

ISN Global Trials Focus

May 2020



The ISN-ACT (Advancing Clinical Trials) team presents a monthly showcase of randomized trials in nephrology from around the world. Featured trials are not just those with the highest impact, but also trials that highlight the diversity of current research in nephrology. Trials are reviewed in context and risk of bias assessed in seven key areas. We hope our efforts will stimulate improvement in trial quality and promote greater engagement in trial activity.

If you are interested in contributing, either by suggesting a trial or joining the team, please send a brief CV to research@theisn.org.

Join the conversation each month by following us @ISNkidneycare

Key to risk of bias assessment

Random sequence generation	High risk
Allocation concealment	Uncertain risk / not stated
Blinding of participants/personnel	Low risk
Blinding of outcome assessment	
Complete outcome data	
Complete outcome reporting	
No other sources of bias	

Contents

Early bird doesn't get the worm! Early angiography offering little benefit in stable CAD	1
Managing ischemia in CKD: A change of heart?	2
Co-management by primary care physicians and nephrologists does not improve survival without hospitalisation	2
Practice does not necessarily make perfect: no definitive benefit over standard care to regular retraining of PD techniques.....	2
One step forward, one step back?	3
BCM-guided dry weight assessment did not improve short-term survival in dialysis patients.....	3

ISN Academy: [Chronic Kidney Disease](#)

Early bird doesn't always get the worm: Angiography offers little benefit in CKD patients with stable CAD
Management of Coronary Disease in Patients with Advanced Kidney Disease
[Bangalore et al. N Engl J Med. 2020;382\(17\):1608-18.](#)

Population	777 participants with advanced CKD (eGFR <30 mL/min/1.73m ²), stable coronary artery disease, and moderate-severe inducible myocardial ischemia	
Intervention vs Comparator	Angiography with revascularisation (if indicated) vs optimal medical therapy with angiography reserved for failure of medical therapy	Time 3 years
Outcomes	<p>Revascularisation was performed in 85% in invasive vs 50% of conservative arm participants. No was seen in difference in death or nonfatal MI between invasive vs conservative strategy (cumulative incidence, 36.4% vs 36.7%; difference -0.4% [95% CI -8.5 to 7.8]; HR 1.01 [95% CI 0.79 to 1.29]; P=0.9). Results were similar when unstable angina, heart failure, or resuscitated cardiac arrest were added to the composite outcome.</p> <p>The invasive strategy arm experienced a higher risk of stroke (HR 3.76, 95% CI 1.52 to 9.32; P = 0.004) and of the composite of death or need for dialysis (HR 1.48, 95% CI; 1.04 to 2.11; P = 0.02).</p>	

This study (ISCHEMIA-CKD) finds that, in individuals with advanced CKD and stable CAD, an initial invasive strategy did not reduce the risk of death, nonfatal MI or hospitalisation for UA, heart failure or resuscitated cardiac arrest. Previous coronary intervention studies have excluded patients with advanced CKD making this an important finding. However, it is important to note this study does not apply to patients with acute coronary syndrome, left main coronary disease or heart failure with EF < 35%.



ISN Academy: [Chronic Kidney Disease](#)

Managing ischemia in CKD: A change of heart?

Health Status after Invasive or Conservative Care in Coronary and Advanced Kidney Disease

[Spertus et al. N Engl J Med. 2020;382:1408-1419](#)

Population	705 participants with advanced CKD (eGFR <30 mL/min/1.73m ²), stable coronary artery disease, and moderate-severe inducible myocardial ischemia	
Intervention vs Comparator	Angiography with revascularisation (if indicated) vs optimal medical therapy with angiography reserved for failure of medical therapy	Time 2 years
Outcomes	At no point during follow up was there a credible difference between the two groups in terms of Seattle Angina Questionnaire (a measure of angina frequency and severity). Overall mean differences varied from 0.1 to 2.4 (on a 100 point scale). Subgroup analysis suggested benefit for those with at least weekly angina at baseline (mean difference 10.1 points; 95% credible interval, 0.0 to 19.9) at 3 months, however this benefit did not persist after 6 months, with the difference at 12 months being only 2.2 (95% credible interval, -8.0 to 13.1).	

This is an important complementary study to the primary analysis of ISCHEMIA-CKD by Bangalore et al. Spertus et al. find that, in addition to no effect on the hard end-points of non-fatal MI and death, an initially invasive management strategy for stable coronary artery disease with moderate to severe ischemia in patients with advanced chronic kidney disease does not have benefits in patient-reported health status when compared with a conservative strategy. While important to note that a minority of participants with frequent anginal symptoms did experience a credible improvement in symptoms with an early invasive strategy, this appeared to be short-lived.



ISN Academy: [Chronic Kidney Disease](#)

Co-management by primary care physicians and nephrologists does not improve survival without hospitalisation

Impact of superimposed nephrological care to guidelines-directed management by primary care physicians of patients with stable chronic kidney disease: a randomized controlled trial

[Saudan et al. BMC Nephrology. 2020\(21\):128](#)

Population	242 people with stage 3b-4 CKD identified as study participants during a hospitalisation event.	
Intervention vs Comparator	Co-management by primary care physicians and nephrologists vs management by primary care physicians guided by written renal clinical practice guidelines (KDOQI) with on demand email, telephone and face-to-face review by nephrologists.	Time 2 years
Outcomes	There was no difference in the primary outcome of death or emergency rehospitalisation between groups (P=0.2). Similarly, there was no difference in eGFR decline, elective dialysis initiation or quality of life.	

