Peripheral Ultrafiltration for Acute Decompensated Heart Failure

Number: 0741

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers ultrafiltration medically necessary for the acute management of inpatient members hospitalized with acutely decompensated congestive heart failure (CHF) who have dyspnea at rest or with minimal activity, and have confirmed diuretic resistance defined as dose escalation beyond a person's previously recognized dose ceiling or a dose approaching the maximum recommended daily dose without incremental improvement in diuresis.

Aetna considers intermittent peripheral ultrafiltration in persons who are not acutely decompensated or scheduled repetitive peripheral ultrafiltration experimental and investigational, as is use of peripheral ultrafiltration for all other indications because of insufficient evidence of their effectiveness.

Policy History

Last Review
11/11/2020
Effective: 11/20/2007
Next Review: 09/09/2021

Review History

Definitions

Additional Information

Clinical Policy Bulletin
Notes
Aetna considers peritoneal ultrafiltration experimental and investigational as an adjunctive therapy in end-stage heart failure because the effectiveness of this approach has not been established. See also CPB 0541 - Dialysis (../500_599/0541.html).

See also: CPB 0610 - Biventricular Pacing (Cardiac Resynchronization Therapy)/Combination Resynchronization-Defibrillation Devices for Congestive Heart Failure (../600_699/0610.html), and CPB 0709 - Nesiritide (Natrecor) (0709.html).

Background

Approximately 5 million Americans are currently diagnosed with heart failure (HF), and more than 500,000 new cases are diagnosed each year. Heart failure is the leading cause of hospitalizations in the United States (U.S.) and is associated with significant morbidity, mortality and resource utilization. The New York Heart Association (NYHA)'s classification of HF was the first rating system developed to quantify the degree of functional limitations exhibited by patients with HF. It is a 4-tier system that categorizes patients based on subjective impression of the degree of functional compromise. The 4 NYHA functional classes are as follows:

Class I:

Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain. Symptoms only occur on severe exertion.

Class II:
Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity (e.g., moderate physical exertion such as carrying shopping bags up several flights or stairs) results in fatigue, palpitation, dyspnea, or anginal pain.

**Class III:**

Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity (i.e., mild exertion) causes fatigue, palpitation, dyspnea, or anginal pain.

**Class IV:**

Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

The NYHA's functional classification of HF entails a continuum of increasing symptom severity, in which patients in Class I report no symptoms of HF, while those in Class IV exhibit severe symptomatology at rest. Patients with acute decompensated heart failure (ADHF) are usually characterized by an acute change in their baseline NYHA status (usually NYHA Class I or II) to NYHA Class IV disease (Hunt et al, 2001). Although no formal definition of ADHF exists, traditional signs of ADHF include pitting edema greater than 2 mm, presence of rales on pulmonary examination, pulmonary capillary wedge pressure (greater than 18 mm Hg), elevated right atrial pressure (greater than 10 mm Hg), and an increase in body weight (greater than 4.5 kg for patients below 5 feet in height or greater than 6.8 kg for patients over 5 feet in height). The level of brain B-type natriuretic peptide is now recommended to confirm the diagnosis of ADHF, with a level greater than 80 pg/ml being indicative of
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-decompensation. While ADHF can occur in patients with almost any stage of HF, episodes occur frequently in those with structural heart disease and either a history or current symptoms of HF (Bleske et al, 1998; Gottlieb et al, 1998; Hunter et al, 2001).

In contrast to chronic HF, where there have been numerous advances in care and corresponding decreases in morbidity and mortality, treatment for patients with ADHF remains largely empiric, and outcomes of these patients have remained relatively unchanged with an approximate 10% 30-day mortality and almost 40% 1-year re-hospitalization rate (Howlett, 2005). Acute decompensated heart failure is an important milestone in the clinical course of HF. It is an event associated with a significant deterioration in the prognosis of HF (Onwuanyi and Taylor, 2007).

Allen and O'Connor (2007) stated that ADHF represents a heterogeneous group of disorders that typically present as dyspnea, edema and fatigue. Despite the high prevalence of this condition and its associated major morbidity and mortality, diagnosis can be difficult, and optimal treatment remains poorly defined. Identification of the acute triggers for the decompensation as well as non-invasive characterization of cardiac filling pressures and output is central to management. Diuretics, vasodilators, continuous positive airway pressure and inotropes can be used to alleviate symptoms. However, few agents currently available for the treatment of ADHF have been definitively shown in large prospective randomized clinical trials to provide meaningful improvements in intermediate-term clinical outcomes. Multiple novel therapies are being developed, but previous treatment failures indicate that progress in the management of ADHF is likely to be slow.

