Management and prevention of heart failure in dialysis patients

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INTRODUCTION

Patients with end-stage kidney disease requiring dialysis are at increased risk for development of heart failure (HF).

Factors that may contribute to HF in the dialysis patient : fluid overload, poorly-controlled hypertension increasing afterload, left ventricular (LV) diastolic dysfunction (often associated with LV hypertrophy), arterial stiffness , Lv systolic dysfunction, uremic toxin accumulation, anemia, and valvular heart disease,

- A high-output state caused by shunting through hemodialysis arteriovenous access can also precipitate HF, particularly in patients with underlying ventricular dysfunction.

- **Ventricular dysfunction** and **cardiovascular drugs** can also reduce hemodynamic reserve, making the patient more vulnerable to episodes of hypotension during dialysis

- **HF is a clinical diagnosis based upon identification of symptoms (eg, dyspnea and fatigue) that are caused by impairment of ventricular filling ejection of blood**

Major
Paroxysmal nocturnal dyspnea
Orthopnea
Elevated jugular venous pressure
Pulmonary rales
3rd heart sound
Cardiomegaly on chest radiograph
Pulmonary edema on chest radiograph
Weight loss ≥4.5 kg in 5 days in response to treatment of presumed heart failure*
Minor
Bilateral leg edema
Nocturnal cough
Dyspnea on ordinary exertion
Hepatomegaly
Pleural effusion
Tachycardia (heart rate ≥120 beats/min)
Weight loss ≥4.5 kg in 5 days
Diagnosis
The diagnosis of heart failure requires that **2 major or 1 major and 2 minor criteria** cannot be attributed to another medical condition.

heart failure classification:

American College of Cardiology/American Heart Association (ACC/AHA) stages of HF:

- stage A :at high risk for HF but without structural heart disease or symptoms of HF, no symptom
- stage B :structural heart disease without current or prior signs or symptoms of HF, Dyspnea on exertion
- stage C :structural heart disease with prior or current symptoms of HF, Dyspnea with activities of daily life (ADLs)
- stage D: refractory HF requiring specialized interventions Dyspnea at rest

Functional classification

- The three elements of the proposed HF staging system for patients with ESKD are:

- ✓ Standardized echocardiographic evidence of structural and/or functional cardiac abnormalities
- ✓ Dyspnea occurring in the absence of primary lung disease, including isolated pulmonary hypertension (ie, not due to elevation in pulmonary capillary wedge pressure)
- ✓ Response of congestive symptoms to renal replacement therapy (RRT)/ultrafiltration(uf)

Echocardiography criteria*

LVH (LV mass index >110 g/m^2 for women and >130 g/m^2 for men or >47 g/m$^{2.7}$ for women and >50 g/m$^{2.7}$ for men). Latter measure is LV mass calculated by the area-length method and indexed to height [1-3].
Increased LV volume index >86 mL/m^2 diastolic or >37 mL/m^2 systolic.
Left atrial enlargement (left atrial volume index ≥34 mL/m^2).
Diastolic dysfunction (ASE grade ≥2).
Moderate to severe mitral or aortic valvular disease (stenosis or regurgitation).
RV systolic dysfunction by accepted criteria (eg, TAPSE <17 mm).
LV ejection fraction ≤45%.
Regional wall motion abnormality of LV (>10% of the myocardium).

LVH: left ventricular hypertrophy; LV: left ventricle; ASE: American Society of Echocardiography; RV: right ventricle; TAPSE: tricuspid annular plane systolic excursion.

* At least one (of eight) listed criteria must be abnormal to fulfill the definition of echocardiographic evidence of heart disease.

