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Abstracts

□ ASSOCIATION OF SCHEDULED VS EMERGENCY-ONLY DIALYSIS WITH HEALTH OUTCOMES AND COSTS IN UNDOCUMENTED IMMIGRANTS WITH END-STAGE RENAL DISEASE.

Nguyen OK, Vasquez MA, Charles LLCSW, et al.
JAMA Internal Medicine. 2019;179(2):175-183

Scheduled dialysis has been proven effective at prolonging life for patients with end stage renal disease (ESRD) and is thus considered standard of care. Most people living in the United States are able to receive scheduled dialysis through either Medicare or Medicaid coverage. However in 40 out of 50 states, uninsured individuals ineligible for federal assistance, often undocumented immigrants, are denied that right and receive emergency only dialysis. Previous studies have suggested that this "compassionate" dialysis results in higher stress levels for patients, worse quality of life, and increased medical costs. Currently, there is little data that comparatively evaluates the cost, health outcomes, and utilization for scheduled versus emergency only dialysis.

The objective of this study was to measure the efficacy of scheduled versus emergency only dialysis in undocumented immigrants who live in Dallas, Texas. Due to the passage of the Affordable Care Act and the ban on exclusions for preexisting conditions, uninsured individuals were given an opportunity to gain access to private health insurance and charitable premium assistance, which ultimately led to them securing scheduled dialysis. Researchers conducted a retrospective observational study of uninsured individuals with ESRD who were 18 years old or older and were receiving emergency only dialysis in February 2015 at Parkland Hospital. Baseline data was gathered from 6 months prior to enrollment and patients were followed until 1 year after enrollment. Primary outcomes included death and healthcare utilization. Secondary outcomes focused on cost.

Of the 181 individuals enrolled, 105 were approved and enrolled in scheduled dialysis and 76 were denied placement in a dialysis center and remained on emergency only dialysis. These individuals were denied, not due to their comorbidities or documentation issues, but for issues related to the dialysis center such as lack of availability. At baseline, the patients who were enrolled for scheduled dialysis were younger, had more frequent presentations to the emergency department, and were on dialysis for a longer period of time. At 12 months they found that the mortality rates were lower in the scheduled dialysis group with an absolute risk reduction of 14% and a number needed to treat (NNT) of 7 (HR: 4.6 (95% CI: 1.2-18.2). Rates of health care utilization, defined as the number of emergency room visits, hospitalizations, and hospital days, decreased significantly in the scheduled dialysis group. Those having scheduled dialysis had 5.2 fewer ED visits per month, for example (Difference-in-Difference: −6.2 ED visits per month, 95% CI(−7.0 to −5.4)). With respect to cost, baseline price per person per month (PPPM) decreased significantly a year after enrollment, showing a net decrease of $4316 PPPM for patients who were enrolled in scheduled dialysis (Difference-in-Difference: −$5768, 95% CI(−8332 to −3204)).

The authors conclude that scheduled dialysis is superior to emergent dialysis and leads to lower mortality, cost, and healthcare utilization. The authors recommend that scheduled dialysis should be the standard of care for **all** persons with ESRD in the United States.

[Alisa Fujihashi, MD
Jerrilyn Jones, MD
University of Arkansas for Medical Sciences, Little Rock, Arkansas]

Comment: Emergency departments and hospitals across the country feel the burden of emergency only dialysis and would benefit from a safe and cost-effective solution. This is the first evaluation of scheduling dialysis in patients who previously were only able to obtain emergent dialysis. While this is retrospective and some of the outcomes may not be generalizable across the country, this important study indicates that scheduled dialysis is preferred to save lives and money.

□ EARLY USE OF NOREPINEPHRINE IN SEPTIC SHOCK RESUSCITATION (CENSER): A RANDOMIZED TRIAL.

Permpikul C, Tongyoo S, Viarasilpa T, et al. *Am J Respir Crit Car Med*. 2019, Feb 1. doi: 10.1164/rccm.201806-1034OC

Recent retrospective analyses have indicated a possible utility in early administration of norepinephrine (NE). Permipikul and colleagues designed single center, double blinded RCT to evaluate these claims prospectively.

The goal of the study was to evaluate the utility of early low-dose NE in septic shock. Patients were eligible if they were aged > 18 years and presented with MAP < 65mmHg and suspected sepsis. They were randomized to receive early low dose NE through a peripheral IV at a rate of 0.05μg/kg/hr in addition to standard of care (fluids, antibiotics, and open label

vasopressors). The control group received placebo plus standard of care. The primary composite endpoint was control of shock within 6 hours of the diagnosis of sepsis with hypotension. Shock control was defined by a MAP >65mmHg plus either urine output > 0.5mL/kg/h or a decrease of baseline lactate by 10%. Secondary outcomes included 28-day mortality and hospital mortality. Multiple safety outcomes were also recorded.

Three hundred ten patients were randomized. The groups were well matched with regard to prognostic factors. The median door-to-norepinephrine time was 99 minutes less in the treatment group (93 vs 192 minutes, P<0.001), with a 27.7 % increase in shock control at 6 hours (OR=3.4; 95% confidence interval [CI]: 2.09–5.53). There were no differences in rates of ICU admissions, hospital length of stay, 28-day mortality rates or hospital mortality rates.

