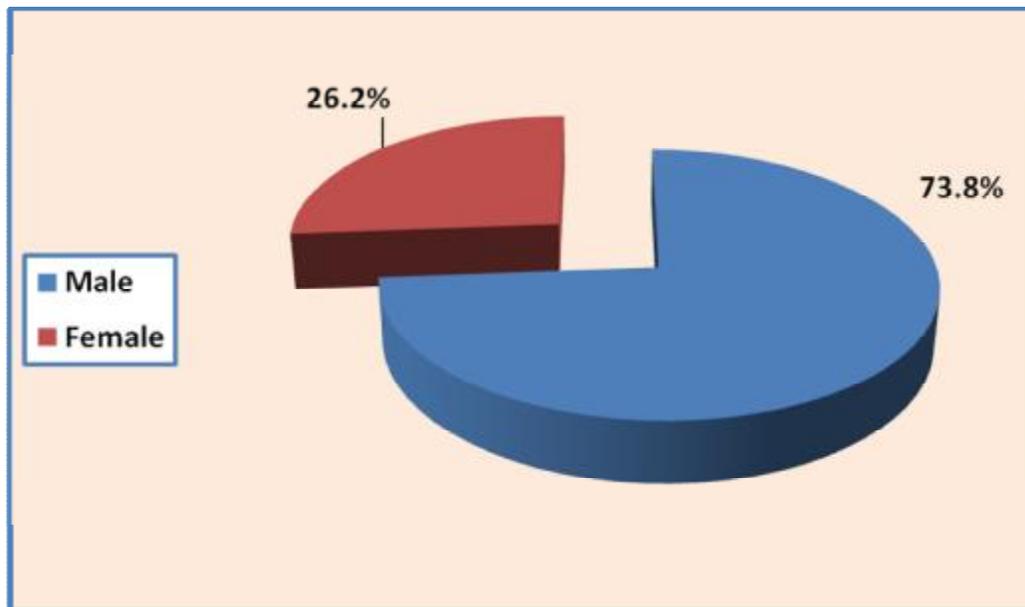


Fig. 2:Distribution of patients according to the sex.

Table 3 : Distribution of patients according to the comorbid illness.

| Comorbid illness | No. | % |
|--|------------|-------------|
| Hypertension | 70 | 57.4 |
| Diabetic | 70 | 57.4 |
| Ischemic heart disease | 97 | 79.5 |
| Coronary artery bypass grafting | 11 | 9 |
| PCI | 28 | 23 |
| VHD | 12 | 9.8 |
| Peripartum cardiomyopathy | 2 | 1.6 |
| Atrial fibrillation | 30 | 24.6 |

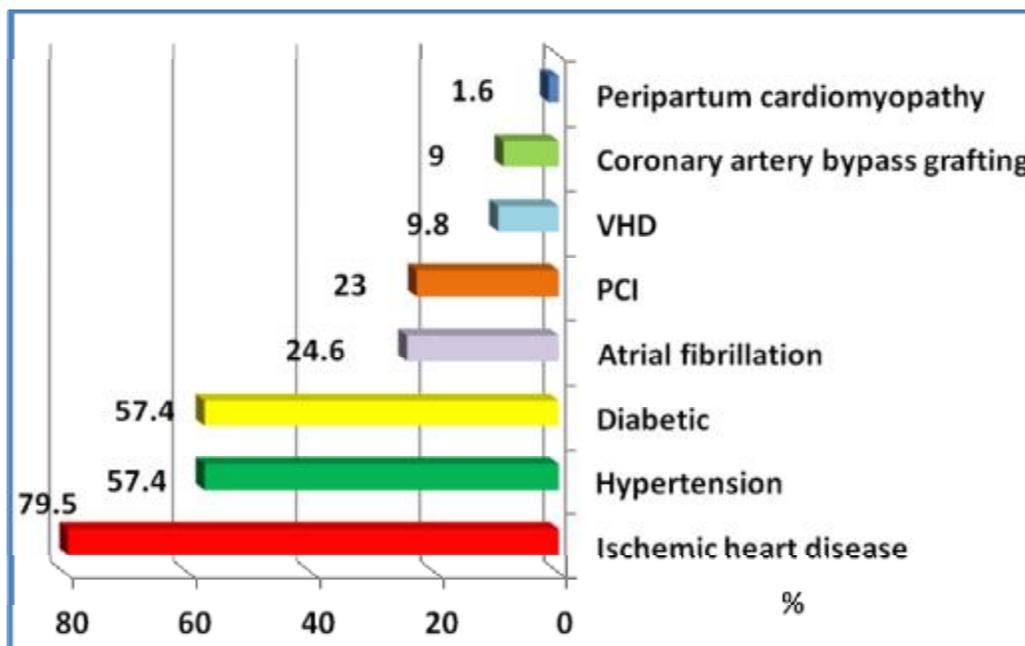


Fig.3 Distribution of patients according to the comorbid illness.

