ULTRAFILTRATION FOR FLUID MANAGEMENT IN COVID-19 PATIENTS

START-UP GUIDE
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Dear Physicians and Caregivers:

As highlighted recently by multiple news sources (e.g., New York Times, CNN, Fox News, NPR, and CJASN) hospitals around the country are facing shortages of dialysis machines and supplies as well as trained personnel to care for critically ill COVID-19 patients.

In response to these shortages, several hospitals across the country have included a simplified form of ultrafiltration (Aquadex FlexFlow® or Aquadex SmartFlow™) into their treatment protocol for fluid management. As a company, we want to help you manage this situation and are making every effort to ensure the use of Aquadex is financially feasible.


"Acute kidney injury is a significant risk for critically ill patients with COVID-19," said Dr. DeVita. "Adequate access to dialysis equipment is a growing concern as is the growing number of patients who need fluid removal but are poor candidates for traditional dialysis. We see ultrafiltration as a valuable treatment in both instances and are seeing a clear benefit to including Aquadex therapy as a vital part of our armamentarium to treat COVID-19."

In the April 3rd Clinical Journal of the American Society of Nephrology, a similar approach was recommended: "The use of other machines to replace a standard dialysis machines may have merit such as machines that only do isolated ultrafiltration to perform all isolated ultrafiltration procedures, thereby keeping standard full-size dialysis machines available to perform treatments." (CJASN ePress. Dwyer, et. al. published on April 3, 2020 as doi: 10.2215/CJN.03750320.)

Every day, Aquadex SmartFlow is helping to alleviate the dialysis supply and staffing burden by:

• Providing fluid removal for dialysis patients while waiting for equipment and staff to become available
  • Unmanaged fluid overload due to long wait times to receive dialysis may negatively impact the kidneys
• Performing fluid removal in patients who may not require daily dialysis support
• Expanding staff capability as Aquadex SmartFlow can be managed with fewer nursing resources (up to 4:1 patient to nurse ratio)
• Reducing nurse exposure by not requiring staff to be bedside for the entire therapy
• Quick removal of excess fluid in septic patients who are hemodynamically unstable
• Fluid overload in the post-op period is associated with greater length of stay in ICU, increased hospital mortality, and prolonged ventilation.1,2
• Providing simple, gentle, and predictable fluid management when a patient only requires fluid removal

I understand that you are busy, but a brief discussion may lead to a solution to your needs. Do you have a short window of time to talk this or next week?

Kind Regards,

CHF Solutions

Sources:
ULTRAFILTRATION FOR FLUID MANAGEMENT IN COVID-19 PATIENTS
Aquafex Smartflow™ Indication

**RX ONLY**

The Aquafex SmartFlow System is indicated for:
Continuous ultrafiltration therapy for temporary (up to 8 hours) or extended (longer than 8 hours in patients who require hospitalization) use in adult and pediatric patients weighing 20 kilograms or more whose fluid overload is unresponsive to medical management, including diuretics.

All treatments must be administered by a healthcare provider, within an outpatient or inpatient clinical setting, under physician prescription, both of whom having received training in extracorporeal therapies.

Example of Early & Late Use of Aquafex for Fluid Management & Removal

- Patients with co-morbidities (e.g. HF, etc.) that are known to exacerbate fluid retention
- Patients who present to the ICU with fluid overload (FO)
- Patients given fluids for resuscitation (e.g. sepsis)
- Hemodynamically unstable fluid overload dialysis patients that can’t tolerate dialysis, but still need fluid removal
- Patients who need fluid removal between dialysis treatments, but not enough dialysis machines exist

DAY 1 2 3 4 5 6 7 8 9 10 11 12 13 14

SUPPLEMENTAL O2
INTUBATION
COVID Hotspots Are in Severe Short Supply of Dialysis Equipment/Staff

- **NPR** – Shortage Of Dialysis Equipment Leads To Difficult Decisions In New York ICUs
- **CNN** – New Covid-19 Crisis Hits ICUs as More Patients Need Dialysis
- **Fox News** – Hospitals Face Shortage of Dialysis Machines Amid Coronavirus Crisis