The ADQI heart failure in ESKD classification

includes the following classes, ranging from least to most severe symptoms:

- Class 1 – Asymptomatic patients with echocardiographic evidence of heart disease
- Class 2R – Dyspnea on exertion that is relieved with RRT/UF to a NYHA class I level
- Class 2NR - Dyspnea on exertion that CANNOT be relieved with RRT/UF to a NYHA class I level
- Class 3R – Dyspnea with activities of daily life (ADLs) that is relieved by RRT/UF to a NYHA class II level
- Class 3NR – Dyspnea with ADLS that CANNOT be relieved by RRT/UF to a NYHA class II level
- Class 4R – Dyspnea at rest that is relieved by RRT/UF to a NYHA Class III level
- Class 4NR - Dyspnea at rest that CANNOT be relieved by RRT/UF to a NYHA Class III level

ASSESSMENT OF CLINICAL STATUS

- The evaluation should address the following key questions, which relate to management and prevention of HF:

  - What type and cause of HF? HF with reduced left ventricular ejection fraction [HFrEF; LVEF ≤40 percent], HF with midrange ejection fraction [HFmrEF; LVEF 41 to 50 percent], or HF with preserved ejection fraction [HFpEF; LVEF >50 percent]).
  - Presence/absence of asymptomatic LV systolic dysfunction (LVEF ≤40 percent).
  - Identification contributing factors (eg, hypertension).

- Common causes of HF in dialysis patients include ischemic heart disease and hypertensive heart disease

APPROACH TO MANAGEMENT

- The approach to management or prevention of HF in the dialysis patient varies depending upon the clinical presentation

- For all dialysis patients, general measures to manage or prevent HF apply .
- For dialysis patients without HF with left ventricular systolic dysfunction (ALVSD; left ventricular ejection fraction [LVEF] ≤40 percent), specific measures apply.
- For dialysis patients with HF: Additional general measures (eg, HF self-management, palliative services as appropriate) apply to all dialysis patients with HF

Treatment goals

- General measures to prevent or treat HF in dialysis patients are aimed at optimizing functional status and improving clinical outcomes (prolong survival and reduce cardiovascular event rates)

- there is interest in left ventricular hypertrophy (LVH) regression as a surrogate outcome(available data have not established that specifically targeting LVH improves outcomes)

- progression of LVH is associated with increased risk of HF cardiovascular death ,and all-cause mortality

GENERAL MEASURES

- General measures for all dialysis patients to prevent or treat HF: monitoring for the development or worsening of HF and management of contributing or concurrent conditions (including hypertension, coronary heart disease).

- following measures that may improve clinical outcome also cause regression of LVH: control of hypertension, mineralocorticoid receptor antagonist (MRA) therapy, correction of anemia, more frequent hemodialysis, and kidney transplantation

Specific measures

to manage HF are indicated for the following groups:

- For patients with HF with reduced ejection fraction (HFrEF; LVEF ≤40 percent)
- For patients with HF with mid-range ejection fraction (LVEF 41 to percent) 50 percent)
- For patients with HF with preserved ejection fraction (HFpEF; LVEF >50 percent)
- In dialysis patients with arteriovenous access who have HF
- Patients with HF caused by valve disease

Monitoring

- Dialysis patients with HF should be monitored by routine serial (eg, at least every month) review of symptoms and signs, functional classification and medications.
- The frequency of monitoring by clinicians will need to be individualized based on factors such as clinical stability and duration of HF
- Care should be taken to avoid drugs that may cause worsening HF
- Patients with worsening symptoms or signs of HF should undergo clinical evaluation with follow-up echocardiography as clinically appropriate.

Management of contributing conditions

- Conditions that may cause or exacerbate HF in patients with ESKD include the following:

- volume overload: Renal failure with accompanying oliguria or anuria contributes to volume overload
- Hypertension
- Anemia
- Atrial and ventricular arrhythmias occur in patients with HF and may cause or exacerbate HF
- Valvular heart disease, particularly aortic stenosis,high-output states (eg, from shunting via the arteriovenous access)

Control of volume overload

- A key component of therapy to prevent or manage HF in dialysis patients is treatment of volume overload with diuretic therapy (if there is significant urine output) and dialysis.

- For dialysis patients with HF who have significant urine output, loop diuretic therapy is helpful to increase urine output and sodium excretion and decrease the need for volume removal with dialysis.

- Dialysis patients receiving diuretics should be monitored for hearing loss and skin changes.

- Diuretics should be stopped when urine output becomes negligible.

Management of renal failure

- Management of renal failure in patients with ESKD includes identification and preparation of patients who require renal replacement therapy (RRT), choice of dialysis modality, optimizing the dialysis prescription, and identification candidates for renal transplantation.