The therapeutic objective in patients with ADHF is volume and sodium removal, and the restoration of diuretic sensitivity. A number of drugs have been demonstrated to lower morbidity and mortality in patients with chronic HF. Despite these
advances, the frequency of hospitalization for HF has continued to rise, and evidence is lacking in demonstrable benefit of pharmacotherapy for patients hospitalized with ADHF. In particular, Sackner-Bernstein and Aaronson (2007) noted that nesiritide is approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with ADHF who suffer from symptoms at rest or with minimal exertion. Its approval was based on a clinical development program that focused on surrogates and short-term effects on symptoms rather than clinical outcomes. Aggregate data analysis has suggested that it may be associated with a risk of excess mortality and worsening renal insufficiency. The association between its use and subsequent risk of death raises the question of whether the endpoints assessed in the clinical development program were adequate, and provides the opportunity to evaluate the process of weighing risks with benefits. The authors concluded that with nesiritide, the risks of therapy outweigh the benefits demonstrated to date.

Several percutaneous/peripheral devices have been developed to improve symptoms and clinical outcomes in patients hospitalized with HF. These include devices such as continuous aortic flow augmentation and ultra-filtration (UF) devices. Peripheral UF therapy offers the potential of greater volume and sodium removal as compared with conventional therapies in a more expeditious manner. Ultrafiltration differs from dialysis because it acts via convection rather than diffusion, which lowers the risk for induced metabolic abnormalities. Conventional UF devices required central venous access with a double lumen catheter, monitoring by a dialysis technician, and specialized hospital units. More recently, devices have been developed that allow UF to be carried out via large peripheral venous catheters (CTAF, 2007).

One device for ultrafiltration is the Aquadex FlexFlow system; Aquapheresis is the trademarked term for removal of salt and water with the Aquadex system. The Aquadex
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FlexFlow technology received initial 510(k) marketing clearance from the FDA in June 2002. An updated/amended 510(k) clearance (classified as a high permeability dialysis system) was given in February 2006 following some modifications. That Aquadex FlexFlow System is indicated for temporary (up to 8 hours) ultrafiltration treatment of patients with fluid overload who have failed diuretic therapy, and extended (longer than 8 hours) ultrafiltration treatment of patient with fluid overload who have failed diuretic therapy and require hospitalization.

Costanzo (2006) stated that 90% of one million annual hospitalizations for HF in the U.S. are due to symptoms of volume over-load. Hypervolemia contributes to HF progression and mortality. Current treatment guidelines recommend that therapy for patients with HF be aimed at achieving euvolemia. Intravenous loop diuretics induce a rapid diuresis that reduces lung congestion and dyspnea. However, the effectiveness of loop diuretics decreases with repeated treatments. Unresolved congestion may contribute to high re-hospitalization rates. Furthermore, loop diuretics may be associated with increased morbidity and mortality due to deleterious effects on neuro-hormonal activation, electrolyte balance, as well as cardiac and renal function. Peripheral UF is an alternative method of sodium and water removal that may improve hemodynamics in patients with HF.

Bart et al (2005) evaluated the safety and effectiveness of UF in patients admitted with decompensated congestive HF (CHF). Ultrafiltration for CHF is usually reserved for patients with renal failure or those unresponsive to pharmacological management. These researchers performed a randomized trial of UF versus usual medical care using a simple UF device that does not require special monitoring or central intravenous access. Patients admitted for CHF with evidence of volume overload were randomized to a single, 8-hour UF session in addition to usual care or usual care alone. The primary end point was weight loss 24 hours after the time of enrollment. A
total of 40 patients were enrolled (20 UF, 20 usual care). Ultrafiltration was successful in 18 of the 20 patients in the UF group. Fluid removal after 24 hours was 4,650 ml and 2,838 ml in the UF and usual care groups, respectively (p = 0.001). Weight loss after 24 hours, the primary end point, was 2.5 kg and 1.86 kg in the UF and usual care groups, respectively (p = 0.240). Patients tolerated UF well. The authors concluded that the early application of UF for patients with CHF was feasible, well-tolerated, and resulted in significant weight loss and fluid removal. They noted that a larger trial is underway to determine the relative effectiveness of UF versus standard care in ADHF.