Uses and Potential Benefits of Aquadex SmartFlow in COVID-19 Patients

**USES**

- Provides fluid management for patients while waiting for dialysis equipment and/or staff to become available
- Offers fluid management option for patients who may not require daily dialysis support but still need fluid removed
- Affords fluid management solution when a patient only requires fluid removal
- Provides gentle, safe, and precise fluid removal when rapid resuscitation of septic patients who are hemodynamically unstable is necessary

**POTENTIAL BENEFITS**

- Frees up hospital staff as the system doesn’t require 1 to 1 nurse to patient support
- Reduces nurse exposure time by not requiring staff to be bedside for the entire therapy

"Acute kidney injury is a significant risk for critically ill patients with COVID-19. Adequate access to dialysis equipment is a growing concern as is the growing number of patients who need fluid removal but are poor candidates for traditional dialysis. We see ultrafiltration as a valuable treatment in both instances and are seeing a clear benefit to including Aquadex therapy as a vital part of our armamentarium to treat COVID-19."¹

Maria DeVita, MD  
Nephrologist, Lenox Hill Hospital (Northwell Health), New York, NY

"We came up with what we called an Aquadex renal rescue protocol in trying to temporarize and stabilize the patient while the hemodialysis machine wasn’t available...And that allowed, I don’t know, stabilization for the next, at least 24 hours until a hemodialysis machine became available."²

Giovanni Piovesana, MD  
Cardiothoracic Surgeon, Phoebe Putney Hospital, Albany, Georgia

"Besides everything going on with our [COVID-19] patient, we are very aware about the volume overload on the patient...We need a reliable way [to diuresis the patient], which the Aquadex can help us do."²

Mehdi Oloomi, MD  
Intensivist, Mount Sinai, New York, NY

Sources:
# COVID-19 Discussion Guide

## Clinical Manifestations

- Patients with co-morbidities (e.g. HF, etc.) that are known to exacerbate fluid retention
- Patients who present to the ICU with fluid overload (FO)
- Hemodynamically unstable fluid overload dialysis patients that can’t tolerate dialysis, but still need fluid removal
- Patients who need fluid removal between dialysis treatments, but not enough dialysis machines
- Patients given fluids for resuscitation (e.g. sepsis)

## Clinical Needs

### Fluid Management
- "In severe cases, COVID-19 can be complicated by acute respiratory distress syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury and cardiac injury."¹
- In the absence of shock, conservative fluid therapy is recommended to achieve a negative fluid balance of 0·5 to 1·0 L per day²
- "Fluid resuscitation may lead to volume overload, including respiratory failure, particularly with Acute Respiratory Distress Syndrome (ARDS)."³

## How Aquadex SmartFlow™ Meets Needs

### Effective Fluid Management & Treatment of Fluid Overload
- Low extracorporeal volume (35mL) may help mitigate hemodynamic instability
- Precise control of rate and amount of fluid removed
- No clinically significant change to electrolytes

### More Efficient Use of Human & Capital Resources
- Simplified form of ultrafiltration - can be prescribed by any physician trained in extracorporeal therapy
- Easy set-up and monitoring allows a 4:1 patient to nurse ratio, compared to 1:1 for CRRT devices
- Can be used intermittently with patients who need dialysis for end stage renal disease (ESRD)
- Therapy can be started in minutes due to highly automated setup and operation

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### Key Message:
Aquadex SmartFlow is a simplified form of ultrafiltration that safely, gently, and predictably removes isotonic fluid from critically ill patients, while reducing the resource burden to hospitals.