Modality

- dialysis modality selection is based upon many factors including the patient's ability and willingness to perform peritoneal dialysis.
- HF patients with ESKD may potentially benefit more from peritoneal dialysis than conventional thrice-weekly hemodialysis.
- Peritoneal dialysis avoids the risks associated with arteriovenous fistula creation and allows better control of volume status via daily ultrafiltration
- In practice, patients with HF are often unable to perform peritoneal dialysis and lack the required support at home, so they frequently default to in-center hemodialysis.

Optimizing dialysis prescription

- Optimal management of dialysis includes optimizing volume status, optimizing the frequency and duration of dialysis, and additional measures to reduce the risk of intradialytic hypotension.

- Optimizing volume status: is an important goal in the management of HF in hemodialysis patients

- **According (KDOQI) guidelines that the maintenance of euvolemia is a major component of effective treatment in such patients**

- **Euvolemia may be defined as a state of normal biventricular filling pressure (right atrial pressure and pulmonary capillary wedge pressure) or as the lowest filling pressure that can be achieved without compromising cardiac output, without significant extravascular fluid accumulation**

- In clinical settings, the term euvolemia is often used interchangeably with "being at the prescription target weight," which guides the amount of ultrafiltration

- The optimal target weight is usually determined empirically by trial and error ("probing"). Using a trial-and-error approach, the target weight is set just above the weight at which unacceptable symptoms, such as cramping, nausea, vomiting, or hypotension, occur.

- Although bioimpedance is used by some nephrologists to assess extravascular volume, its use is controversial, and its role is uncertain

- **The flactuated nature of fluid volume in relation to the hemodialysis schedule makes the maintenance of euvolemia difficult .specially in anuric patients**

- **A balance between tolerability of hypovolemia and hypervolemia needs to be sought in individual patients**

- **In Many chronic hemodialysis patients are, hypotension during dialysis is common due to attempting to achieve post dialysis euvolemia, especially when interdialytic fluid gain is large**

- **The screening echocardiogram enables assessment of intravascular and intracardiac volumes, ventricular function, and any valve disease.**

- In most clinical settings, filling pressures are not directly measured by invasive hemodynamic assessment, and instead noninvasive methods are used (eg, assessment of jugular venous pressure, peripheral edema, third heart sound, lung rales, and echocardiographic finding such as inferior vena cava diameter and collapsibility)

- When volume status can be accurately assessed by noninvasive assessment (which may include echocardiography), invasive hemodynamic assessment is not required.

- when the volume status of a patient remains uncertain (eg, if the patient has persistent HF symptoms despite apparently optimized volume status), referral to a cardiologist is suggested to evaluate the risks and benefit of invasive hemodynamic assessment

Optimizing the duration or frequency of dialysis.

- **Greater duration or frequency of dialysis is an option for difficult -to-manage HF. Increasing the duration of hemodialysis or instituting daily hemodialysis is likely to provide better volume control and minimize intradialytic hypotension than that provided by a standard dialysis schedule.**

Additional measures may help reduce the risk of intradialytic hypotension

- A cool (35°C) dialysate bath may reduce symptomatic hypotensive episodes by increasing both systemic vascular resistance and cardiac contractility

- Managing the hypotensive effect of prescribed medications is challenging in chronically hypotensive dialysis patients. The most common (but not evidence-based) strategy is to alter dosing schedules on dialysis days, particularly withholding the dose before dialysis.

Kidney transplantation

- Dialysis patients with HF require careful evaluation and management in determining whether they are candidates for kidney transplantation.

- Patients with HFrEF and ESKD are often not referred for kidney transplantation, because of concerns about risk of poor outcomes.

- some data suggest that kidney transplantation may result in improved LV systolic function and diastolic function and reduce LVH and improved survival in these patients

Control of hypertension

- Control of hypertension is a key intervention in preventing and managing HF in dialysis patients. The management of hypertension in dialysis patients includes gradual targeting euvolemia as well as administering antihypertensive medications.