Table 4: Distribution of patients by sex and according to comorbid illness

| Comorbid illness | Sex | | | | P value |
|--|-----------|-------------|-----------|-------------|-------------------|
| | Male | | Female | | |
| | No. | % | No. | % | |
| Hypertension | 48 | 53.3 | 22 | 68.8 | 0.130(N.S) |
| Diabetic | 49 | 54.4 | 21 | 65.6 | 0.272(N.S) |
| Ischemic heart disease | 74 | 82.2 | 23 | 71.9 | 0.213(N.S) |
| Coronary artery bypass grafting | 9 | 10 | 2 | 6.3 | 0.525(N.S) |
| PCI | 21 | 23.3 | 7 | 21.9 | 0.866(N.S) |
| VHD | 8 | 8.9 | 4 | 12.5 | 0.556(N.S) |
| Peripartum cardiomyopathy | 0 | 0 | 2 | 6.3 | 0.017(S) |
| Atrial fibrillation | 23 | 25.6 | 7 | 21.9 | 0.678(N.S) |

N.S= Not significant. S = Significant

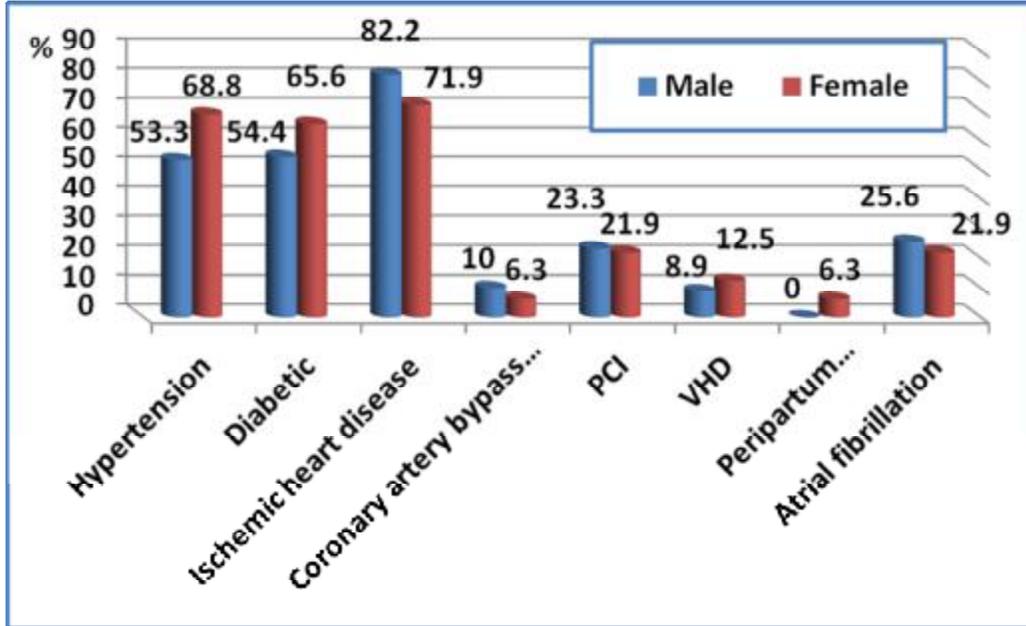


Fig. 4: Distribution of patients by sex and according to comorbid illness

Table 5 :Distribution of patients according to smoking status of male.

| Smoking status | No. | % |
|-----------------------|------------|-------------|
| Smoker | 47 | 52.2 |
| None smoker | 43 | 47.8 |
| Total | 90 | 100 |

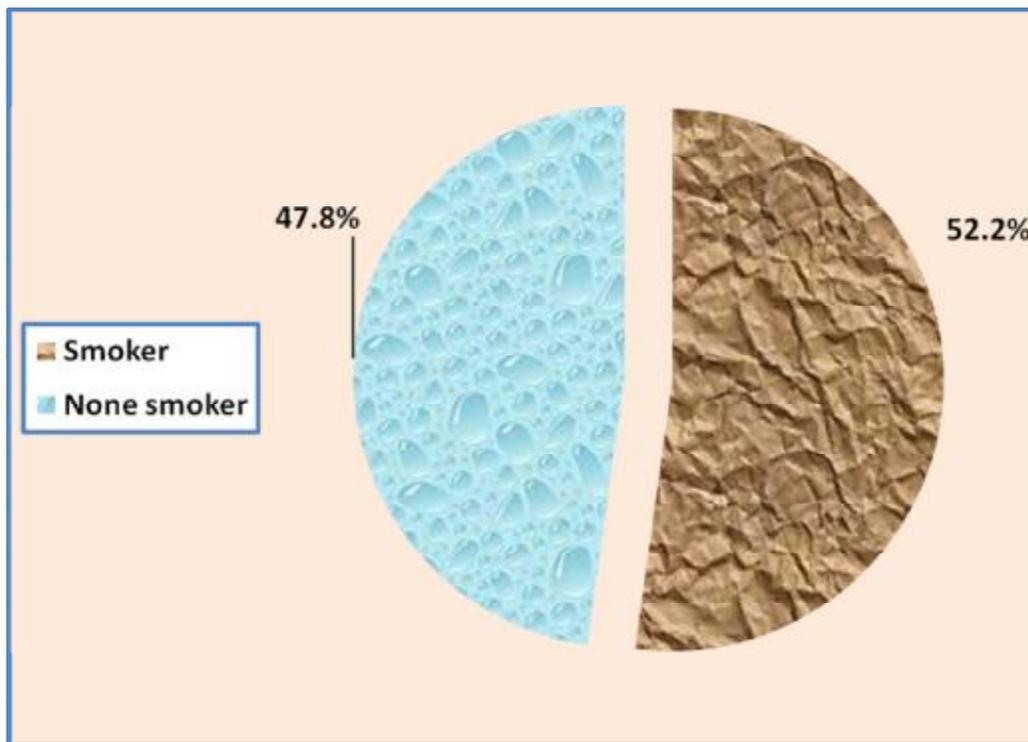


Fig. 5:Distribution of patients according to smoking status of male.

Ejection fraction percentage : All patients had percentage $\leq 45\%$

Mean EF%= 34.6% \pm 8%. Median= 35%.Minimum =17%.

Maximum =45%.

Table 6 :Distribution of patients according to creatinin level.

| Creatinine level / mg/dl | No. | % |
|---------------------------------|------------|-------------|
| < 0.6 | 3 | 2.5 |
| 0.6 – 1.2 | 59 | 48.3 |
| >1.2 | 60 | 49.2 |
| Total | 122 | 100 |

Mean= 1.5 mg/dl ±0.89 mg/dl. Median= 1.2 mg/dl. Minimum =0.4 mg/dl. Maximum = 5.5 mg/dl.