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³ Clinical Management of Severe Acute Respiratory Infection (SARI) when COVID-19 disease is suspected. Interim Guidance, 13 March 2020.
Suggested Pathways for Fluid Management in Critically Ill Patients

**FLUID OVERLOAD**

- NEED CLEARANCE

**NO**
- Only needs fluid removal and BP > 90 (hemodynamically stable)
  - Presents with fluid overload
  - At risk for fluid overload and needs fluid resuscitation

**YES**
- CRRT/Dialysis Equipment Available
  - Develops fluid overload during resuscitation
    - Hemodynamically stable
      - YES
        - CRRT or HEMODIALYSIS
          - Continue with CRRT or HD
      - NO
        - Use CRRT for clearance and intermittent AQ for fluid removal

BP= Blood Pressure
CRRT= Continuous Renal Replacement Therapy
HD= Hemodialysis
AQ= Aquadex

Source: [1] Aquapheresis: An Institutional Experience at Lenox Hill Hospital
(Abstract presented at the 2019 American Society of Nephrology Conference)
Critical Care: Ultrafiltration Critical to Success in Fluid Overloaded, Critically Ill Patients

- Large-volume hospitals use Aquadex as a treatment for fluid overload in the ICU setting
- The clinical reason for fluid overload in critically ill patients is related to the need for fluid resuscitation (infusion of fluids to maintain hemodynamic stability)
- In a retrospective study of Aquadex FlexFlow® at Lenox Hill Hospital in NYC, 23 patients were treated safely in situations, other than heart failure, without adversely affecting renal function

<table>
<thead>
<tr>
<th>Hospital Locations Where Aquadex FlexFlow is Used in Critically Ill Patients</th>
<th>Indications for Prescribing Aquadex FlexFlow in Critically Ill Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiothoracic Intensive Care Unit (CICU)</td>
<td>Cardiogenic shock, including post CTS</td>
</tr>
<tr>
<td>Critical Care Unit (CCU)</td>
<td>Anasarca (general tissue fluid accumulation)</td>
</tr>
<tr>
<td>Medical ICU (MICU)</td>
<td>Acute Tubular Necrosis (ATN) with volume overload</td>
</tr>
<tr>
<td>Surgical ICU (SICU)</td>
<td>End-stage renal disease between hemodialysis</td>
</tr>
<tr>
<td></td>
<td>Post-operative volume overload</td>
</tr>
</tbody>
</table>

Source: Aquapheresis: An Institutional Experience at Lenox Hill Hospital (Abstract presented at the 2019 American Society of Nephrology Conference)

COVID-19 and the Inpatient Dialysis Unit

“The use of other machines to replace a standard dialysis machine may have merit such as machines that only do isolated ultrafiltration to perform all isolated ultrafiltration procedures, thereby keeping standard full-size dialysis machines available to perform treatments.”
Severe COVID-19 Risk Mapping

This tool shows projected US county-level demand of severe COVID-19 cases and supply estimates of hospital critical care beds, including ICU beds and other hospital beds that could be made available for critical care, under various scenarios of hospital response to patient surges. The maps also show the expected time to patient demand exceeding hospital capacity for a 42-day horizon from April 2, 2020. Data related to patients at high risk for severe COVID-19 are also shown, including: the number of people age 65+ and people with underlying health conditions that make them vulnerable to severe COVID-19.

https://columbia.maps.arcgis.com/apps/webappviewer/index.html?id=ade6ba85450c4325a12a5b9c09ba796c
Aquadex SmartFlow™ System

The Aquadex SmartFlow System uses a simplified approach to ultrafiltration for the removal of salt and water in patients with hypervolemia, or fluid overload. Compared to renal replacement devices used for ultrafiltration, the Aquadex SmartFlow System is smaller and more portable. Physicians can specify and adjust the exact amount and rate of fluid to be removed from each patient, resulting in a gradual reduction that has been shown to have no significant clinical impact on blood pressure, heart rate, or the balance of electrolytes (e.g. sodium, potassium, etc.) in the body. Up to 500 mL per hour of excess fluid can be removed with no clinically significant impact on electrolyte balance.\(^1,^2\)

**Features & Benefits**

**SIMPLE**
- Easy set-up and monitoring allows for up to 4:1 patient to nurse ratio
- Highly automated with only one setting required to begin
- Smart alarms/alerts prompt action when necessary

**FLEXIBLE**
- Perform therapy through peripheral or central venous access
- Portable system with small 35 ml extracorporeal volume meets patient needs in a multitude of clinical settings
- Customizable HCT monitor can be tailored to individual patient needs

