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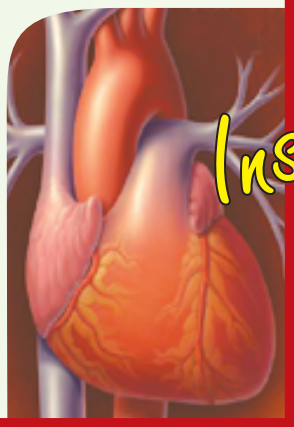

Insight HEART

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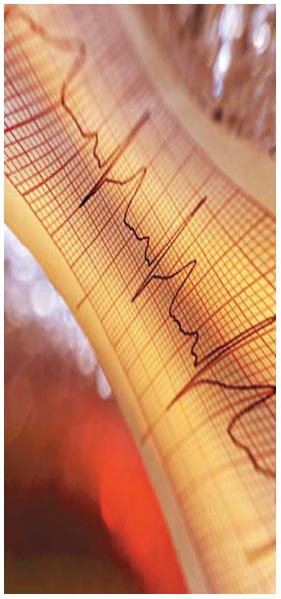

'Rule-out' Test for Heart Failure

Introduction:

B-type natriuretic peptide (BNP) is one of a family of structurally similar peptide hormones that also includes atrial natriuretic peptide (ANP). Both are secreted by cardiac myocytes. Major site of production of BNP is the left ventricle. BNP, which is produced by cleavage of a precursor protein (proBNP) into BNP and the biologically inactive peptide NT-proBNP, causes natriuresis, diuresis, vasodilatation and smooth muscle relaxation.

Plasma BNP concentrations are raised in patients with heart failure (HF), rising in line with NYHA class. 'Normal' values of BNP have yet to be fully established, although plasma BNP concentrations are known to be affected by age, gender, renal failure and drug use, particularly drugs such as diuretics and beta-blockers.

Natriuretic peptide assays

At present, there are two natriuretic peptide assays commercially available. The first is a rapid fluorescence immunoassay for BNP, which provides results within 15 min at bed side (Biosite Diagnostics). This method may be attractive in clinical situations where access to a laboratory is difficult or when a rapid result is required. The second is an electrochemiluminescent assay for measuring NT-proBNP with a processing time of only 18 min (Roche Diagnostics).

BNP & NT-proBNP testing in clinical practice

Testing for either BNP or NT-proBNP has a number of possible uses in HF practice:

- Diagnosis
- Screening for asymptomatic LV dysfunction
- Risk stratification and prognostication
- Treatment monitoring.

Diagnosis of HF

Patients in primary care/outpatient setting

- In new patients with suspected HF, BNP testing is useful as a **'rule-out' test** for HF.
- A clinical history & examination should be performed. If BNP is below the decision cut-point (normal) then HF is unlikely. If BNP concentration is raised then there is a strong possibility of HF, which should be investigated.
- For practical purposes a 'decision cut point' of 100 pg/ml give diagnostic accuracy. If BNP is <100 pg/ml in untreated patients, then HF is unlikely. The decision cut-points in Europe for NT-proBNP are 100 pg/ml for males and 150 pg/ml for women, and in the USA 125 pg/ml for both.

Patients in the emergency care setting

- In patients presenting to emergency services with dyspnoea, a history, physical examination and a chest X-ray and ECG should be undertaken together with measurement of BNP.
- If the BNP is <100 pg/ml, then HF is highly unlikely.

Screening for left ventricular systolic dysfunction

- BNP testing is not appropriate for screening asymptomatic LV systolic dysfunction.
- There may be some value in using plasma BNP to screen high risk patients, such as after MI, with diabetes or those with chronic history of poorly controlled hypertension.

BNP and NT-proBNP as prognostic indicators in HF

Measurement of plasma BNP concentrations may prove a useful addition to clinical assessment in situations where risk stratification is required. Further studies are needed to determine whether measuring plasma BNP should be used as a stand-alone test or in conjunction with scoring systems. Similarly, further work is needed to determine whether a single measurement is sufficient to predict the patient's prognosis.