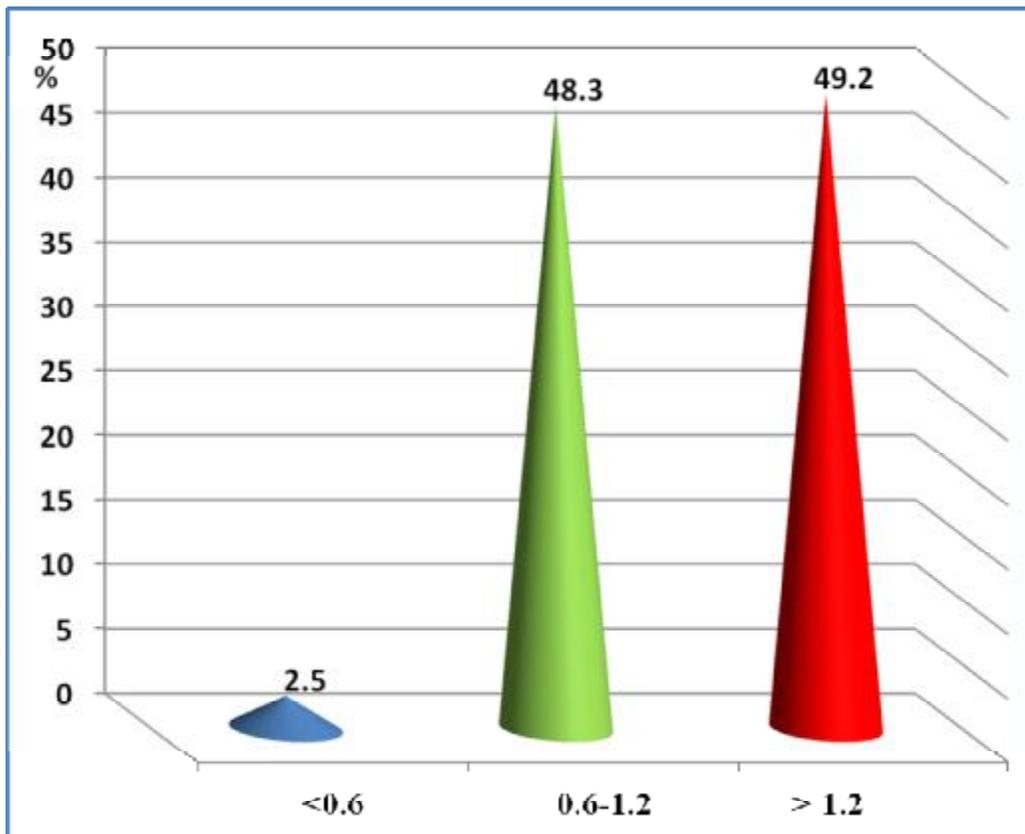


Fig. 6 :Distribution of patients according to creatinin level.

Table 7 :Distribution of patients according to hemoglobin level for male.

| Hemoglobin level g/dl | No. | % |
|-----------------------|-----|------|
| <13 | 66 | 73.3 |
| 13 -16 | 24 | 26.7 |
| Total | 90 | 100 |

Mean= 11.5g/dl \pm 1.9g/dl. Median= 11.9 g/dl. Minimum = 7.4 g/dl.
Maximum =15.5g/dl.

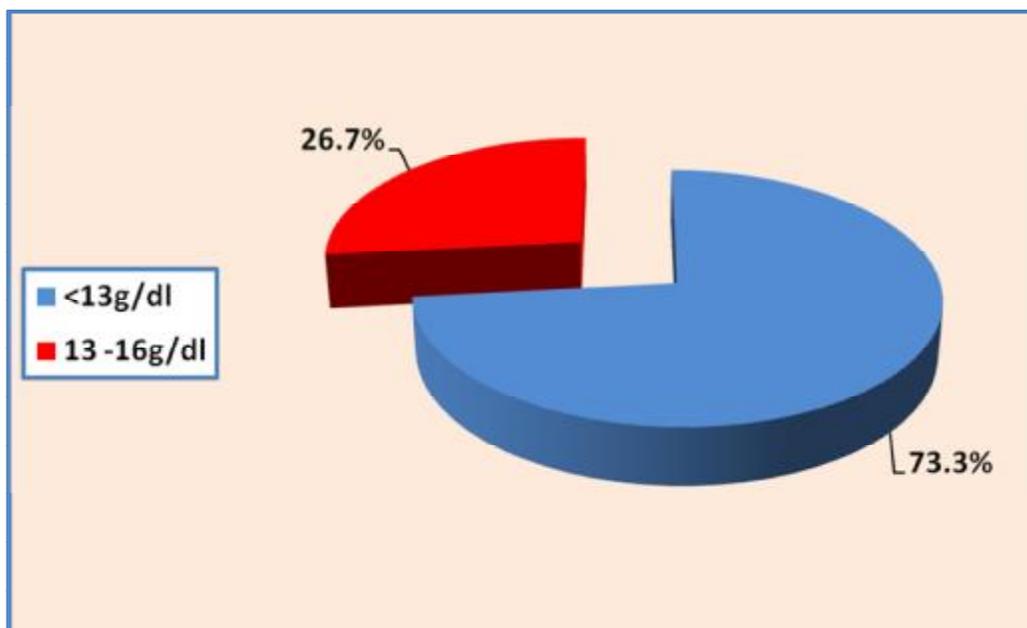


Fig.7 :Distribution of patients according to hemoglobin level for male.