This study trialed two models of renal care that did not differ in its primary or secondary outcomes. Its authors argue that some of its design limitations prevented a true impact of interventions to be observed. These limitations included only 60% receiving randomised treatment and being underpowered to detect a difference in survival or rehospitalisation. However this provocative study encourages further assessment of utility and cost-effectiveness of co-management of CKD by nephrologists and primary care physicians versus primary care physician led management with on-demand nephrology consultation.



ISN Academy: [Peritoneal Dialysis](#)

Practice does not necessarily make perfect: no definitive benefit over standard care to regular retraining of PD techniques

Prevention of peritoneal dialysis-related peritonitis by regular patient retraining via technique inspection or oral education: a randomized controlled trial

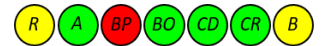
[Xu et al. Nephrol Dial Transplant. 2020;35:676-686.](#)

Population	150 participants who had recently completed peritoneal dialysis training	
Intervention vs Comparator	1:1:1 randomisation to second-monthly retraining on performance of PD bag exchange via technique inspection; retraining via oral education, or usual care.	Time 2 years

Outcomes

There was both a low event rate for errors at each retraining session in both intervention arms (≤ 1) and PD peritonitis episodes. There was no difference in time to first episode of peritonitis among groups [HR 0.87 (95% CI 0.47-1.62) for inspection group and 0.82 (95% CI 0.45-1.53) for oral education]. In terms of secondary outcomes, the technique inspection group, but not the oral education group had a lower risk of first non-enteric peritonitis than control [HR 0.33 (95% CI 0.12-0.92) and HR 0.77 (95% CI 0.36-1.67), respectively]. There were no differences between arms for enteric or culture-negative peritonitis event rates.

International consensus guidelines recommend periodic retraining of PD patients, but this has not been supported with high level evidence. This single centre study was unable to justify this additional retraining protocol with either of its education programmes although they were limited by a high degree of drop out (82/150 patients) that at least halved numbers in each arm by study completion. Secondary outcomes for the inspection group may suggest that touch contamination may be reduced (lower non-enteric infection rates) but was associated with the withdrawal of 14% of patients due to unwillingness to be re-observed. There will need to be further fine tuning of education techniques before uptake of these strategies can be supported.



ISN Academy: [Hemodialysis](#)

One step forward, one step back?

A Walking Intervention to Increase Weekly Steps in Dialysis Patients: A Pilot Randomized Controlled Trial

[Sheshadri et al. Am J Kidney Dis. 2020;75\(4\):488-496](#)

Population	60 dialysis recipients (48 HD / 12 PD)	
Intervention vs Comparator	Pedometer plus weekly phone-based coaching for 3 months vs. usual care (with pedometer provided for only one week at baseline, 3 months and 6 months)	Time 6 months
Outcomes	Baseline step counts were $3,578 \pm 3,680$ and $3,924 \pm 3,422$ in the control and intervention groups, respectively. The intervention group increased their daily step count at 3 months by 2,256 steps (95% CI 978 to 3,537; $P=0.001$) relative to controls. This difference was not apparent at 6 months (-34 steps, 95% CI -1,179 to 1,111; $P=0.9$). Dialysis Symptom Index scores were higher in the intervention group at 3 and 6 months and vitality scores were lower (6 month mean difference in total symptom burden 4.9, 95% CI 2.6 to 7.2; $P<0.01$; vitality score mean difference -13.7, 95% CI -25.0 to -2.5; $P=0.02$)	

This study emphasises the difficulty engendering durable behaviour change in the dialysis population. The intervention group increased their step count by an impressive 50% while the phone-based coaching was in place. However, this gain disappeared entirely at 3 months and was, unexpectedly, associated with worsening of symptom scores and vitality. The authors speculate that the patient's expectations changed, resulting in a perceived worsening of symptoms following the intervention period. Nevertheless, the benefits of regular exercise seem such that researchers should continue to strive for sustainable exercise programs in this population.



ISN Academy: [Hemodialysis](#)

BCM-guided dry weight assessment did not improve short-term survival in dialysis patients

BOdy COMposition MONitor (BOCOMO) study, a randomised trial

[Liu et al. BMC Nephrology 2020;21:135](#)

Population	445 participants on maintenance hemodialysis	
Intervention vs Comparator	Use of body composition monitoring (BCM) (bioimpedance measurement every 2 months) to determine dry weight vs control (standard clinical practice)	Time 1 year
Outcomes	During a median follow-up of 13.7 months, 18 (4.0%) patients died. Kaplan-Meier survival analysis showed no significant difference in survival between two groups (HR 0.51, 95% CI 0.24-1.08; log-rank test p-value = 0.07) after one-year follow-up. There was no difference in the primary composite outcome of death, acute myocardial infarction, cerebral infarction, cerebral haemorrhage, and peripheral vascular disease.	

There is a well-known association between fluid overload and increased mortality in dialysis patients. Bioimpedance is a non-invasive technique which represents an attractive way of more accurately assessing fluid status in dialysis patients. Previous studies had shown that strict BCM-guided fluid management led to better blood pressure control, a decrease in arterial stiffness, a reduction of intradialytic symptoms and improved survival. These findings were not reflected in this study. This may be due to a small sample size, differences in study population or short follow-up duration.