BNP & NTproBNP in monitoring of HF

Rising BNP concentrations should alert the clinician to decompensation. Regular monitoring of BNP may also help to stratify the follow-up interval for more rational planning of discharge and clinical review.

European Society of Cardiology Recommendation

ESC recommended the BNP and NT-proBNP as **'rule out' test** to exclude significant cardiac diseases particularly in primary care and also some aspects of secondary care. The cost-effectiveness of the test suggests that a normal result should obviate the need for further cardiological tests.

Conclusion

BNP testing is of most value in the diagnostic arena to improve the performance of non-specialist physicians in diagnosing HF. It is not a replacement for echocardiography and full cardiological assessment, which will be required with an elevated BNP. For cardiologists, measurement of BNP level is helpful in guiding therapy and monitoring of HF, particularly in alerting clinicians to decompensation.

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Chronic Heart Failure : A Review Update

DEFINITION

Definition of heart failure includes

I. Symptoms of heart failure (at rest or during exercise)

and

II. Objective evidence (preferably by echocardiography) of cardiac dysfunction (systolic and/or diastolic) (at rest)

and

(in cases where the diagnosis is in doubt)

III. Response to treatment directed towards heart failure

Heart failure should never be the only diagnosis.

Acute vs. chronic heart failure

The term acute heart failure (AHF) is often used exclusively to mean de novo AHF or decompensation of chronic heart failure (CHF) characterized by signs of pulmonary congestion, including pulmonary oedema. CHF often punctuated by acute exacerbations, is the most common form of heart failure.

Diastolic vs. systolic heart failure

Diastolic and systolic heart failures should not be considered as separate patho-physiological entities. Diastolic heart failure is often diagnosed when symptoms and signs of heart failure occur in the presence of a PLVEF (Preserved Left Ventricular Ejection Fraction) at rest. PLVEF is more common in elderly & women, in whom systolic hypertension and myocardial hypertrophy with fibrosis are contributors to cardiac dysfunction.

Heart Failure as a Progressive Disorder

Left ventricular dysfunction begins with injury to or stress on the myocardium and is a progressive process. The manifestation of such progression is a change in the geometry of the left ventricle such that the chamber dilates, hypertrophies, and becomes spherical - referred as cardiac remodelling. The evolution and progression of HF characterized by 4 stages (Fig. 1).

DIAGNOSIS IN CLINICAL PRACTICE

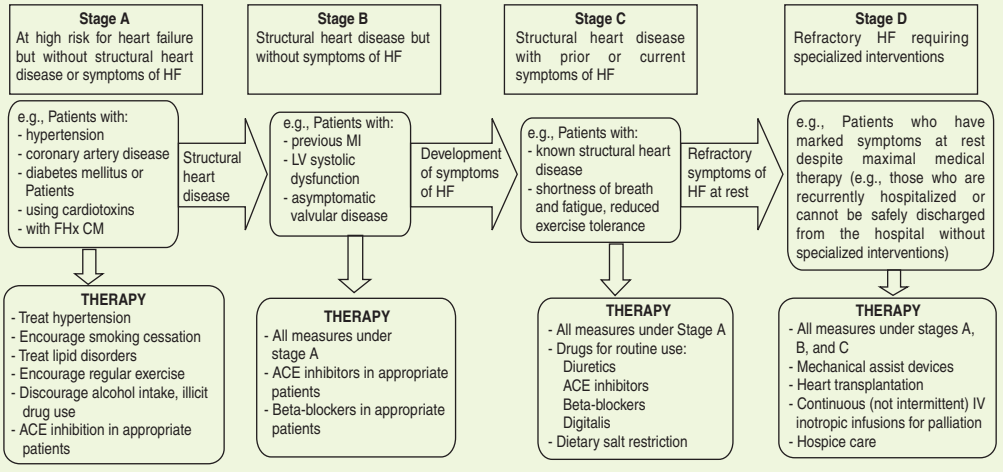
Symptoms and signs

Breathlessness, ankle swelling, and fatigue are the characteristic symptoms and signs of heart failure but may be difficult to interpret, particularly in elderly, obese and women. It should be interpreted carefully and different modes (e.g. effort and nocturnal) should be assessed. Fatigue is also an essential symptom in heart failure. The origins of fatigue are complex including low cardiac output, peripheral hypoperfusion, skeletal muscle deconditioning, and confounded by difficulties in quantifying this symptom. Peripheral oedema, raised venous pressure, and hepatomegaly are the characteristic signs of congestion of systemic veins.