In a case-series study, Dahle and colleagues (2006) reported the feasibility and effectiveness of performing large volume UF via peripherally inserted standard intravenous catheters in hospitalized patients with ADHF (n = 9). The mean length of time of peripheral UF therapy was 33.3 +/- 20.0 hours with a mean volume removed of 7.0 +/- 4.9 L. All patients experienced a statistically significant mean weight loss of 6.2 +/- 5.0 kg (p = 0.01). There was no statistically significant change in renal function. The authors noted that this was the first successful implementation of UF via standard peripheral intravenous catheters to remove a large volume of fluid over an extended period of time reliably in a small group of patients. The ability to use peripheral UF therapy via intravenous catheters will potentially allow this therapy to be implemented more easily in a variety of care settings to treat patients with refractory HF.

Costanzo and associates (2007) compared the safety and effectiveness of peripheral (veno-venous) UF and standard intravenous diuretic therapy for patients with hypervolemic HF. Patients hospitalized for HF with greater than or equal to 2 signs of hypervolemia were randomized to UF or intravenous diuretics. Primary end points were weight loss and dyspnea assessment at 48 hours after randomization. Secondary end points included net fluid loss at
48 hours, functional capacity, HF re-hospitalizations, and unscheduled visits in 90 days. Safety end points included changes in renal function, electrolytes, and blood pressure. A total of 200 patients (138 men and 62 women, mean age of 63 +/- 15 years, 71 % ejection fraction less than or equal to 40 %) were randomized to UF or intravenous diuretics. At 48 hours, weight loss (5.0 +/- 3.1 kg versus 3.1 +/- 3.5 kg; p = 0.001) and net fluid loss (4.6 versus 3.3 L; p = 0.001) were greater in the UF group. Dyspnea scores were similar. At 90 days, the UF group had fewer patients re-hospitalized for HF (16 of 89 [18 %] versus 28 of 87 [32 %]; p = 0.037), HF re-hospitalizations (0.22 +/- 0.54 versus 0.46 +/- 0.76; p = 0.022), re-hospitalization days (1.4 +/- 4.2 versus 3.8 +/- 8.5; p = 0.022) per patient, and unscheduled visits (14 of 65 [21 %] versus 29 of 66 [44 %]; p = 0.009). No serum creatinine differences occurred between groups. Nine deaths occurred in the UF group and 11 in the diuretics group. The authors concluded that in patients with decompensated HF, peripheral UF safely produces greater weight and fluid loss than intravenous diuretics, reduces 90-day resource utilization for HF, and is an effective alternative therapy.

In an editorial that accompanied the afore-mentioned study, Elkayam et al (2007) stated that "[t]he use of this therapy should be considered early in patients not responding to intravenous diuretics and vasoactive medications and in patients in whom such therapy is discontinued or reduced because of worsening of renal function or other drug-induced complications". Furthermore, Guglin and Polavaram (2007) stated that managing volume over-load is essential for the treatment of symptomatic HF. Traditionally, it is achieved via oral and intravenous diuretics. Alternatively, the excess fluid can be removed via UF. Advent in technology has made UF more feasible than before for routine clinical practice. Zevitz (2006) stated that patients with HF who are fluid over-loaded should be treated with diuretics, or, if necessary in patients with renal failure, hemodialysis with UF.
In contrast, in an editorial regarding the efficacy of vasopressin antagonism in heart failure outcome study with tolvaptan (EVEREST) clinical trials program, Yancy (2007) noted that UF represents at best an emerging technology with intriguing preliminary data but limited applications.

There is also a lack of consensus among several specialty societies and a technology assessment agency regarding the clinical value of peripheral UF in the treatment of patients with ADHF. The European Society of Cardiology Task Force's guidelines on the diagnosis and treatment of acute HF (Dickstein et al, 2008) stated that ultrafiltration should be considered to reduce fluid overload in selected patients, and to correct hyponatremia in symptomatic patients that are refractory to diuretics. The guidelines noted, however, that the appropriate selection criteria for UF have not been established. The Heart Failure Society of America's guidelines on evaluation and management of patients with ADHF (2006) stated that when congestion fails to improve in response to diuretic therapy, UF may be considered (strength of evidence = C [expert opinion, observational studies, epidemiologic findings, safety reporting from large-scale use in practice]). Furthermore, the Institute for Clinical Systems Improvement's guidelines on HF in adults (2006) noted that patients with persistent volume over-load may be candidates for continuous intravenous diuretics, UF, or hemodialysis (all out of guideline).