**SMART**
- HCT sensor provides real time measurement of % blood volume change
- SvO2 monitoring provides insights into tissue oxygen delivery
- Filter Alert prompts action to extend filter life and reduce therapy time

**Sources:**
Simplified approach to ultrafiltration for the removal of isotonic fluid.

Easy to Operate, Safe to Use

- Controllable fluid reduction and individualized patient fluid removal
- Perform therapy through peripheral or central venous access
- Highly automated with only one setting required to begin
- Hematocrit sensor provides real time measurement of % blood volume change
- User defined hematocrit limit
- SvO2 monitoring provides insights into tissue oxygen delivery
Blood Circuit Set

Uniquely designed for the removal of isotonic fluid with a low extracorporeal blood volume of approximately 35 ml.

Aquadex System Fluid Path

Fully Integrated Blood Circuit Set

- Patented filter designed to reduce clotting
- Air and blood leak detectors to ensure correct operation
- Needleless access ports for aspiration or infusion of fluids
- Filter Resistance Alert prompts action to help extend circuit life
CHFS Resources

Click on the links below to access the complete product resource.

**Therapy Guidelines Card**

**Dual Lumen Extended Length Catheter**

- Two independent 5 Fr lumens
- parachute tip for smooth insertion
- Silt reinforcement for enhanced resistance

**Quick Reference Guide**

**Console and Blood Set Brochure**

**Venous Access Considerations**

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ULTRAFILTRATION ORDERS USING THE AQUADEX SMARTFLOW™

CHF Solutions is providing this template in association with the delivery of Aquapheresis therapy with the Aquadex SmartFlow (Rx Only) to patients with fluid overload who have failed diuretic therapy. This template is intended to be customized for standardization & compliance with an institution’s standard operating procedures and does not take the place of the Aquadex SmartFlow User’s Guide. Physician & hospital staff judgment should be exercised at all times in the care of the patient. For HCP use only.

1. **Indication:** The Aquadex SmartFlow System is indicated for: Continuous ultrafiltration therapy for temporary (up to 8 hours) or extended (longer than 8 hours in patients who require hospitalization) use in adult and pediatric patients weighing 20 kilograms or more whose fluid overload is unresponsive to medical management, including diuretics. All treatments must be administered by a healthcare provider, within an outpatient or inpatient clinical setting, under physician prescription, both of whom having received training in extracorporeal therapies.

2. **Patient selection:**
   a. Fluid overload and two of the following
      i. ___ lbs/kg over dry weight (estimated)
      ii. IV Diuretic Dose > ___ mg furosemide or equivalent (1 mg bumetanide or 20 mg torsemide=40 mg furosemide)
      iii. Diuresis < ______ cc/hr, and/or > ______ mg/dl sCr rise
      iv. ___ hospitalizations in ______ days
      v. readmission

3. **Labs:**
   a. CBC prior to treatment and every_____hour_____days during treatment
   b. BMP prior to treatment and every_____hour_____days during treatment
   c. CMP prior to treatment and every_____hour_____days during treatment
   e. Other Labs:_______________________________________________________________

4. **Anticoagulation therapy (e.g. aPTT, PTT, INR, etc):**
   a. Keep the patient is contraindicated
   b. Labs: obtain anticoagulation level prior to treatment
      i. ___PT/INR, PTT now and every _____ hrs. Every _____ day
      ii. ___ACT now and every _____ hrs
      iii. ___AntiXa level and every _____ day(s)
      iv. follow PTT based on heparin protocol
   c. Therapy
      i. Heparin with DVT protocol dosing or
      ii. Alternative therapy
         ______ Continuous slow infusion of heparin (e.g. 500 units/hr)
         ______ ECMO Heparin protocols, narrower range of PTT (for example 40-60 sec general range)²
         ______ Heparinized saline to prime/reprime the circuit (for example 5000 units in 500 ml normal saline or 5000 units in 1L normal saline)³⁴
         Bolus of Heparin prior to initiation of therapy:
            ______ Priming circuit with Heparin in saline 5000 Units/L in saline (9 mg/ml)³
            ______ Weight based option: patient on Heparin gtt, with subtherapeutic PTT, bolus units/kg per Heparin protocol⁵
ULTRAFILTRATION ORDERS USING THE AQUADEX SMARTFLOW