Structural abnormality or cause of heart failure:

A complete history and physical examination are the first steps in evaluating the cause responsible for the development of HF. Direct inquiry may reveal evidence of myocardial infarction, valvular disease, or congenital heart disease, whereas examination may suggest the presence of cardiac enlargement, murmers or a third heart sound. Physicians should inquire about a history of hypertension; diabetes; hypercholesterolemia; coronary, valvular or peripheral vascular disease, rheumatic fever; chest irradiation; exposure to cardiotoxic agents; illict drug use; alcohol consumption; and exposure to sexually transmitted diseases. The history and physical examination should include consideration of noncardiac diseases including thyroid or collagen-vascular disease, bacterial or parasitic infection and pheocromocytoma. A detailed family history should be obtained.

Figure 1. Stages in the evolution of heart failure and recommended therapy by stage.



FHx CM indicates family history of cardiomyopathy; MI, myocardial infarction; LV, left ventricular; and IV, intravenous.

Symptoms and the severity of heart failure

There is a poor relationship between symptoms and the severity of cardiac dysfunction. The New York Heart Association (NYHA) classification is in widespread use in this regard (Table 1).

Table 1 New York Heart Association classification

Class I No limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea, or palpitations.

Class II Slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations, or dyspnoea.

Class III Marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms.

Class IV Unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity.

Electrocardiogram

Abnormal ECG has little predictive value for the presence of heart failure. The presence of pathological Q-waves may suggest MI as the cause of cardiac dysfunction. A QRS width >120 ms suggests that cardiac dyssynchrony may be present and a target for treatment. A normal ECG suggests that the diagnosis of CHF should be reviewed.

The chest X-ray

Chest X-ray is the initial diagnostic work-up in heart failure to detect cardiomegaly and pulmonary congestion.

Haematology and biochemistry

CBC, S-electrolytes, S-creatinine, S-glucose, S-hepatic enzymes, and urinalysis should be done routinely. In acute exacerbations, acute MI is excluded by specific enzyme analysis.

Natriuretic peptides (Mentioned in page 1)

Echocardiography

The most important measurement of ventricular function is the left ventricular ejection fraction (LVEF) for distinguishing cardiac systolic dysfunction from preserved systolic function. Transthoracic Doppler Echocardiography (TDE) is rapid, safe, and widely available. This test determines whether the abnormality is pericardial, myocardial or valvular, and if myocardial, whether the dysfunction is primarily systolic or diastolic.

Diagnostic criteria of diastolic dysfunction

A diagnosis of primary diastolic heart failure requires three conditions to be simultaneously satisfied: (1) presence of signs or symptoms of CHF, (2) presence of normal or only mildly abnormal left ventricular systolic function (LVEF > 45-50%), and (3) evidence of abnormal left ventricular relaxation, diastolic distensibility, or diastolic stiffness. Furthermore, it is essential to exclude pulmonary disease.

The three filling patterns 'impaired relaxation' (with a decrease in peak transmitral E-velocity, a compensatory increase in the atrial-induced (A) velocity and therefore a decrease in the E/A ratio.), 'pseudonormalized filling' (the E/A ratio and the deceleration time are normal), and 'restrictive filling' (an elevated peak E-velocity, a short E-deceleration time, and a markedly increased E/A ratio) represent mild, moderate, and severe diastolic dysfunction, respectively.

Repeated echocardiography recommended in follow-up of HF only when clinical status suggesting significant improvement or deterioration in cardiac function.