On the other hand, a technology assessment on peripheral UF for the management of ADHF by the California Technology Assessment Forum (CTAF, 2007) concluded that the use of peripheral UF does not meet Technology Assessment Criterion 3, 4 and 5 for safety, effectiveness and improvement in health outcomes when used to treat ADHF. The CTAF assessment also discussed a number of methodological issues regarding the study by Costanzo et al (2007). These issues include a lack of blinding for patients, investigators, staff, or those evaluating and adjudicating outcomes as well as inadequate reporting of recruitment and
follow-up. Furthermore, data for the primary endpoints (weight loss at 48 hours and dyspnea scores at 48 hours) were only available on 80% to 84% of the patients randomized. This high rate of incomplete data 48 hours after randomization in a hospitalized patient population was not explained by the researchers. Also, patients studied in this trial did not meet the FDA indication for peripheral UF as they had not previously failed diuretic therapy. The authors of the CTAF assessment noted that the benefits of peripheral UF remain to be proven; and the findings by Costanzo et al (2007) need to be replicated before they can be accepted with confidence.

The McGill University Health Center Technology Assessment Unit (Pan and Dendukuri, 2010) found that there is sufficient evidence to conclude that UF is an effective technology for the management of ADHF, and is the method of choice when patients have become resistant to diuretics or have developed secondary renal failure. The assessment found limited evidence that UF may have long-term health benefits including improved exercise performance for up to 3, and possibly 6 months, and that these effects are associated with a reduction in re-hospitalization rates.

An assessment of UF for HF by the Veterans Health Administration Technology Assessment Program (Flynn, 2010) found no recently published evidence to materially change conclusions from a previous report by the Centre for Evidence-based Purchasing (CEP) of the UK National Health Services, which found: “CEP finds that UF has significant potential to become a routine therapy for excess fluid removal in patients with CHF. However, further work is needed to establish the patient groups who would benefit most, the optimal rates of fluid removal, the conditions for termination of therapy, and the cost savings associated with long-term quality of life benefits.”
The VATAP report stated that these conclusions can be transferred to the United States in 2010 (Flynn, 2010). Additional shortcomings of the available literature include those elaborated by the CEP report: lack of blinding, which may be understandably difficult in the case of a bulky bedside device; lack of explicit power calculations and correspondingly small numbers of patients in clinical trials, which may reflect the relative lack of reliable estimates of clinically significant effects for UF in available research on which such calculations would be based; lack of follow-up beyond 2 to 3 months; reliance on intermediate or surrogate outcomes such as fluid volume removed or weight lost, rather than longer term outcomes such as quality of life or HF-specific mortality. The VATAP report noted that the device manufacturer is a significant presence in the only published (Costanzo et al, 2007; Costanzo et al, 2010) and ongoing trials. The VATAP report found that systematic reviews and assessments do not report significant adverse events or safety concerns with ultrafiltration for HF, but studies may not have been adequately powered or followed patients for long enough to detect uncommon adverse events. Post-marketing surveillance for a device only available since late 2006 may also be inadequate for detecting uncommon or late adverse events. The VATAP report notes that kidney dysfunction with over-zealous volume reduction has been observed and is under investigation for UF.

The American College of Cardiology/American Heart Association's updated guidelines on the diagnosis and management of chronic HF in adults (Hunt et al, 2005) did not discuss the use of peripheral UF as a therapeutic option for patients at various stages of HF. Similarly, the National Heart Foundation of Australia/the Cardiac Society of Australia and New Zealand's guidelines on the prevention, detection and management of chronic HF (2006) did not address the use of peripheral UF as a therapeutic option.
The potential for peripheral UF devices to normalize underlying cardiac function and thus improve long-term clinical outcomes in patients with ADHF needs to be further investigated.

