ARTICLE:
- **Citation:** Diuretic Strategies in Patients with Acute Decompensated Heart Failure
- **Country:** USA
- **Funding Sources:** National Heart, Lung, and Blood Institute
  - Authors have consulting and lecture support from multiple pharmaceutical companies: Amgen, Cytokinetics, Corthera, Otsuka, Novartis, Medtronic, Johnson & Johnson and Roche Diagnostics.

PURPOSE:
- **Research Question(s):**
  
  Which IV diuretic strategy works best for CHF exacerbation?

  - **Hypothesis:** What is the anticipated outcome or alternatively, the null hypothesis (there will be no difference between groups).

N/A

DESIGN:
- **Study Design:**
  - Prospective, randomized, double-blind, controlled trial
  - Utilized double blind and double dummy control (basically patients got a Q12H med and a continuous med)

  - **Dependent / outcome Variable(s):** What is the variable of interest / outcome being studied.
    - Is there a best strategy when it comes to IV diuretic therapy

  - **Independent / research Variable:** What is the variable that is modified among groups?
    - Dose, bolus vs continuous

SETTING / SUBJECTS:
- **Research Setting:** Inpatient hosp, academic centers
- **Subjects:**
  - Study population: 308 pts at 26 different clinical sites

Pt’s presenting with CHF if they had presented within the last 24 hrs they could be enrolled

  - Inclusion / Exclusion criteria:
Inclusion
- one sign (rales, peripheral edema, ascites, or pulmonary vascular congestion)
- one symptom (dyspnea, orthopnea, or edema)
- diagnosis of CHF
- Rx on loop diuretic 1 month prior to admission

Exclusion
- systolic BP less than 90
- Creatinine level >3.0
- Pt’s requiring vasodilators or inotropic agents
  - Number (control / intervention groups): roughly 75 each
  - Demographics: average age 66, 75% male, 75% white. Everyone had baseline Cr of 1.5 +/- 0.5, EF was very similar across groups with ~33-35%
  - Attrition: no one lost during study, however they do not provide comment on the percentage of study participants they were able to do 60 day follow up with.

METHODS:
- Interventions: high vs. low dose, continuous vs. bolus
- Study Groups: What were the various study groups (eg: control / placebo, intervention 1, intervention 2, etc)
  - IV bolus Q12H of daily dose
  - IV bolus Q12H of 2.5 daily dose
  - Continuous of daily dose
  - Continuous of 2.5 daily dose
- Instruments:
  - Visual analog scales
  - Wanted to assess 2 primary end points – safety and efficacy
- Data Collection: does not say who collected data

DATA ANALYSIS:
- Level of Data: Ordinal
- Statistics Used:
  - Linear model – for continuous end points
  - Logistic regression – for binary end points
  - Cox or Kaplan-Meier curves – for time to event end points
- What, if any, variables were controlled for
  - n/a

RESULTS:
- Brief answers to research questions:
Patient’s in the bolus group require more dose increases

- No significant different in primary efficacy as measured by global assessment of symptoms
- No significant difference in primary safety end point of change in serum creatinine
- **Patient’s on high dose strategy were more likely to be changed to oral diuretic agent at 48 hours**
- No statistical significant difference in rates of death, rehospitalization, or ED visit within 60 days.
- 23% in high dose group met safety end point of worsening renal function (rise in serum Cr >0.3) vs 14% in low dose (P=0.04)
- **High dose group was associated with greater relief of dyspnea, greater fluid loss, and fewer SAE.**
- The low dose group had more serious adverse effects than the high dose group (p=0.033). Yet severe SAEs were not statistically significant.
  - SAE = MI, Afib, cardiac arrest, VT, hyperK, hypoK, hypoNa, renal failure, renal failure requiring dialysis

- **Other possible explanation for findings/Limitations**
  - Treatment was really not standardized -> they had 24 hours to enroll a subject. Large boluses of diuretic are given in the first day. After 48 hours, other drugs could be added and doses titrated. Open label use of diuretic could therefore take place for the first day and after the 3rd day
  - This study is likely only applicable to people with a known diagnosis of CHF. Patients whom are “lasix naïve” are likely to not fit into one of these treatment groups.
  - *They do not mention the amount of fluid given as a “placebo” from the continuous infusion dummy group. This could certainly have adverse affects.
  - *The use of a visual analog scale is not great when comparing large groups of people. It is trying to produce interval data when it really should be ordinal.
  - *Most study subjects were white men

**IMPLICATIONS FOR PRACTICE:**

- **Applicable to this clinical practice:** Is the study population generalizable to the population likely to be affected by this intervention / outcome in your clinical practice? If not, what setting may this be applicable to?
  - **High dose strategy, bolus type, is the way to go.** Although it raised serum Cr more so than low dose group, this study shows that at 60 days there is no worse clinical outcomes. Therefore transient worsening of renal function during hospitalization for CHF may not affect outcomes.
• Feasible? – Yes – bolus is easier and cheaper, easier on the patient too

• Clinically Relevant: Yes – although it has faults in its design, the 60 day follow up is potentially relevant

LEVEL OF EVIDENCE / DECISION FOR USE:
• Background    Consider Replication    Ready for use

• Level of Evidence:
  Ia Evidence obtained from meta-analysis of randomized controlled trials
  Ib Evidence obtained from at least one RCT
  Iia Evidence obtained from at least one well-designed controlled study without randomization
  Iib Evidence obtained from at least one other type of well-designed quasi-experimental study
  III Well-designed non-experimental studies
  IV Expert committee reports, opinions of experts