Cardiac catheterization

Coronary angiography should be considered in:

- Patients with acute or acutely decompensated CHF and in patients with severe heart failure (shock or acute pulmonary oedema) not responding to initial treatment.
- Patients with angina pectoris or any other evidence of myocardial ischaemia if they are not responding to appropriate anti-ischaemic treatment.
- Patients with refractory heart failure of unknown aetiology.
- Patients with evidence of severe mitral regurgitation or aortic valve disease.

PROGNOSIS

The problem of defining prognosis in heart failure is complex. Half of patients carrying a diagnosis of heart failure will die within 4 years, and in patients with severe heart failure >50% will die within 1 year.

TREATMENT

Aims of treatment in heart failure

(i) Prevention- a primary objective

a. Prevention and/or controlling of diseases leading to cardiac dysfunction and heart failure,

b. Prevention of progression to heart failure once cardiac dysfunction is established.(See Fig-1)

(ii) Maintenance or improvement in quality of life

(iii) Improved survival

Management of chronic heart failure

Management outline & treatment option is given table 2. It includes general advice, non-pharmacological measures, pharmacological therapy, mechanical devices, and surgery.

Table 2 Management outline & Treatment options

Management outline

Establish that the patient has heart failure

Ascertain presenting features: pulmonary oedema, exertional breathlessness, fatigue, peripheral oedema

Assess severity of symptoms

Determine aetiology of heart failure

Identify precipitating and exacerbating factors

Identify concomitant diseases

Estimate prognosis

Assess complicating factors

Counsel patient and relatives

Choose appropriate management

Monitor progress and manage accordingly

Treatment options

Non-pharmacological management
- General advice and measures
- Exercise and exercise training

Pharmacological therapy
- ACE-inhibitors
- Diuretics
- Beta-adrenoceptor antagonists
- Aldosterone receptor antagonists
- Angiotensin receptor antagonists
- Cardiac glycosides
- Vasodilator agents (nitrates/hydralazine)
- Positive inotropic agents
- Anti-coagulation
- Anti-arrhythmic agents
- Oxygen

Devices and surgery
- Revascularization
- Other forms of surgery (mitral valve repair)
- Bi-ventricular (multi-site) pacing
- Implantable cardioverter defibrillator (ICD)
- Heart transplantation, ventricular assist devices

Non-pharmacological management

Educating patients and family

General information about CHF should be given.

Weight monitoring

Patients are advised to weigh on a regular basis to monitor weight gain (as part of a regular daily routine, for instance after morning toilet) and, in case of a sudden unexpected weight gain of >2 kg in 3 days, to alert a physician or adjust their diuretic dose accordingly.

Dietary measures :

Moderate sodium restriction in advisible. A fluid restriction of 1.5-2 L/day is advised in advanced heart failure with or without hyponatremia. Weight reduction in obese patients is advisible. Smoking cessation aids should be actively encouraged including nicotine replacement therapies.

Immunization for influenza should be used.

Drug counselling

Self-management (when practical) of the dose of the diuretic, based on changes in symptoms and weight, should be encouraged. Within pre-specified & individualized limits, patients can adjust their diuretics.

Drugs to avoid or beware

(i) NSAIDS and coxibs (ii) Class I anti-arrhythmic agents (iii) Calcium antagonists (verapamil, diltiazem, & short-acting dihydropyridine derivatives) (iv) Tricyclic anti-depressants (v) Corticosteroids (vi) Lithium

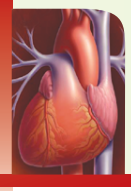
Rest, exercise, and exercise training

In AHF or destabilization of CHF, physical rest or bed rest is recommended. Patients (NYHA class II-III) should be encouraged & advised on how to carry out daily physical and leisure time activities that do not induce symptoms.