Fiaccadori et al (2011) stated that fluid over-load is a key pathophysiologic mechanism underlying both the acute decompensation episodes of HF and the progression of the syndrome. Moreover, it represents the most important factor responsible for the high re-admission rates observed in these patients and is often associated with renal function worsening, which by itself increases mortality risk. In this clinical context, UF has been proposed as an alternative to diuretics to obtain a quicker relief of pulmonary/systemic congestion. These researchers reviewed technical issues, mechanisms, efficacy, safety, costs, and indications of UF in HF. The available evidence does not support the widespread use of UF as a substitute for diuretic therapy. Owing to its operative characteristics, UF can not be expected to directly influence serum electrolyte levels, azotemia, and acid-base balance, or to remove high-molecular-weight substances (e.g., cytokines) in clinically relevant amounts. Ultrafiltration should be used neither as a quicker way to achieve a sort of mechanical diuresis nor as a remedy for an inadequately prescribed and administered diuretic therapy. Instead, it should be reserved to selected patients with advanced HF and true diuretic resistance, as part of a more complex strategy aiming at an adequate control of fluid retention.

Bart et al (2012) stated that UF is an alternative strategy to diuretic therapy for the treatment of patients with ADHF. Little is known about the safety and effectiveness of UF in patients with ADHF complicated by persistent congestion and worsened renal function. These researchers randomly assigned a total of 188 patients with ADHF, worsened renal function, and persistent congestion to a strategy of stepped pharmacologic therapy (94 patients) or UF (94 patients). The primary end-point was the bivariate change from baseline in
the serum creatinine level and body weight, as assessed 96 hours after random assignment. Patients were followed for 60 days. Ultrafiltration was inferior to pharmacologic therapy with respect to the bivariate end-point of the change in the serum creatinine level and body weight 96 hours after enrollment (p = 0.003), owing primarily to an increase in the creatinine level in the UF group. At 96 hours, the mean change in the creatinine level was -0.04 ± 0.53 mg/dL (-3.5 ± 46.9 μmol/L) in the pharmacologic-therapy group, as compared with +0.23 ± 0.70 mg/dL (20.3 ± 61.9 μmol/L) in the UF group (p = 0.003). There was no significant difference in weight loss 96 hours after enrollment between patients in the pharmacologic-therapy group and those in the ultrafiltration group (a loss of 5.5 ± 5.1 kg [12.1 ± 11.3 lb] and 5.7 ± 3.9 kg [12.6 ± 8.5 lb], respectively; p = 0.58). A higher percentage of patients in the UF group than in the pharmacologic-therapy group had a serious adverse event (72 % versus 57 %, p = 0.03). The authors concluded that in a randomized trial involving patients hospitalized for ADHF, worsened renal function, and persistent congestion, the use of a stepped pharmacologic-therapy algorithm was superior to a strategy of UF for the preservation of renal function at 96 hours, with a similar amount of weight loss with the two approaches. Ultrafiltration was associated with a higher rate of adverse events.

Wen and colleagues (2013) compared the safety and effectiveness of UF and conventional intravenous diuretic therapy for patients with acute HF and volume overload. These investigators searched the following databases through November 2012: Cochrane Library (1993-), PubMed (1988-), OVID (1984-), EBSCO (1984-), CBM (1978-), VIP (1989-), and CNKI (1979-). In addition, they manually searched relevant references and review articles. Randomized controlled trials comparing the effectiveness of UF and intravenous diuretics in patients diagnosed with hyper-volemic acute HF were included. Five trials were found to satisfy all the inclusion criteria. Two reviewers independently determined study eligibility, assessed methodological quality and extracted the
data. They analyzed the data and pooled them, when appropriate, using Revman 5.0. They assessed the risk of bias in the included studies using guidelines in the Cochrane Handbook 5.0 for Systematic Reviews of Interventions, taking into account sequence generation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting. Data from the initial phase of five trials involving 477 participants were included. Meta-analysis of the pooled data showed that UF was significantly better than diuretic drugs based on 48-hr weight loss ($Z = 3.72; p < 0.001$, weighted mean difference [WMD] = 1.25 kg, 95 % confidence interval [CI]: 0.59 to 1.91) and based on 48-hr fluid removal ($Z = 4.23; p < 0.001$, WMD = 1.06 L, 95 % CI: 0.57 to 1.56).

Adverse events did not differ significantly between the UF and intravenous diuretic treatment groups. The authors concluded that the available evidence suggested that early UF is safe and effective for patients with hyper-volemic acute HF. It allows greater fluid removal and weight loss by 48 hours than do intravenous diuretics, with no significant increase in adverse effects.