- Antihypertensive drug therapy is indicated for dialysis patients who remain hypertensive despite achieving optimal dry weight

Goal blood pressure

- Hypertension is an important contributor to HF. Elevated cardiac afterload increases can worsen congestion and impair forward output

- For nondialysis patients at risk for HF or with HF, the goal blood pressure is 130/80 mmHg or less

- A target blood pressure is more difficult to define for dialysis patients given blood pressure fluctuated in predialysis, postdialysis, and home settings. Some experts suggest maintaining interdialytic self-recorded home blood pressure at less than 130/80 mmHg, but this recommendation is contingent upon patient tolerance.

Choice of therapy

- The choice of antihypertensive agents should take into account their dialyzability, interdialytic fluid gain, propensity of the patient to experience intradialytic hypotension, interdialytic home blood pressure values if available

- The choice of antihypertensive therapy varies depending upon whether HF is present and, if so, what type:

For dialysis patients with an LVEF >50 percent with or without HF

- In the absence of other specific indications, initial therapy with a beta blocker. Some clinicians prescribe carvedilol or labetalol in this setting, while others use atenolol.

- if the beta blocker is not tolerated or is not sufficient to achieve target blood pressure, dihydropyridine calcium channel blocker (amlodipine) can be added.

- if the beta blocker plus calcium channel blocker is not sufficient an angiotensin-converting enzyme (ACE) inhibitor could be added. If an ACE inhibitor is not tolerated due to cough or angioedema, an angiotensin receptor blocker (ARB; candesartan or valsartan) is used.

For dialysis patients with HFrEF (LVEF ≤40 percent), HF with midrange ejection fraction (HFmEF; LVEF 41 to 50 percent), or with asymptomatic LVEF ≤40 percent

- initial therapy is with a beta blocker. Carvedilol is prefered to other beta blockers in this setting

- If the beta blocker is not tolerated or is not sufficient to achieve target blood pressure, an ACE inhibitor is suggested. If an ACE inhibitor is not tolerated due to cough or angioedema, an ARB (candesartan or valsartan) is used.

- If maximum tolerated disease of beta blocker plus ACE inhibitor is not sufficient, adding a dihydropyridine calcium channel blocker is suggested (, amlodipine 5 to 10 mg daily).

Pharmacologic therapy for HFrEF

- approach to drug therapy for HFrEF (LVEF ≤40 percent) in the dialysis patient is similar to that for HFrEF in nondialysis patients

- For dialysis patients with HF who have significant urine output, diuretic therapy is helpful to increase urine output and sodium excretion and decrease the need for volume removal with dialysis.

- Loop diuretics are the preferred choice in most circumstances given their greater potency compared with other diuretics. Dialysis patients receiving diuretics should be monitored for hearing loss and skin changes. Diuretics should be stopped when urine output becomes negligible.

- For dialysis patients with HFrEF, we use combined beta blocker (carvedilol preferred) and ACE inhibitor therapy. An ARB is used in place of an ACE inhibitor in patients with a history of angioedema or ACE inhibitor-induced cough

- Start low-dose carvedilol (eg, 3.125 mg twice daily) and titrate as tolerated to a moderate dose (eg, 12.5 mg twice daily). Titrate carvedilol as tolerated up to target dose (25 to 50 mg daily).

- Add low-dose ACE inhibitor (eg, lisinopril 2.5 mg daily) and titrate as tolerated to a moderate dose (eg, lisinopril 20 mg daily).

- **Titrate ACE inhibitor (or ARB if ACE inhibitor intolerant) as tolerated up to target dose (for ACE inhibitor, lisinopril 40 mg daily; for ARB, candesartan 32 mg daily,valsartan 360mg daily)**

- **For dialysis patients with HFrEF who have persistent symptoms of HF despite treatment with optimally titrated beta blocker plus ACE inhibitor therapy, the role of additional pharmacologic therapy is uncertain. For patients who can be closely monitored, some clinicians weigh the potential risks and benefit of addition of an ARB or MRA**

- **In most dialysis patients with HFrEF, using digoxin is not suggested routinly, and reserve its use only for selected patients with atrial fibrillation who have not achieved adequate rate control with optimum beta blocker therapy and who can be closely monitored to maintain a digoxin level <0.1 ng/ml.**

Uncertain role of mineralocorticoid receptor antagonist

- **Low-quality evidence from randomized trials (limited by risk of bias and inadequate information size) suggests that MRA therapy in dialysis patients reduces all-cause mortality and cardiovascular mortality despite an increased risk of hyperkalemia.**

- **It has been postulated that MRA therapy may reduce the risk of HF through reduction in myocardial fibrosis and adverse remodeling**

- A difficult question is how to optimally manage the hypotensive effects of these agents in chronically hypotensive patients.