Table 8 :Distribution of patients according to hemoglobin level for female.

| Hemoglobin level g/dl | No. | % |
|-----------------------|-----------|------------|
| <12 | 28 | 87.5 |
| 12 -15 | 4 | 12.5 |
| Total | 32 | 100 |

**Mean= 10.1g/dl ± 1.6g/dl. Median=10.4g/d. Minimum =4.2 g/dl.
Maximum =12.5 g/dl**

(t –test the difference between the mean hemoglobin level of male and female)t = 6.243 with 120 degrees of freedom; P = 0.000(Significant)

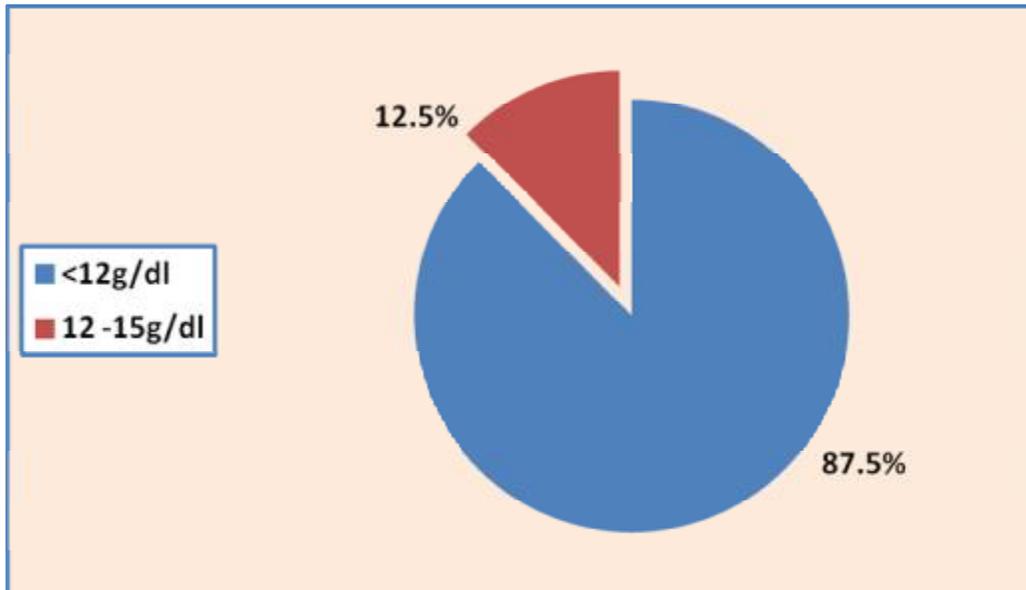


Fig. 8:Distribution of patients according to hemoglobin level for female.

Table 9: Distribution of patients according to the adherence to guidelines for managing congestive heart failure at the Hospital management .

| Type of drug | No.(122) | % |
|-----------------------|-----------------|-------------|
| Diuretic | 99 | 81.1 |
| ACEI & ARB | 100 | 82 |
| β-Blocker | 90 | 73.8 |
| Spironolactone | 46 | 37.7 |
| Aspirin | 98 | 80.3 |
| Clopidogrel | 59 | 48.4 |
| Warfarin | 27 | 22.1 |
| Digoxin | 17 | 13.9 |
| Nitrate | 60 | 49.2 |
| Hydralazine | 0 | 0 |
| Statin | 83 | 68 |
| Amiodarone | 17 | 13.9 |

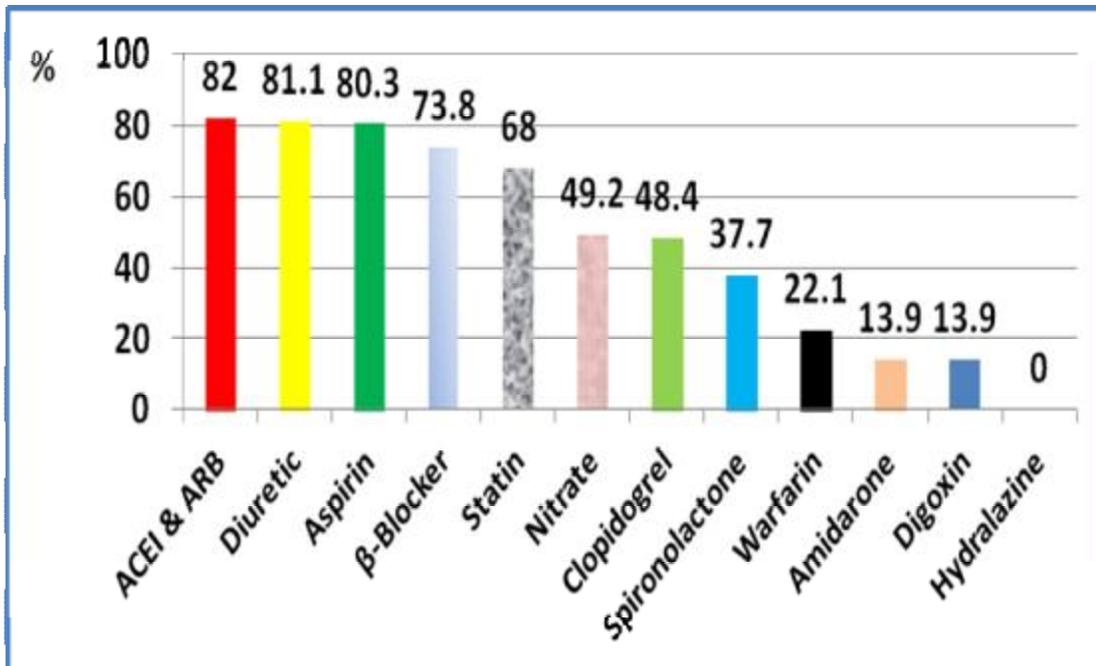


Fig. 9: Distribution of patients according to the adherence to guidelines for managing congestive heart failure at the Hospital management .