De Vecchis et al (2014) compared intravenous diuretics versus isolated ultrafiltration (IUF) regarding their respective safety and effectiveness in ADHF patients through systematic review and meta-analysis of data derived from relevant randomized controlled trials. A total of 6 studies (477 patients) were included in the systematic review. By contrast, data from only 3 studies were pooled for the meta-analysis, because of different adopted outcomes or marked dissimilarities in the data presentation. Weight loss at 48 hours was greater in IUF group compared to the diuretics group [weighted mean difference (WMD) = 1.77 kg; 95 % confidence interval [CI]: 1.18 to 2.36 kg; $p < 0.001$]. Similarly, greater fluid loss at 48 hours was found in IUF group in comparison with diuretics group (WMD = 1.2 L; 95 % CI: 0.73 to 1.67 L; $p < 0.001$). In contrast, the probability of exhibiting worsening renal function (WRF), i.e., increase in serum creatinine greater than 0.3 mg/dL at 48 hours, was similar to the one found in the diuretics group.
group (OR = 1.33; 95 % CI: 0.81 to 2.16 p = 0.26). The authors concluded that on the basis of this meta-analysis, IUF induced greater weight loss and larger fluid removal compared to iv diuretics in ADHF patients, whereas the probability of developing WRF was not significantly different in the comparison between intravenous diuretics and IUF.

The National Institute for Health and Care Excellence’s clinical guideline on “Acute heart failure: Diagnosing and managing acute heart failure in adults” (NICE, 2014) stated that “Do not routinely offer ultrafiltration to people with acute heart failure. Consider ultrafiltration for people with confirmed diuretic resistance. Diuretic resistance is defined as dose escalation beyond a person's previously recognized dose ceiling or a dose approaching the maximum recommended daily dose without incremental improvement in diuresis”.

Ebrahim et al (2015) noted that although diuretics are mainly used for the treatment of ADHF, inadequate responses and complications have led to the use of extracorporeal UF as an alternative strategy for reducing volume overloads in patients with ADHF. These investigators performed meta-analysis of the results obtained from studies on extracorporeal venous UF and compared them with those of standard diuretic treatment for overload volume reduction in ADHF. MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials databases were systematically searched using a pre-specified criterion. Pooled estimates of outcomes after 48 hours (weight change, serum creatinine level, and all-cause mortality) were computed using random effect models. Pooled weighted mean differences were calculated for weight loss and change in creatinine level, whereas a pooled risk ratio was used for the analysis of binary all-cause mortality outcome. A total of 9 studies, involving 613 patients, met the eligibility criteria. The mean weight loss in patients who underwent UF therapy was 1.78 kg [95 % CI: -2.65 to -0.91 kg; p < 0.001] more than those who received standard diuretic therapy. The post-intervention creatinine level, however, was not significantly different (mean
change = -0.25 mg/dL; 95 % CI: -0.56 to 0.06 mg/dL; p = 0.112). The risk of all-cause mortality persisted in patients treated with UF compared with patients treated with standard diuretics (pooled RR = 1.00; 95 % CI: 0.64 to 1.56; p = 0.993).

The authors concluded that compared with standard diuretic therapy, UF treatment for overload volume reduction in individuals suffering from ADHF, resulted in significant reduction of body weight within 48 hours. However, no significant decrease of serum creatinine level or reduction of all-cause mortality was observed.

Peritoneal Ultrafiltration as an Adjunctive Therapy in End-Stage Heart Failure

Heart failure (HF) is a major cause of morbidity and mortality. Extracorporeal (EC) therapy, including ultrafiltration (UF) and haemodialysis (HD), peritoneal dialysis (PD) and peritoneal ultrafiltration (PUF) are potential therapeutic options in diuretic-resistant states. Cionh, et al. (2020) conducted a systematic review to assess outcomes of PD and compared the effects of PD to EC. A comprehensive search of major databases from 1966 to 2017 for studies utilizing PD (or PUF) in diuretic-resistant HF was conducted, excluding studies involving patients with end-stage kidney disease. Data were extracted and combined using a random-effects model, expressed as odds ratio (OR). Thirty-one studies (n = 902) were identified from 3195 citations. None were randomized trials. Survival was variable (0 to 100%) with a wide follow-up duration (36 hours to 10 years). With follow-up greater than 1 year, the overall mortality was 48.3%. Only four studies compared PD with EC. Survival was 42.1% with PD and 45.0% with EC; the pooled effect did not favor either (OR 0.80; 95% confidence interval (CI): 0.24-2.69; p = 0.710). Studies on PD in patients with HF reported several benefits. Left ventricular ejection fraction (LVEF) improved after PD (OR 3.76, 95% CI: 2.24-5.27; p < 0.001). Seven of nine studies saw LVEF increase by greater than 10%. Twenty-one studies reported the New York Heart Association status and 40% to 100% of
the patients improved by 1 or more grades. Nine of 10 studies reported reductions in hospitalization frequency and/or duration. When treated with PD, HF patients had fewer symptoms, lower hospital admissions and duration compared to diuretic therapy. However, there is inadequate evidence comparing PD versus UF or HD. Further studies comparing these modalities in diuretic-resistant HF should be conducted.