Of the safety outcomes, cardiogenic pulmonary edema and new onset arrhythmias had a lower incidence in the early NE group compared to control. Episodes of cardiogenic pulmonary edema were 14.4% in the NE group compared to 27.7% in the control group (p=0.04). Interestingly, there was no difference in fluid resuscitation within the first 3 days. Total volume status during hospital stay was not calculated which may have elucidated the etiology of the cardiogenic pulmonary edema. Given that early NE when compared to control achieved both MABP and target urine output earlier (35.5% vs 24.% (p=0.04)), the authors inferred that the patient's ability to diurese unnecessary volume early in their course could have played a part in the lower rates of pulmonary edema found in the NE group. Their second safety endpoint, new onset arrhythmias, also occurred less often in the treatment group (11% vs 20%; p=.03). As NE has been shown to increase global perfusion without significant improvement in coronary perfusion, the authors postulated that the reduction in arrhythmias was due to a shorter duration of myocardial oxygen demand secondary to early shock control. Currently, no safety data exists regarding NE and its association with arrhythmias in the setting of sepsis.

The authors found a statistically significant association between early norepinephrine and increased shock control within 6 hours and suggest this protocol may be superior to current standards of care.

[Alex Rahnema, MD
Jerrilyn Jones, MD, MPH
University of Arkansas for Medical Sciences, Little Rock, Arkansas]

Comment: This RCT is the first to date that has analysed prospective early administration of norepinephrine in management of sepsis with hypotension. While there was robust randomization, the rapid effect that early NE had blood pressure could have potentially unblinded physicians. Also, while patients often do suffer from iatrogenic fluid overload in the management of sepsis, future studies should consider total volume status from admission to discharge in order to understand the relationship between early NE use and observed lower rates of cardiogenic pulmonary edema. Unfortunately this study found no differences between mortality or length of stay so we can't say if NE truly provides a clinically significant benefit, however we suspect the study may have been underpowered for those outcomes.

☐ KETAMINE INFUSION FOR PAIN CONTROL IN ADULT PATIENTS WITH MULTIPLE RIB FRACTURES: RESULTS OF A RANDOMIZED CONTROL TRIAL.

Carver TW, Kugler NW, Juul J, et al. *J Trauma Acute Care Surg*. 2019;86(2):181-188

For trauma patients with rib fractures, adequate pain control is critical to decreasing mortality from respiratory complications. Historically rib fracture pain management has predominantly depended on narcotics; however growing concerns about the side effects as well as dependency issues associated with opioids has sparked interest in alternative therapies. Although ketamine is usually used as adjunct therapy for patients with pain refractory to traditional multimodal pain protocols, there is data to suggest that use of low-dose ketamine (LDK) may decrease a patient's opioid requirement.

The goal of this study was to evaluate the use of LDK for primary pain management of traumatic rib fractures as opposed to adjunct therapy. Adult blunt trauma patients with three or more rib fractures were randomized to receive LDK infusion ($2.5\mu g \cdot kg^{-1} \cdot min^{-1}$) or similar volume of placebo (0.9% sodium chloride) for 48 hours. Patients were excluded from the trial for various reasons, including age over 65 years, Glasgow Coma Scale (GCS) less than 14, a history of psychosis, use of more than 2 psychotropic medications, chronic opioid use, currently had substance abuse issues, active acute coronary syndrome, and severe hypertension. The primary outcome of this prospective, randomized, double-blinded, placebo-controlled trial was a reduction in numeric pain scores (NPS) 24 hours after initiation of LDK infusion compared to NPS of patients receiving placebo. The authors defined a clinically significant reduction in NPS as a two-point reduction on the 11-point scale. Secondary outcomes included reduction in NPS at 48 hours, oral morphine equivalents (OME) required at 24 and 48 hours, total for hospitalization, hospital length of stay, time spent in the intensive are unit (ICU), epidural placement rate, and incidence of pulmonary complications and adverse events.

Ninety-one patients who presented to Froedtert Memorial Lutheran Medical Center, a Level I Trauma Center, from August 2015 to December 2017 after blunt trauma were randomized into the trial. Forty-five patients received LDK infusion and 46 were randomized to receive placebo. Motor vehicle collision (MVC) accounted for 45.7% of injuries and patients were predominantly male (74.7%) with a median age of 49 years and median Injury Severity Score (ISS) of 14. Seventy-five patients received more than 36 hours of infusion with no difference in infusion duration between the experimental (LDK) arm and placebo. Patients received standard multimodal pain management with oral nonsteroidal anti-inflammatory medications, acetaminophen, and muscle relaxants, however the groups had similar utilization of these medications. There was no difference in NPS or OME totals between the two groups. Rate of adverse events or epidural placement was not significantly different between the two groups. Subset analysis did show, however, a significant reduction in OME for severely injured patients (ISS > 15) receiving LDK (OME 180.3 for LDK group versus 328.5 in placebo, p<0.05).