Table 10: Distribution of patients according to the adherence to guidelines for managing congestive heart failure at the discharge.

| Agents | No. | % |
|-----------------------|------------|-------------|
| Diuretic | 81 | 66.4 |
| ACEI & ARB | 98 | 80.3 |
| β-Blocker | 92 | 75.4 |
| Spironolactone | 52 | 42.6 |
| Aspirin | 97 | 79.5 |
| Clopidogrel | 56 | 45.9 |
| Warfarin | 28 | 23 |
| Digoxin | 14 | 11.5 |
| Nitrate | 51 | 41.8 |
| Hydralazine | 0 | 0 |
| Statin | 84 | 68.9 |
| Amiodarone | 19 | 15.6 |

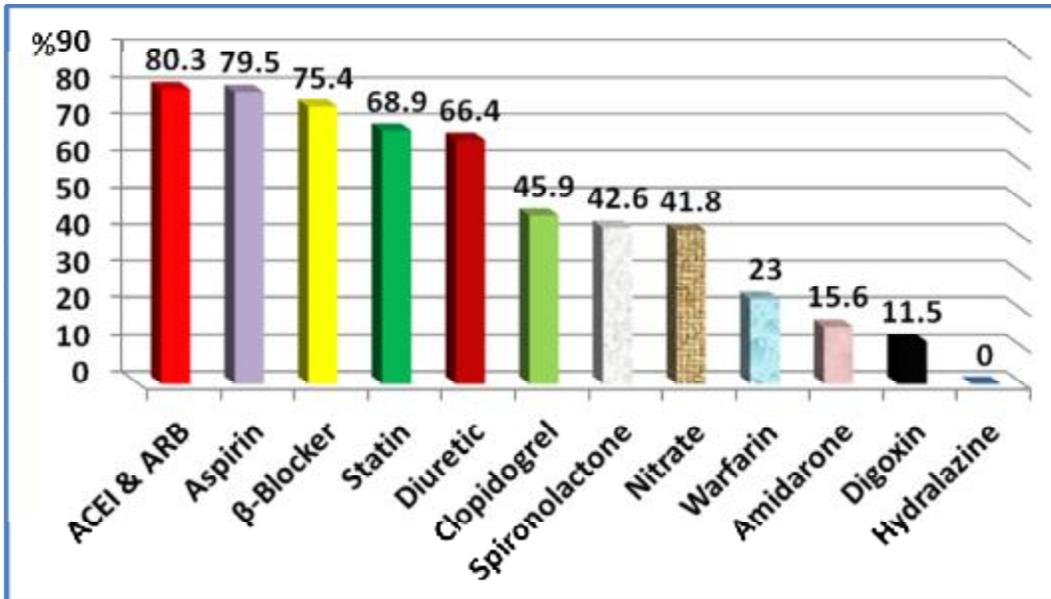


Fig.10:Distribution of patients according to the adherence to guidelines for managing congestive heart failure at the discharge.

Table 11: Distribution of patients by sex and the adherence to guidelines for managing congestive heart failure at the Hospital.

| Agents | Sex | | | | P value |
|-----------------------|-----------|-------------|-----------|-------------|-------------------|
| | Male | | Female | | |
| | No. | % | No. | % | |
| Diuretic | 72 | 80 | 27 | 84.4 | 0.587(N.S) |
| ACEI & ARB | 77 | 85.6 | 23 | 71.9 | 0.144(N.S) |
| β-Blocker | 66 | 73.3 | 24 | 75 | 0.854(N.S) |
| Spironolactone | 35 | 38.8 | 11 | 12.2 | 0.651(N.S) |
| Aspirin | 77 | 85.6 | 21 | 65.6 | 0.015(S) |
| Clopidogrel | 45 | 50 | 14 | 43.8 | 0.543(N.S) |
| Warfarin | 21 | 23.3 | 6 | 18.8 | 0.592(N.S) |
| Digoxin | 13 | 14.4 | 4 | 12.5 | 0.785(N.S) |
| Nitrate | 45 | 50 | 15 | 46.9 | 0.761(N.S) |
| Statin | 60 | 66.7 | 23 | 71.9 | 0.587(N.S) |
| Amiodarone | 12 | 13.3 | 5 | 15.6 | 0.748(N.S) |

N.S= Not significant. S = Significant

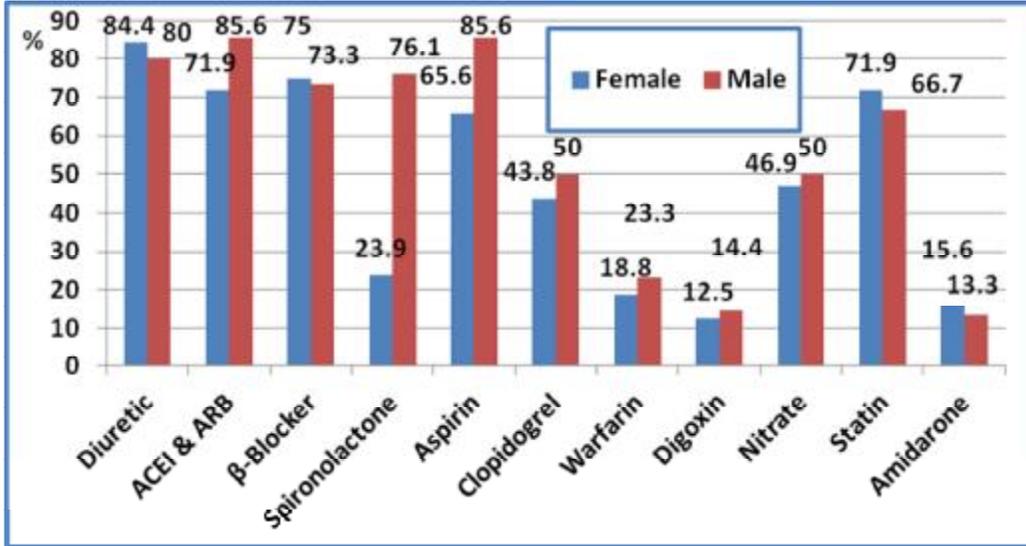


Fig.11: Distribution of patients by sex and the adherence to guidelines for managing congestive heart failure at the Hospital.