5. **Venous access:**
   a. ____ CHF 6Fr. dual, triple or quad lumen (with at least 2 lines 16ga or larger) Peripheral Extended Length Catheter (DELc), -- OR --
   b. ____ 7-8Fr. dual lumen central line (dual 14ga or dual 16ga). -- OR --
   c. ____________________________________________________________________
   d. Remove all extensions and needle-less systems from the lines when connecting blood circuit (e.g. hub to hub)

6. **Before starting treatment:**
   a. Diuretic and electrolyte replacement therapies may be discontinued for duration of Aquapheresis treatment.
   b. Ensure venous access is patent and can deliver required blood flow.
   c. Ensure blood circuit set is loaded properly (press the PRIME then HELP keys on device).
   d. Prime blood circuit with a minimum of 250 ml NS and ensure prime is successfully completed.

7. **Treatment:**
   a. Connect blood circuit to venous access.
   b. NET Fluid removal at a rate of _____ ml/hr (0-500 ml/hr) for ____ hours OR until _____ liters of fluid removed.
      i. Monitor patient for clinical signs of hypovolemia and hypotension as appropriate.
   c. Vital signs Q____ minutes or first ____ hour(s), then Q____ hour for duration of treatment and PRN patient status.
   e. IV drug therapy can be administered through the access ports on the blood circuit.
   f. For laboratory testing, blood can be removed through the access port on the withdrawal side of the blood circuit.

8. **Monitoring**
   a. Vital signs every _____ minutes for the first hour(s), then every _____ hr(s)
      i. Aline monitoring every _____ hr(s)
   b. Hemodynamic Monitoring
      i. CVP monitor every ___ hr(s)
      ii. PA monitoring every ______ hr(s)
      iii. CO/Cl every ______ hr(s)
   c. SVO2 Monitoring
      i. Keep the SVO2 monitor every ___ hr(s)
      ii. add contact provider for ______%  
      iii. if SVO2 < ____% contact provider
      iv. if SVO2 < ___% set UF rate to 0 and contact provider
   d. Hematocrit Monitoring (if prescribed/available):
      i. To enable, place sensor clip on the blood set chamber and follow the onscreen instructions.
      ii. After baselining is complete, accept the default or set the prescribed Hct Limit:
         Accept the default Hct limit, or
         Set Hct limit to (%) _______
   e. Strict I& O record every _____ hr(s)
   f. Daily weight ________
   g. Fluid restriction ______ ml/24 hours
9. **Call the physician or provider if:**
   a. SBP < ______ mm HG
   b. Heart rate > ____ and decreased UF rate by ______ ml/hr, or place at 0 ml/hr until stabilized.
      
      Once stable, Resume UF at lower rate (i.e. 50-100 ml/hr less than last rate)
   c. If the Hct Limit is consistently exceeded (e.g. at least ____ “Extended UF Pump Stoppage” alerts have occurred) and the patient is otherwise stable and obviously fluid overloaded, consider the following:
      i. Returning the patient to the baseline position.
      ii. Reducing the UF Rate by _______ (e.g. 100 ml/hr)
      iii. Increasing Hct Limit to ________ (e.g. 34.5 to 35.5)
      iv. 50-100 ml/hr by reducing UF rate add increasing Hct limit by ____%

10. **Post therapy:**
   a. Maintain IV access per unit protocol ________________________________________________
   b. Discontinue anticoagulation as appropriate.
   c. Resume diuretics as appropriate.

**Additional Orders**

<table>
<thead>
<tr>
<th>Physician signature</th>
<th>□ Sent to pharmacy ______ (initials)</th>
<th>Date/Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Printed physician name</td>
<td>RN Name</td>
<td></td>
</tr>
</tbody>
</table>

**Sources:**
Additional Reading on Role of Ultrafiltration in the Treatment of COVID-19 Patients

https://cjASN.asnjournals.org/content/early/2020/04/13/CJN.03750320

https://jamanetwork.com/journals/jama/fullarticle/2763879

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30127-2/fulltext