Pharmacological therapy

Angiotensin Converting Enzyme (ACE) inhibitors

- Recommended as first-line therapy in patients with a reduced left ventricular systolic function expressed as a subnormal ejection fraction, i.e. <40-45% with or without symptoms.
- Asymptomatic patients with a documented left ventricular systolic dysfunction should be treated with an ACE-inhibitor to delay or prevent the development of heart failure. ACE-inhibitors also reduce the risk of myocardial infarction and sudden death in this setting.
- Improves survival, symptoms, functional capacity, and reduces hospitalization in moderate and severe heart failure and left ventricular systolic dysfunction.
- Should be given as the initial therapy in the absence of fluid retention. In patients with fluid retention, ACE-inhibitors should be given together with diuretics.
- Should be given in patients with a recent or remote history of MI regardless of ejection fraction.



- Should be uptitrated to the dosages shown to be effective in the large, controlled trials in heart failure , and not titrated based on symptomatic improvement alone.

Table 3 The recommended procedure for starting an ACE-inhibitor or an angiotensin receptor blocker

Review the need for and dose of diuretics and vasodilators.

Avoid excessive diuresis before treatment. Consider reducing or withholding diuretics, if being used for 24 h.

It may be advisable to start treatment in the evening, when supine. Start with a low dose (Table 5) and build-up to maintenance dosages shown to be effective in large trials.

If renal function deteriorates substantially, stop treatment.

Avoid potassium-sparing diuretics during initiation of therapy.

Avoid NSAIDs and coxibs.

Check blood pressure, renal function, and electrolytes 1 - 2 weeks after each dose increment, at 3 months, and subsequently at 6 regular monthly intervals.

The following patients should be referred for specialist care:

Cause of heart failure unknown
Systolic blood pressure <100 mmHg
Serum creatinine >150 µmol/L
Serum sodium <135 mmol/L
Severe heart failure
Valve disease as primary cause

Table 4 ACE-inhibitor dose ranges for for heart failure

Drug	Initiating dose	Maintenance dose
Captopril	6.25 mg t.i.d.	25-50 mg t.i.d.
Enalapril	2. 5 mg daily	10 mg b.i.d.
Lisinopril	2.5 mg daily	5-20 mg daily
Ramipril	1.25-2. 5 mg daily	2.5-5 mg b.i.d.
Trandolapril	1 mg daily	4 mg daily

Diuretics

Loop diuretics, thiazides, and metolazone

- Diuretics are essential for symptomatic treatment when fluid overload is present and manifest as pulmonary congestion or peripheral oedema. The use of diuretics results in rapid improvement of dyspnoea and increased exercise tolerance.
- Diuretics should always be administered in combination with ACE-inhibitors and beta-blockers if tolerated.

Table 5 Diuretics

Initial diuretic treatment.

Loop diuretics or thiazides. Always administered in addition to an ACE-inhibitor.

If GFR <30 mL/min, do not use thiazides, except as therapy prescribed synergistically with loop diuretics

Insufficient response:

Increase dose of diuretic

Combine loop diuretics and thiazides

With persistent fluid retention: administer loop diuretics twice daily

In severe heart failure add metolazone with frequent measurement of creatinine and electrolytes

Potassium-sparing diuretics: triamterene, amiloride and spironolactone

Use only if hypokalaemia persists after initiation of therapy with ACE, inhibitors and diuretics

Start one-week low-dose administration; check serum potassium and creatinine after 5-7 days and titrate accordingly. Recheck every 5-7 days until potassium values are stable

GFR = glomerular filtration rate.

Aldosterone receptor antagonists

- Recommended in addition to ACE-inhibitors, beta-blockers & diuretics in advanced HF (NYHA III-IV) with systolic dysfunction to improve survival and morbidity.
- Recommended in addition to ACE-inhibitors and beta-blockers in HF after MI with left ventricular systolic dysfunction and signs of HF or diabetes to reduce mortality and morbidity.