Table 12: Distribution of patients by sex and the adherence to guidelines for managing congestive heart failure at the discharge.

| Agents | Sex | | | | P value |
|-----------------------|-----------|-------------|-----------|-------------|-------------------|
| | Male | | Female | | |
| | No. | % | No. | % | |
| Diuretic | 58 | 64.4 | 23 | 71.9 | 0.445(N.S) |
| ACEI & ARB | 75 | 83.3 | 23 | 71.9 | 0.254(N.S) |
| β-Blocker | 67 | 74.4 | 25 | 78.1 | 0.678(N.S) |
| Spironolactone | 39 | 43.3 | 13 | 40.6 | 0.790(N.S) |
| Aspirin | 75 | 83.3 | 22 | 68.8 | 0.079(N.S) |
| Clopidogrel | 41 | 45.6 | 15 | 46.9 | 0.898(N.S) |
| Warfarin | 23 | 25.6 | 5 | 15.6 | 0.251(N.S) |
| Digoxin | 11 | 12.2 | 79 | 87.8 | 0.664(N.S) |
| Nitrate | 41 | 45.6 | 10 | 31.3 | 0.159(N.S) |
| Statin | 61 | 67.8 | 23 | 71.9 | 0.667(N.S) |
| Amiodarone | 14 | 15.6 | 5 | 15.6 | 0.993(N.S) |

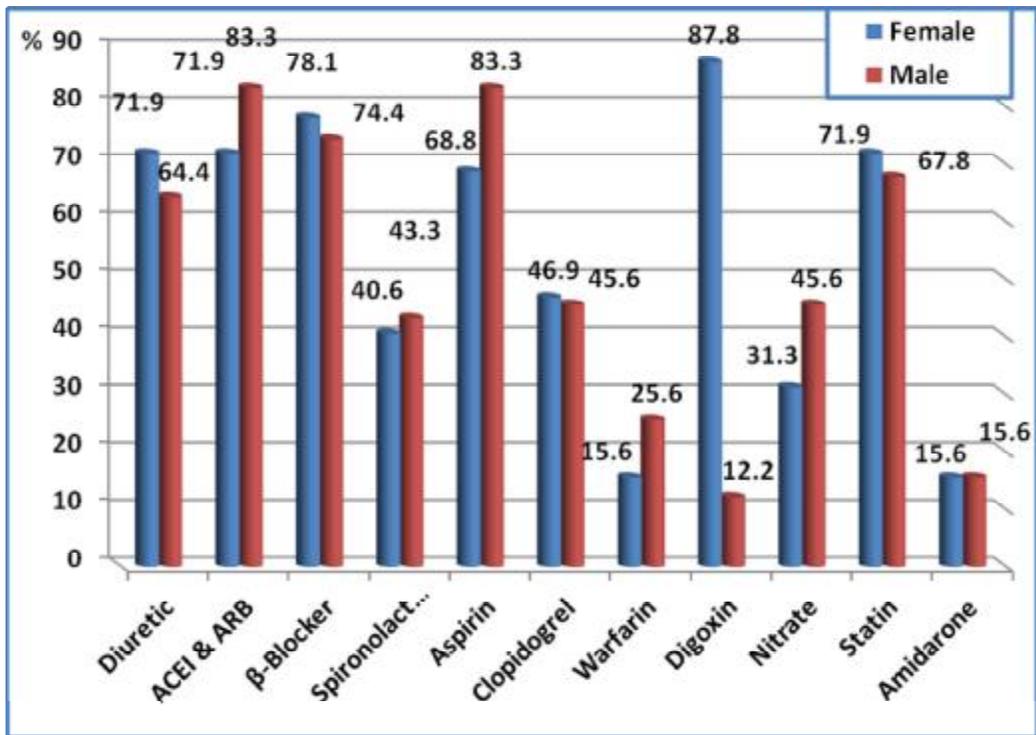


Fig.12: Distribution of patients by sex and the adherence to guidelines for managing congestive heart failure at the discharge.

Discussion:

Of 122 CHF patients, there were 90 male accounting for 73.8% and 32 female accounting for 26.2%, the male to female ratio was 2.8:1, the mean age was 61.2 ± 14 years, with minimum age 17 years and maximum age 95 years, and 80% of the patients were above 50 years of age. The mean age of 61.2 ± 14 years in our study is lower than 67.8 ± 12.8 years reported by Alqahtani M, et al in Saudi study⁽⁷⁹⁾. In another studies the mean age was higher than this study 78.4 years and 75.5 ± 11.6 ^(80,81).

In similar study more than half were males 53.1%⁽⁷⁹⁾.

While in other studies 53.1% and 46.7% of patients were females^(80,81). In another study done by members of European society of cardiology male patients were 71.2% and female patients were 28.8%.⁽⁸⁹⁾

Ischemic heart disease, was the predominant comorbid illness, accounting for 79.5% followed by hypertension and diabetes, 57.4% for each, while 24% had atrial fibrillation.

