What’s Hot, What’s New

Randall Faull
IPP ANZSN
What’s HOT?
What else is hot?
Maybe not so hot
What’s NEW?
More new
Very New
NEW
England Journal of Medicine
Effect of home testing of INR on clinical events – Matchar et al, NEJM 2010; 363: 1608

- 2922 patients, randomised to weekly self-testing or monthly clinic testing
- Followed for 2.0-4.75 years
- Primary end point – time to first major event (stroke, major bleed, death)
- No difference in primary end point
- Self care group slightly more minor bleeds, slightly more time in target range, and slightly better patient satisfaction
Rivaroxaban for symptomatic venous thromboembolism – EINSTEIN investigators, NEJM 2010; 363: 2499

- Oral factor Xa inhibitor
- Fixed dose regime, no lab monitoring
- 3449 patients, randomised comparison of Rivaroxaban vs SC Enoxaparan, then warfarin or acenocoumarol
- Followed by additional 6-12 months of Rivaroxaban vs placebo (1196 patients)
- No difference in first study in either recurrent venous thromboembolism or safety
- Less recurrent thrombosis (8 vs 42) in second study; 4 nonfatal major bleeds vs 0 with placebo
Apixaban vs Enoxaparin for thromboprophylaxis after hip replacement – Lassen et al, NEJM 2010; 363: 2487

- 5407 patients, randomised – Apixaban 12-24 hours post surgery; Enoxaparin 12 hours before

- For 35 days, then bilateral venography, then followed additional 60 days

- Less thrombosis with Apixaban (27 [1.4%] vs 74 [3.9%])

- No difference in bleeding
Apixaban in patients with atrial fibrillation – Connolly et al, NEJM 2011; 364: 806

- 5599 patients with AF but unsuitable for warfarin randomised to Apixaban or aspirin
- Mean follow-up 1.1 years
- Study terminated early due to clear benefit of Apixaban – 51 vs 113 events per year; death rate 3.5 vs 4.4%
- Major bleeds – 44 vs 39 (11 vs 13 intracranial)
Thoughtful interlude
Two thoughtful people

- 358 patients unsuitable for surgery randomly assigned to standard therapy (inc. valvuloplasty) vs balloon-expandable bovine pericardial valve
- Death rate @ 1 year 50.7 vs 30.7%
- Among survivors, cardiac symptoms 58 vs 25.2%
- At 30 days, higher rate of stroke and vascular complications in valve replacement group
Cardiac resynchronization therapy for mild-to-moderate heart failure – Tang et al, NEJM 2010; 363: 2385

- 1798 patients with NYHA class II or III heart failure, LVF <30%, and wide QRS complex, followed mean of 40 months
- Randomly assigned to implantable cardioverter-defibrillator (ICD) or that plus cardiac-resynchronization therapy (CRT)
- Lower rate of primary outcome in combined group (33.2 vs 40.3%), but higher rate of adverse event at 30 days (124 vs 58)
ACCORD study (1238 collaborators)

- Combination lipid therapy vs statin alone – did not reduce CV events (NEJM 2010; 362: 1563)
- Intensive blood pressure control in type II DM (NEJM 2010; 362: 1575) – did not reduce CV events
- Intensive glycaemic and lipid control reduced progression of retinopathy, but not intensive BP control (NEJM 2010; 363: 233)
- Intensive glycaemic control reduced nonfatal MI, but increased 5 year mortality
Time for some kidney stuff
Changes to funding of dialysis in the USA

- NEJM February 16, 2011
  - “Special treatment – the story of Medicare’s ESRD treatment”
  - “Bundled payment for ESRD – including ESAs in Medicare’s dialysis package”

- As of January 2011, await with interest the effect on use of ESAs, IV iron, and IV vitamin D

- The impact of the financial model on the renal literature
Further effects of funding changes

- JASN 2011; 22, 426
  - Clinical technical expert panel
  - “….concluded unanimously that the single most important measure (to decrease vascular access-related infections) would be to remove financial and regulatory barriers to timely placement and revision of hemodialysis fistulas and the concurrent avoidance of cathether use….“
Japanese experience with funding changes

  - Introduced bundling policy to incorporate ESA in dialysis reimbursement
  - Hb maintained
  - Mean dose of ESA decreased 11.8%
  - % of patients prescribed IV iron increased significantly, but not mean dose
Enough about money
Treatment of ADPCKD

- Sirolimus and kidney growth in ADPCKD – Serra et al, NEJM 2010; 363: 820
  - No effect of 18 months of sirolimus on cyst growth
- Everolimus in patients with ADPCKD – Budde et al, NEJM 2010; 363, 830
  - 2 years treatment, slowed increase in total kidney volume, but not progression of renal impairment
Treatment of vasculitis

  - Not superior/not inferior for induction therapy
  - May be more effective in relapsing disease
  - Comparable adverse effects
IDEAL trial

- Cooper et al, NEJM 2010; 363: 609
- “…planned early initiation of dialysis in patients with stage V chronic kidney disease was not associated with an improvement in survival or clinical outcomes”
In-center hemodialysis six times per week versus three times per week

- FHN Trial Group, NEJM 2010; 363: 2287
- 245 patients, randomised
- weekly Kt/V 3.54 vs 2.49
- frequent HD
  - significant benefits (death, LV mass, physical health composite score (SF-36), HT, phosphate)
  - more frequent interventions related to vascular access
Intensive blood-pressure control in hypertensive chronic kidney disease