- dosing schedules to avoid intradialytic hypotension it should be modified , such as not administering these agents before dialysis on hemodialysis days.

- blood pressure measurements may vary when assessed in different positions, particularly in the setting of peripheral arterial disease. The goal is to reduce central aortic pressure, which may be higher than brachial pressures if there is vascular stenosis present.

ADDITIONAL GENERAL MEASURES FOR HF

- **HF self-management :** Dialysis patients with HF should be counseled on daily monitoring of weights

- **Palliative care:** supportive palliative care services should be integrated into the care of patients with HF

Management of coronary heart disease

- The treatment of coronary heart disease is aimed at relieving symptoms and improving outcomes

- Management options include pharmacologic therapy (antithrombotic therapy, antianginal therapy, and treatment of anemia, hypertension, and other cardiovascular risk factors) and revascularization (percutaneous or surgical).

- In some cases, revascularization of obstructive coronary artery disease may improve systolic and diastolic ventricular function

Management of anemia and iron deficiency

- The management of iron deficiency and anemia is part of the routine care of dialysis patients.
- iron deficiency treatment in patients with or without HF is similarly
- The use of erythropoiesis-stimulating agents involves a balance between avoiding symptomatic anemia and avoiding adverse outcomes from therapy to correct anemia
- targeting hemoglobin levels in the range of 10 to 11.5 g/dL is suggested.

Management of arrhythmias

- Cardiac arrhythmias may precipitate HF or be caused by HF.

✓Atrial fibrillation :

- Dialysis patients are at risk for developing atrial fibrillation with higher risk among those with older age, HF, or coronary heart disease.
- Patients with atrial fibrillation and HF may be treated with either a rate control or rhythm control strategy, although the subset of patients on dialysis are more commonly treated with rate control. For patients with atrial fibrillation and HF, a beta blocker is generally the primary agent for rate control.

- **The use of digoxin in the dialysis population is challenging since the risk of digoxin toxicity may be higher than in individuals with normal kidney function**

- **for most dialysis patients with HF, using digoxin is not suggest ; its use for selected patients with atrial fibrillation who do not achieve adequate rate control with optimum doses of beta blocker.**

- **When digoxin is used by a dialysis patient, dosing of digoxin should be adjusted for renal failure and levels followed very closely to maintain a digoxin level < 0.1 ng/ml**

Ventricular arrhythmias and sudden death

- Dialysis patients (with and without HF) are at risk for ventricular arrhythmias and sudden cardiac death. Management of ventricular arrhythmias and risk of sudden cardiac death are largely the same in patients with and without ESRD

- Indications for implantable cardioverter defibrillator(ICD) therapy for primary or secondary prevention of sudden cardiac arrest are the same as for patients with preserved renal function.

SUMMARY

- For all dialysis patients, a key general measure to manage or prevent heart failure (HF) is adequate volume control with loop diuretic therapy (if there is significant urine output) and dialysis

- For dialysis patients with HF with reduced ejection fraction (HFrEF; defined as HF with left ventricular EF ≤40 percent), the mainstays of therapy are treatment of volume overload and pharmacologic therapy including combined beta blocker and angiotensin converting enzyme (ACE) inhibitor therapy

- For dialysis patients with HFrEF, we recommend beta blocker therapy (Grade 1B). We suggest carvedilol rather than other beta blockers in this setting (Grade 2C)

- For dialysis patients with HFrEF who tolerate beta blocker therapy, we suggest adding ACE inhibitor therapy (Grade 2B)

- For dialysis patients with HFrEF who have persistent symptoms of HF despite treatment with optimally titrated beta blocker plus ACE inhibitor therapy, the role of additional pharmacologic therapy is uncertain.

- For most dialysis patients with HFrEF, we suggest not routinely using digoxin (Grade 2B).

- We treat dialysis patients with HFmrEF with a combination of pharmacologic agents similar to that for HFrEF


Thank
You!