Table 6 Administration of aldosterone antagonists

- Consider whether a patient is in severe heart failure (NYHA III-IV) despite ACE-inhibition/diuretics.
- Check serum potassium (<5.0 mmol/L) and creatinine (<250 (jimol/L).
- Add a low dose (spironolactone 12.5-25 mg, eplerenone 25 mg) daily.
- Check serum potassium and creatinine after 4-6 days.
- If at any time serum potassium 5-5.5 mmol/L, reduce dose by 50%. Stop if serum potassium >5.5 mmol/L.
- If after 1 month symptoms persist and normokalaemia exists, increase to 50 mg daily. Check serum potassium/ creatinine after 1 week.

Beta-adrenoceptor antagonists

- Should be considered for the treatment of all patients (in NYHA class II-IV) with stable, mild, moderate, & severe HF from ischaemic or non-ischaemic cardiomyopathies and reduced LVEF on standard

treatment, including diuretics, ACE-inhibitors, unless there is a contraindication.

- Reduces hospitalizations, improves the functional class and leads to less worsening of heart failure.
- In left ventricular systolic dysfunction, with or without symptomatic HF, following an acute MI long-term beta-blockade is recommended in addition to ACE inhibition to reduce mortality.
- Only bisoprolol, carvedilol, metoprolol succinate and nebivolol can be recommended in CHF.

Table 7 Procedure for starting a beta-blocker

I Patients should be on a background therapy with ACE inhibition, if not contraindicated.

II The patient should be in a relatively stable condition, without the need of intravenous inotropic therapy and without signs of marked fluid retention.

III Start with a very low dose and titrate up to maintenance dosages shown to be effective in large trials. The dose may be doubled every 1-2 weeks if the preceding dose was well tolerated. Most patients can be managed as out-patients.

IV Transient worsening failure, hypotension, or bradycardia may occur during the titration period or thereafter.

a. Monitor the patient for evidence of HF symptoms, fluid retention, hypotension, and symptomatic bradycardia.

b. If worsening of symptoms, first increase the dose of diuretics, or ACE-inhibitor; temporarily reduce the dose of beta-blockers if necessary.

c. If hypotension, first reduce the dose of vasodilators; reduce the dose of the beta-blocker if necessary.

d. Reduce/discontinue drugs that may lower heart rate in presence of bradycardia; reduce dose of beta-blocker if needed, discontinue only if clearly necessary.

e. Always consider the reintroduction and/or uptitration of the beta-blocker when the patient becomes stable.

If inotropic support is needed to treat a decompensated patient on beta-blockade, phosphodiesterase inhibitors should be preferred because their haemodynamic effects are not antagonized by beta-blocker agents.

Following patients should be referred for specialist care:

a. Severe heart failure Class III/IV
b. Unknown aetiology
c. Relative contraindications: asymptomatic bradycardia, and/or low blood pressure
d. Intolerance to low doses
e. Previous use of beta-blocker and discontinuation because of symptoms
f. Suspicion of asthma or severe pulmonary disease

Contraindications to beta-blockers in heart failure

- Asthma bronchiale
- Severe bronchial disease
- Symptomatic bradycardia or hypotension

Table 8 Dose and titration of beta-blocking agents

Beta-blocker	First dose (mg)	Increments (mg/day)	Target dose (mg/day)	Titration period
Bisoprolol	1.25	2.5, 3.75, 5, 7.5, 10	10	Weeks- month
Metoprolol Sunccinate CR	12.5 / 25	25, 50, 100, 200	200	Weeks- month
Carvedilol	3.125	6.25, 12.5, 25, 50	50	Weeks- month
Nebivolol	1.25	2.5, 5, 10		Weeks- month

Angiotensin II receptor blockers (ARBs)

For patients with left ventricular systolic dysfunction:

- ARBs can be used as an alternative to ACE inhibition in symptomatic patients intolerant to ACE-inhibitors to improve morbidity and mortality .
- ARBs and ACE-inhibitors seem to have similar efficacy in CHF on mortality and morbidity. In acute myocardial infarction with signs of heart failure or left ventricula dysfunction ARBs and ACE-inhibitors have similar or equivalent effects on mortality.
- ARBs can be considered in combination with ACE-inhibitors in patients who remain symptomatic, to reduce mortality and hospital admissions.