- Appel LJ et al, NEJM 2010; 363: 918
- 1094 black Americans, intensive (130/78) vs standard (141/86) BP control
- no effect on kidney disease progression, except possibly those with more proteinuria
Racial variation in medical outcomes among living kidney donors

- Lentine et al, NEJM 2010; 363: 724
- retrospective study of 4650 kidney donors
- compared with white donors
  - black donors had increased risk of HT (1.52x), DM (2.31x), and CKD (2.32x)
  - similar for Hispanic donors
  - ESRD in <1%, but more common in blacks
Rosuvastatin and cardiovascular events in patients undergoing hemodialysis (AURORA)

- Fellstrom et al, NEJM 2009; 360: 1395
- 2776 patients, 50-80 years old
- “…initiation of…rosuvastatin lowered the LDL… but had no significant effect on the composite primary end point of death from cardiovascular causes, nonfatal MI, or nonfatal stroke”
Erythropoietic response and outcomes in kidney disease and type 2 diabetes (TREAT)

- Solomon et al, NEJM 2010; 363: 1146
- 1872 patients, not on dialysis
- poorer initial response
  - lower Hb at follow up, despite high dose of ESA
  - higher rate of composite cardiovascular end point or death
Outcomes of kidney transplantation in HIV-infected recipients

- Stock et al, NEJM 2010; 363: 2004
- prospective study of 150 stable patients
- followed for median 1.7 years
- patient survival – 1 yr 94.6%, 3 yrs 88.2%
- graft survival – 90.4 and 73.7%
- higher than expected rejection rate – 31 and 41% at 1 and 3 years
- HIV infection remained well controlled
Prevention of dialysis catheter malfunction with recombinant tissue plasminogen activator

- Hemmelgam et al, NEJM 2011; 364: 303
- 225 patients with newly inserted central vein catheter for long-term HD
- randomised to heparin lock 3/week, or rTPA in mid-week lock (heparin for other 2)
- catheter malfunction in 34.8 vs 20.0%
- bacteraemia in 13.0 vs 4.5%
- other adverse effects similar
Yes, there is more
Molecular architecture of the Goodpasture autoantigen in anti-GBM nephritis

- Pedchenko et al, NEJM 2010; 363: 343
- compared antibody epitopes in anti-GBM and Alport’s post-transplantation nephritis
M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy

- Beck et al, NEJM 2009; 361: 11
- Serum from 26 of 37 with idiopathic membranous (not secondary) identified 185kD glycoprotein from glomeruli
- Antibodies against conformation-dependent epitope M-type phospholipase A(2) receptor – present in podocytes and immune deposits in membranous
Risk HLA-DQA1 and PLA2R1 Alleles in idiopathic membranous nephropathy

- Stanescu et al, NEJM 2011; 364: 616
- Genomewide association studies of SNPs in three white populations with membranous (556 patients)
- HLA-DQA1 allele most closely associated
- Also associated with gene encoding M-type phospholipase A2 receptor (previously shown to be target of autoimmune response)
- Odds ratio 78.5 if homozygous for both risk alleles
PLA2R autoantibodies and recurrent membranous nephropathy after transplantation

- Stahl et, NEJM 2010; 363: 496 (letter)
- anti-PLA2R autoantibody detected in patient with membranous as cause of renal failure, and when it recurred post-transplantation
PLA2R autoantibodies and PLA2R glomerular deposits in membranous nephropathy

- Debiec et al, NEJM 2011; 363: 689 (letter)
- assessed their presence in 42 patients with idiopathic membranous
Other journals
Role of residual renal function in phosphate control and anemia management in chronic hemodialysis patients

- Penne et al, CJASN 2011; 6: 281
- 552 patients from Convective Transport Study (CONTRAST)
- residual function = lower phosphate and less resistance to ESA cf anuric patients
Long-term experience with kidney transplantation from hepatitis C-positive donors into hepatitis C-positive recipients

- Morales et al, AJT 2010; 10: 2453
- 162 Hep C +ve recipients of hep C +ve kidney, vs 306 recipients of hep C –ve kidney
- 1990-2007, mean follow-up 74.5 months
- 5/10 yr survival
  - patient 84.8 and 72.7% vs 86.6 and 76.5%
  - graft 58.9 and 34.4% vs 65.5 and 47.6% (p=0.006)
- decompensated liver disease 10.3 vs 6.2%
Immunosuppression with belatacept-based, corticosteroid-avoiding regimens in de novo kidney transplant recipients

- Ferguson et al, AJT 2010; 11: 66
- 2 belatacept regimes (MMF or sirolimus) vs Tac/MMF; all received thymoglobulin plus short course of steroids
- 89 patients
- acute rejection in 4/1/1 patients by month 6
- >2/3 belatacept CNI/steroid free at 12/12, and GFR 8-10 ml/min higher than TAC
- Comparable safety between groups
ANCA-associated glomerulonephritis in the very elderly

- Bomback et al, KI 2011; 79: 757
- retrospective evaluation of 78 patients >80 years old (72% p-ANCA)
- treated vs untreated at 12/12
  - ESRD – 36% vs 73% (p=0.03)
  - mortality 46 vs 64% (p=0.3)
  - at 2 years, mortality lower in treated group
Prize for most interesting name
Grainyhead-like 2 is expressed in the distal nephron and regulates the composition of epithelial junctions.

- Werth et al, Development 2010; 137: 3835
- Critical role in regulating composition of epithelial junctions and epithelial differentiation in the kidney (proximal tubules vs collecting duct)
No Discussion

Thank u 4 coming