However, In another study hypertension was the predominant comorbid illness 84.9% and diabetes in 61.7%⁽⁷⁹⁾. In another studies it was documented that both diabetes mellitus and hypertension are common in Saudi Arabia,⁽⁸²⁾ and in the Middle East in general⁽⁸³⁾. While in another study hypertension and

ischaemic heart disease were present in 64.7% of patients⁽⁸⁰⁾ and in an Australian study hypertension was recorded in 62.5% of patients⁽⁸¹⁾. In another study done by members of ESC hypertension was the predominant comorbid illness 58.2%, followed by ischemic heart disease 43%, diabetes mellitus was 31.8% and atrial fibrillation was 37.6%.⁽⁸⁹⁾

Coronary artery bypass grafting recorded in 9% of our patients, was lower than 19.5% reported by Australian study⁽⁸¹⁾.

Comorbid illness were distributed similarly in male and female in most of illness were p value > 0.05.

More than half of the male patients were smokers (52.2%), this result was higher than Saudi study were only 15.3% of the patients were smoker⁽⁷⁹⁾.

Ejection fraction percentage all patients had percentage $\leq 45\%$. Mean EF% was $34.6\% \pm 8\%$, with minimum EF% (17%) and maximum (45%). In another study 76.2% of the patients had ejection fraction $\leq 45\%$.⁽⁸⁹⁾ While in another study all patients had an EF $\leq 45\%$, and 36% of patients had an EF $\leq 30\%$.⁽⁸⁴⁾

Creatinine level ranged between 0.4 to 5.5mg/dl, with mean level 1.5 ± 0.89 mg/dl. Nearly half (48.3%) of the patients had creatinine level 0.6 – 1.2mg/dl and 49.2% had level above

1.2mg/dl. In another study 18.2% of the patient had creatinine level above 1.2mg/dl.⁽⁸⁹⁾

Mean of hemoglobin level for male was 11.5 ± 1.9 g/dl, and ranged between 11.9 to 15.5g/dl, while 73.3% of them had hemoglobin level < 13 g/dl. Hemoglobin level of female was ranged between 4.2 to 12.5 g/dl, with mean level 10.1 ± 1.6 g/dl, with 87.5% had hemoglobin < 12 g/dl.

There was difference between mean hemoglobin level of male and female p value = 0.000. It had been recorded that, CHF patients were more likely to have lower hemoglobin level, and higher serum creatinine level⁽⁸⁵⁾.

ACEI & ARB, diuretic & aspirin were the highest adhered to recommendations in hospital (82%, 81.1% and 80.3% respectively), while the least adhered to recommendations were hydralazine, digoxin and warfarin(0%, 13.9% and 22.1% respectively), while β -blocker was prescribed to 73.8% of the patients. The adherence to β -blocker in our study was higher than 34% reported in Australian study,⁽⁸¹⁾ and 48% in similar study done in Nigeria.⁽⁸⁶⁾

In another study the result of adherence to guidelines in the treatment of patients with chronic heart failure were as follow 75.6% were treated with a beta-blocker, 53.4% received an

ACEI and 37.7% an ARB. While 88.9% of patients used loop diuretics, but only 30.9% patients an aldosterone antagonist⁽⁸⁷⁾. In Australian study, ACE inhibitors & ARBs were prescribed to 58.2% of patients, spironolactone 11.5%, and diuretics 72%.⁽⁸¹⁾ which is lower than that in our study where the use of ACEI & ARB in 82% of patients, spironolactone 37.7%, and diuretics 81.1%. Other common cardiovascular drugs include, digoxin 18.6%, aspirin 38.0%, warfarin 20.8%, statins 21.9%, and nitrates 13.9%⁽⁸¹⁾.

In Riyadh study the majority of patients were taking diuretics (76.8%), statins (70.7%), b-blockers (69.3%) and aspirin (62.3%)⁽⁷⁹⁾.

ACEI & ARB, aspirin & β -blocker were the highest adhered to recommendations in the discharge from hospital (80.3%, 79.5% and 75.4% respectively), while the least adhered to recommendations were hydralazine, digoxin and amidarone (0%, 11.5% and 15.6% respectively). In multi-center, retrospective study in Korea they found that the adherence to drugs at discharge was as follows: Angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor II blocker (ARB), 89.7%, beta-blocker (BB), 69.2%; and aldosterone antagonist(AA), 65.9%. Overall, 82.7% of the patients had

good guideline adherence⁽⁸⁸⁾. While in multi-centre, observational study of patients presenting to 211 Cardiology Centres of 21 European and Mediterranean countries which are members of the European Society of Cardiology (ESC). They found that in chronic HF, with reduced EF, renin–angiotensin system (RAS) blockers, beta-blockers, and mineralocorticoid antagonists (MRAs) were used in 92.2, 92.7, and 67.0% of patients, respectively.⁽⁸⁹⁾ In all drugs there were no significance difference between male and female in adherence to recommendations in hospital or at discharge from hospital, A P-value in all was > 0.05 .

Conclusions:

Majority of patients were males and aged more than 50years. Ischemic heart disease, was the predominant comorbid illness, followed by hypertension and diabetes.

ACEI & ARB, diuretic & aspirin were the highest adhered to recommendations in hospital while the least adhered to recommendations were hydralazine, digoxin and warfarin.

ACEI & ARB, aspirin & β -blocker were the highest adhered to recommendations at discharge from hospital, while the least adhered to recommendations were hydralazine, digoxin and amiodarone. Drug adherence not more than 82% in both hospital and hospital discharge, while many of recommended drugs not reaching even 50%, and some of them not used at all.

So the study revealed poor adherence to current therapeutic guidelines for CHF, particularly of those with better evidence for reducing morbidity and mortality such as spironolactone.

Recommendations:

- 1-There is need for proper education of patients and physicians to increase compliance to medications.
- 2- There is need for continuing medical education and training courses to physicians to properly implement current recommendation in the management of heart failure.
- 3- Further studies on a larger sample are required to improve the use and adherence to medications of heart failure.