Grossekettler and colleagues (2020) noted that peritoneal ultrafiltration (pUF) in refractory HF reduces the incidence of decompensation episodes, which is of particular significance as each episode incrementally adds to mortality. Nevertheless, there are insufficient data regarding which patient cohort benefits the most. These researchers compared pUF in HF with reduced left ventricular ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF), focusing on functional status, hospitalizations, surrogate end-points and mortality. This study entailed 143 patients, who could be classified as either HFpEF (n = 37, 25.9 %) or HFrEF (n = 106, 74.1 %) and who received pUF due to refractory HF. Baseline eGFR was similar in HFrEF (23.1 ± 10.6 mg/dL) and HFpEF (27.8 ± 13.2 mg/dL). Significant improvements in NYHA class were found in HFpEF (3.19 ± 0.61 to 2.72 ± 0.58, p < 0.001) and HFrEF (3.45 ± 0.52 to 2.71 ± 0.72, p < 0.001). C-reactive protein (CRP) decreased in HFrEF (19.4 ± 17.6 mg/L to 13.7 ± 21.4 mg/L, p = 0.018) and HFpEF (33.7 ± 52.6 mg/L to 17.1 ± 26.3 mg/L, p = 0.004). Body weight was significantly reduced in HFrEF (81.1 ± 14.6 kg to 77.2 ± 15.6 kg, p = 0.003) and HFpEF (86.9 ± 15.8 kg to 83.1 ± 15.9 kg, p = 0.005). LVEF improved only in HFrEF (25.9 ± 6.82 % to 30.4 ± 12.2 %, p = 0.046). BCR decreased significantly in HFrEF and HFpEF (55.7 ± 21.9 to 34.3 ± 17.9 p > 0.001 and 50.5 ± 68.9 to 37.6 ± 21.9, p = 0.006). Number of hospitalization episodes as well as number of hospitalization days decreased significantly only in HFpEF (total number 2.88 ± 1.62 to 1.25 ± 1.45, p < 0.001, days 40.4 ± 31.7 to 18.3 ± 22.5 days, p = 0.005). The authors concluded that pUF offered various benefits in HFpEF and HFrEF, however, there
were also substantial differences. In particular, hospitalization rates were found to be significantly reduced in HFpEF patients, indicating a greater medical and economical advantage. However, LVEF was only found to be improved in HFrEF patients. These researchers stated that the findings of this study warrant larger controlled studies to elaborate the differential effects of pUF as an adjunct palliative therapy in end-stage HF.

The authors stated that this study had several drawbacks. This study had a relatively small patient cohort, while cardio-renal patients were included from 18 different centers. Thus, this all-comers population may have resulted in a highly heterogeneous collective that did not allow the exclusion of potential biases. Furthermore, the fact that pUF patients received a rather close monitoring might have resulted in an improved outcome on its own.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

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<td>CPT codes not covered for indications listed in the CPB:</td>
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ICD-10 codes not covered for indications listed in the CPB:

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The above policy is based on the following references:

7. California Technology Assessment Forum (CTAF). Peripheral ultrafiltration for the management...


32. Morpurgo M, Pasqualini M, Brunazzi MC, et al. A multicenter feasibility study on ultrafiltration via a single peripheral venous access in acute heart failure


41. Shin JT, Dec GW. Ultrafiltration should not replace diuretics for the initial treatment of acute


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0741 Peripheral Ultrafiltration for Acute Decompensated Heart Failure

There are no amendments for Medicaid.

revised 11/09/2020