Cardiac glycosides

- Cardiac glycosides are indicated in atrial fibrillation and any degree of symptomatic heart failure, whether or not left ventricular dysfunction is the cause. Cardiac glycosides slow the ventricular rate, which improves ventricular function and symptoms.
- Digoxin has no effect on mortality but may reduce hospitalizations and, particularly, worsening heart failure hospitalizations, in the patients with heart failure caused by left ventricular systolic dysfunction and sinus rhythm.
- The usual daily dose of oral digoxin is 0.125-0.25 mg if serum creatinine is in the normal range (in the elderly 0.0625-0.125 mg, occasionally 0.25 mg).

Nitrates

Nitrates may be used for the treatment of concomitant angina or relief of dyspnoea. Evidence that oral nitrates improve symptoms of heart failure chronically or during an acute exacerbation is lacking.

Anti-arrhythmics

Anti-arrhythmic drugs other than beta-blockers are generally not indicated in patients with CHF.

Beta-blockers may also be indicated alone or in combination with amiodarone or non-pharmacological therapy in the management of sustained or non-sustained ventricular tachy-arrhythmias.

Amiodarone is the only anti-arrhythmic drug without clinically relevant negative inotropic effects. Amiodarone is effective against most supraventricular and ventricular arrhythmias. It may restore and maintain sinus rhythm in patients with heart failure and atrial fibrillation even in the presence of enlarged left atria, or improve the success of electrical cardioversion and amiodarone is the preferred treatment in this condition.

Surgery and devices

Revascularization

There are no data to support the use of revascularization procedures for the relief of heart failure symptoms.

Pacemakers

Resynchronization therapy using bi-ventricular pacing can be considered in patients with reduced ejection fraction and ventricular dyssynchrony.

Implantable cardioverter defibrillators (ICD)

ICD in combination with bi-ventricular pacing considered, those who remain symptomatic with severe heart failure NYHA class III-IV with LVEF < 35% and QRS duration > 120 ms to improve mortality or morbidity.

Heart replacement therapies:

Heart transplantation

Heart transplantation is for end stage heart failure to significantly increase survival, exercise capacity, return to work and quality of life.

Ventricular assist devices and artificial heart

For bridging to transplantation, acute severe myocarditis, and in some patients permanent haemodynamic support .

Choice and timing of pharmacological therapy

The choice of pharmacological therapy in the various stages of heart failure is displayed in Table 9.

Table 9 CHF-choice of pharmacological therapy in left ventricular systolic dysfunction

	ACE-inhibitor	Angiotensin receptor blocker	Diuretic	Beta- blocker	Aldosterone antagonists	Cardiac glycosides
Asymptomatic LV dysfunction	Indicated	If ACE intolerant	Not indicated	Post MI	Recent MI	With atrial fibrillation
Symptomatic HF (NYHA II)	Indicated	Indicated with or without ACE-inhibitor	Indicated if fluid retention	Indicated	Recent MI	(a) when atrial fibrillation (b) when improved from more severe HF in sinus rhythm
Worsening HF (NYHAIII-IV)	Indicated	Indicated with or without ACE-inhibitor	Indicated, combination of diuretics	Indicated (under specialist care)	Indicated	Indicated
End-stage HF (NYHA IV)	Indicated	Indicated with or without ACE-inhibitor	Indicated, combination of diuretics	Indicated (under specialist care)	Indicated	Indicated

Most frequent causes of worsening HF

Non-cardiac :

Non-compliance to the prescribed regimen, Recently co-prescribed drugs, Infection, Alcohol abuse, Renal dysfunction (excessive use of diuretics), Pulmonary embolism, Hypertension, Thyroid dysfunction, Anaemia.

Cardiac:

Atrial fibrillation, Other supraventricular or ventricular arrhythmias, Bradycardia, Myocardial ischaemia (frequently symptomless), including MI, Appearance or worsening of MR or TR, Excessive preload reduction (e.g. due to diuretics + ACE-inhibitors/nitrates).