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|-------------------------|-----|----|
| 5. Spironolactone | YES | NO |
| 6. Aspirine | YES | NO |
| 7. Clopidogrel | YES | NO |
| 8 . Warfarin | YES | NO |
| 9. Nitrate | YES | NO |
| 10. Digoxin | YES | NO |
| 11. Nitrate&Hydralazine | YES | NO |
| 12 . Statin | YES | NO |
| 13. Amiodarone | YES | NO |

Discharge Management :

| | | |
|--------------------------|-----|----|
| 1 . Diuretic | YES | NO |
| 2 . ACEI | YES | NO |
| 3 . ARB | YES | NO |
| 4 . β .Blocker | YES | NO |
| 5 . Spironolactone | YES | NO |
| 6 . Aspirine | YES | NO |
| 7 . Clopidogrel | YES | NO |
| 8 . Warfarin | YES | NO |
| 9 . Nitrate | YES | NO |
| 10 . Digoxin | YES | NO |
| 11 . Nitrate&Hydralazine | YES | NO |

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|----------------|-----|----|
| 12 .Statin | YES | NO |
| 13. Amiodarone | YES | NO |

ملخص

خلفية: قصور القلب المزمن (CHF) هو مشكلة صحية عامة خطيرة على الصعيد العالمي، مع دورة تقدمية وقاتلة .

الهدف: دراسة خصائص المرضى الليبيين المصابين بقصور في القلب الاحتقاني الذين تم إدخالهم في (مستشفى الهوارى العام) ودراسة مدى التزام الأطباء على المبدأ التوجيهي لإدارة المرضى الذين يعانون من قصور القلب الاحتقاني الذي أوصت به الجمعية الأوروبية لأمراض القلب،المبادئ التوجيهية التي صدرت في 2012 التي ينبغي اتباعها لتحسين نتائج هؤلاء المرضى.

المنهجية: شملت دراسة استيعادية وصفية لجميع ملفات المرضى الذين يتم إدخالهم إلى المستشفى العام الهوارى (وحدة أمراض القلب) تشخيصها على أنها قصور القلب الاحتقاني مع طرد جزء $\geq 45\%$ من ضربات القلب .

النتائج: من 122 مريضا CHF،كانت الأغلبية الذكور 73.8 %، وكان متوسط العمر 61.2 ± 14 سنة.وقد كان مرض القلب الإقفاري، هو الأغلب يليه ارتفاع ضغط الدم والسكري. تم توزيع الأمراض بالمثل في الذكور والإناث في معظم الأمراض. كانت 52.2 % من المرضى الذكور المدخنين. وكان يعني EF%. 34.6% $\pm 8\%$ ،وقد بلغت مستوى الكرياتينين في الدم فوق 1.2ملجرام / ديسي لتر في 49.2 % . كان هناك فرق بين متوسط مستوى الهيموجلوبين من الذكور والإناث. كانت ACEI وARB، مدر للبول والأسبرين أعلى استخدام في

المستشفى، في حين أن الأقل استخدام إلى التوصيات كانت هي درالازين،
الديجوكسين والوارفارين . كانت ACEI و ARB، الأسبرين وحاصرات بيتا أعلى
استعمالاً إلى التوصيات اثناء الخروج من المستشفى، في حين أن الأقل استعمالاً
إلى التوصيات كانت هيدرالازين، الديجوكسين و اميودارون. جميع الأدوية لم يكن
هناك فرق واضح بين الذكور والإناث في التمسك بالتوصيات في المستشفى أوفي
الخروج من المستشفى .

الخلاصة: كان ACEI و ARB، والأسبرين وحاصرات بيتا أعلى التزام إلى
التوصيات عند التخرج من المستشفى، في حين أن الأقل التزام إلى التوصيات
كانت الهيدرالازين، الديجوكسين و اميودارون. الالتزام بالأدوية لاتزيد عن 82%
في كل من المستشفى والخروج من المستشفى، في حين أن العديد من الأدوية
الموصى بها لاتصل حتى 50 %، ومنه ممن لم تستخدم على الإطلاق.

خصائص المريض:

• ملف رقم:

• العمر:

• الجنس:

• ارتفاع ضغط الدم نعم لا

• داء السكري نعم لا

• التدخين نعم لا

• مرض القلب الإقفاري نعم لا

• عملية زراعة الشريان التاجي الالتفافي نعم لا

• أمراض صمامات القلب نعم لا

• رأب الوعاء التاجي نعم لا

• هبوط عضلة القلب بعد الولادة نعم لا

• الرجفان الأذيني نعم لا

• طرد جزء %

• الكرياتينين

• الهيموجلوبين

الأدوية التي استخدمت في المستشفى :

1. مدر البول نعم لا

2. مانع تكون أنجيوتنسين نعم لا

3. حاصرات مستقبلات أنجيوتنسين نعم لا

4. حاصرات بيتا نعم لا

5. السبيرونولاكتون نعم لا
6. الأسبرين نعم لا
7. كلوبيدوقرل نعم لا
8. الوارفارين نعم لا
9. نترات نعم لا
10. الديجوكسين نعم لا
11. الهيدرالازين نعم لا
12. أدوية الستاتين نعم لا
13. اميودارون نعم لا

الأدوية التي استخدمت اثناء الخروج من المستشفى :

1. مدر البول نعم لا
2. مانع تكون أنجيوتنسين نعم لا
3. حاصرات مستقبلات أنجيوتنسين نعم لا
4. حاصرات بيتا نعم لا
5. السبيرونولاكتون نعم لا
6. الأسبرين نعم لا
7. كلوبيدوقرل نعم لا
8. الوارفارين نعم لا
9. نترات نعم لا
10. الديجوكسين نعم لا

11. الهيدراالا زين نعم لا

12. أدوية الستاتين نعم لا

13. اميودارون نعم لا