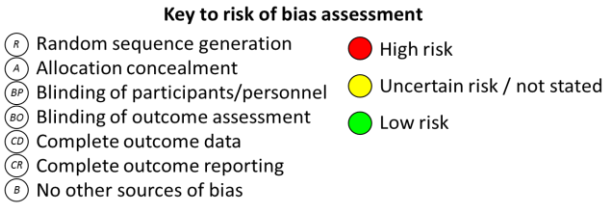
ISN Global Trials Focus

January 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*



Contents

ISN Academy: Interventional Nephrology, Hemodialysis

Brace for it: an external support device may help fistulas to mature

An Implanted Blood Vessel Support Device for Arteriovenous Fistulas: A Randomized Controlled Trial

Karydis et al. Am J Kidney Dis. 2020;75(1):45-53

Population	40 adults undergoing new brachiocephalic arteriovenous fistula (AVF) creation	
Intervention *vs* Comparator	VasQ device (nickel titanium external support implant with a brace wrapped around the brachial artery and mesh braid around cephalic vein to reduce flow disturbances at the juxta-anastomotic region) vs. standard care	**Time** 6 months
Outcomes	There were no severe device-related adverse events (primary outcome) detected. There were no device-related infections or differences in mortality, AVF revascularisation or AVF-related complications between groups. There was no between-group differences in AVF primary patency at 6 months (16/20 vs. 12/18 [treatment vs. control]; P=0.5) or cephalic vein volume flow at 6 months (1394 vs. 1047 ml/min; P=0.1). Cephalic vein stenosis >50% occurred less in the intervention group (3/20 vs. 10/20; P=0.04) though this outcome was not pre-specified.	

This small short-term first-in-human study of the VasQ device in newly created brachiocephalic AVFs showed it to be safe and reduced cephalic vein stenosis. While adequately powered studies are necessary to evaluate the efficacy and safety of the VasQ device on AVF maturation, this exciting new invention could help to straighten the often crooked path to long-term fistula function.

ISN Academy: Peritoneal Dialysis, Fluid and Electrolytes

No benefit from routine bioimpedence spectroscopy in PD

Bioimpedance spectroscopy-guided fluid management in peritoneal dialysis patients with residual kidney function: A randomized controlled trial

Yoon et al. Nephology. 2019;24(12):1279–1289

Population	201 adult peritoneal dialysis patients (on CAPD or CCPD)	
Intervention *vs* Comparator	Fluid status management using bioimpedance spectroscopy (BIS) to reach a target hydration goal of -2.0 to +2.0 vs. clinical method-guided management.	**Time** 12 months
Outcomes	There was no significant difference in the change in residual kidney function, measured by change in renal Cr-urea clearance (P=0.965) and 24 hour urine volume (P=0.596) between the two groups. Neither was there a significant difference in most echocardiographic parameters (apart from a decrease in E/E' ratio in the BIS group, P=0.03), frequency of changes in dialysate or diuretic prescriptions, hospitalisations or CV event-free survival and mortality rates between the groups.	

BIS-guided fluid management did not provide any additional benefit compared with clinical method-guided management in PD patients with residual kidney function. One major limitation of the study was the relatively high drop-out rates, particularly in the BIS group (35.9%). The role of technology in routine volume assessment remains unclear.

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ISN Academy: Hemodialysis

Novel kappa opioid receptor agonist improves itch in people receiving hemodialysis therapy

A Phase 3 Trial of Difelikefalin in Hemodialysis Patients with Pruritus

Fishbane et al. N Engl J Med. 2019 Nov 8. doi: 10.1056/NEJMoa1912770.

Population	378 chronic hemodialysis recipients with moderate to severe pruritis	
Intervention *vs* Comparator	Difelikefalin (0.5 micrograms per kilogram three times per week IV for 12 weeks) vs Placebo	**Time** 12 weeks
Outcomes	82/158 (51.9%) in the difelikefalin group had an improvement of at least 3 points in the 24-hr Worst Itching Intensity Numerical Rating Scale vs 51/165 (30.9%) in the placebo group. Imputed to 49.1% vs 27.9% for difelikafalin and placebo respectively (P<0.001). Diarrhea, vomiting and dizziness were more common in the difelikefalin group.	

This interesting study adds a new agent for patients suffering pruritis. However, the benefit of difelikefalin appears modest (with respect to the estimated minimal clinically important difference in pruritis scores) and has not yet been tested against active comparators. The role of this novel drug remains to be further defined.

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ISN Academy: Anemia, Iron and Trace elements, Hemodialysis

Thinking zinc? Not all replacement formulations are equal

Comparison of zinc acetate hydrate and polaprezinc for zinc deficiency in patients on maintenance hemodialysis: A single-center, open-label, prospective randomized study

Ther Apher Dial. 2019 Dec 3. doi: 10.1111/1744-9987.13461

Population	94 maintenance hemodialysis recipients with zinc deficiency (serum zinc <70ug/dL)	
Intervention *vs* Comparator	Zinc acetate hydrate (ZAH) vs. polaprezinc (PPZ)	**Time** 6 months
Outcomes	Both treatments significantly increased zinc levels at 3 months, with the proportional increase being greater in the ZAH group (73% vs. 43%; P=0.001). Copper levels were significantly lowered in the ZAH group, but did not change in the PPZ group. Adverse events were more common in the ZAH group. No impact on erythropoietin stimulating agent dose was observed.	

Zinc deficiency is reported to be common in people receiving hemodialysis, and has been linked to taste disorders and erythropoietin hyporesponsiveness. This study suggests that zinc replacement formulations may differ in their efficacy and side effects.

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Getting things straight when it comes to peritoneal dialysis catheters

Straight Versus Coiled Peritoneal Dialysis Catheters: A Randomized Controlled Trial.

Am J Kidney Dis. 2020;75(1):39-44

Population	308 adult continuous ambulatory peritoneal dialysis patients	
Intervention *vs* Comparator	Insertion of straight vs. coiled peritoneal dialysis catheters	**Time** 21 months (mean)
Outcomes	Catheter dysfunction/drainage failure occurred in 9/155 (5.8%) participants with coiled vs. 1/151 (0.7%) with straight catheters (difference in catheter dysfunction risk = 5.1% [95% CI 1.2-9.1; P = 0.02]). Coiled catheters were associated with a slightly higher pain score (data not shown), but no increase in peritonitis risk (HR, 0.87; 95% CI, 0.60- 1.27; P = 0.5) or difference in catheter survival (HR, 0.95; 95% CI, 0.73-1.23; P = 0.7).	

This study almost doubles the number of participants randomized in straight vs. coiled catheter trials and, in line with prior meta-analyses, finds a benefit to insertion of straight-tip PD catheters. Although catheter survival does not seem to differ, straight catheters seem to offer a better chance of avoiding twists and turns in the road following commencement of PD.