Heart failure with preserved LV ejection fraction

The percentage of patients hospitalized with heart failure-like symptoms and PLVEF may be as high as 35-45%.

Pharmacological therapy of heart failure with PLVEF or diastolic dysfunction

(1) ACE-inhibitors may improve relaxation and cardiac distensibility directly and may have long-term effects through their anti-hypertensive effects and regression of hypertrophy and fibrosis.

(2) Diuretics should be used when fluid-overload is present.

(3) Beta-blockade could be instituted to lower heart rate and increase the diastolic filling period.

(4) Verapamil-type calcium antagonists may be used for the same reason.

(5) A high dose of an ARB may reduce hospitalizations.

References : 1. ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult, 2001
2. Executive summary of the guidelines on the diagnosis and treatment of acute heart failure; The Task Force on Acute Heart Failure of the European Society of Cardiology, 2005

Insight HEART
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Cardiology News

Even Low Albumin Excretion Levels Tied to Cardiovascular Risk

Urinary albumin excretion of more than 5 mcg/min is associated with coronary heart disease and death, prompting researchers to call for a new definition of microalbuminuria. In future risk assessment in hypertensive individuals, measurement of microalbuminuria has to be included. Microalbuminuria has been defined as urinary albumin excretion of 20-200 mcg/min. After adjustment for factors including blood pressure, diabetes and body mass index, the relative risk of coronary heart disease and death was about doubled in subjects with higher urinary albumin excretion.

Source: Hypertension 2005;46:33-37.

Higher Mortality Seen After Morphine Used to Treat Acute Coronary Syndrome

Patients with unstable angina or non-ST-segment elevation acute MI fare worse when they are treated with intravenous morphine - standard practice when pain is not relieved with nitroglycerin - according to results of a multicenter study. However, the possibility that patients treated with morphine are simply sicker to begin with cannot be ruled out. It is suggested that the worse outcomes are related to morphine's potentially harmful effects such as hypotension, bradycardia and respiratory depression. These deleterious effects can result in decreased myocardial oxygen delivery, decreased arterial oxygenation, increase in arterial carbon dioxide and perhaps even cerebral hypoperfusion. Definite harm of morphine can only be confirmed by a randomized trial.

Source: Am Heart J 2005;149:945-946,1043-1049.

Low-Dose Oral Contraceptives & Cardiovascular Disease Risk

Low-dose oral contraceptives increase the risk of both cardiac and vascular arterial events. The use of low-dose oral contraceptives was associated with a doubling of the risk of cardiovascular outcomes (MI or ischemic stroke). Both second- and third-generation oral contraceptives were associated with increased risk of ischemic stroke but the association between third-generation oral contraceptive and MI proved nonsignificant. The modern use of low-dose oral contraceptives, limited to healthy women and restricted in time, should not increase noticeably the incidence of these adverse outcomes, which might be outweighed by the benefits of contraception. However, prolonged exposure to low-dose oral contraceptives in a population at higher risk may significantly increase the incidence of cardiovascular outcomes.

J Clin Endocrinol Metab 2005;90:3863-3870.

Subclinical UTIs May Trigger Acute Coronary Syndromes

Acute coronary syndromes (ACS) may be precipitated by subclinical urinary tract infections (UTI), perhaps through inflammatory disruption of atherosclerotic plaque. A number of reports have implicated infectious agents, upper respiratory tract infections and inflammation in the development of atherosclerotic complications. UTI leads to cytokine activation that may underlie incident ACS by inducing inflammation and promoting plaque instability and thrombosis formation. Further research, including relationships with other bacterial and viral infections should be done.

Source: Am Heart J 2005;149:1062-1065.

Editorial Note

Dear Doctor

We are happy to present the second issue of *"Insight Heart"*. It is a small endeavor from us to provide you compiled & updated information on cardiovascular diseases and its management. This issue is focused on *"Heart Failure"*. We will appreciate your thoughtful comments on the Newsletter to enrich the publication.

Thanks and regards.