PGY2 Learning activities-Study Appraisal

Second year residents will meet in small groups, once per month, and engage in critical appraisal of studies selected for clinical relevance but also for their value in illustrating key methodological concepts.

- Studies will be selected centrally, in order to correspond with the learning objectives for that session. Residents may choose to present a different study, after consultation with their group facilitators to make sure the learning objectives are still met.
- Resident presenters will be asked to summarize the study using a suggested format and discuss its validity and clinical relevance. Summary should include a table with important methodological aspects and also a table with selected study results (see example below). Resident presentation should last approximately 10-15 minutes to allow time for group discussion.
- After the resident presentation, facilitators will open discussion to the group and ask questions to further clarify methodological concepts specific for that session (also to last 10-15 minutes). Facilitators may refer to tables, graphs and other data from the study during the mini teaching session.
- Resident participants are NOT required to review the study beforehand but will review the summary of the study provided by the resident presenter. This also resembles real clinical settings, where clinicians refer to abstracts or pre-appraised versions of studies rather than the complete article.

Topics to be covered during PGY2 Learning activities:

1. **Randomized Controlled Trials, part 1**: Randomization, Allocation concealment, Blinding
2. **Randomized Controlled Trials, part 2**: Follow up, Addressing missing data, Intention to treat analysis, Patient oriented outcomes, surrogate and composite outcomes
3. **Randomized Controlled Trials, part 3**: Interpreting results, Clinical vs Statistical significance, measures of risk (RR, RRR, ARR, NNT)
4. **Systematic reviews, part 1**: General methodology of systematic reviews, Test of heterogeneity, Publication bias
5. **Systematic reviews, part 2**: Pooled results, Forest plots
6. **Diagnostic trials, part 1**: Diagnostic trial design, diagnostic uncertainty, Reference standard, Blinding
7. **Diagnostic trials, part 2**: Calculating and utilizing sensitivity, specificity, positive and negative predictive value, Likelihood ratios
8. **Evidence based diagnosis**: Types of diagnostic errors and limitations of evidence based diagnosis
9. **Observational studies, part 1**: Types and limitations of observational studies, Studying harm
10. **Observational studies, part 2**: Utilizing odds ratios to express strength of association, differentiating association from causation

EVIDENCE BASED CLINICAL PRACTICE
PGY2 JOURNAL CLUB

Hans-Henrik Parving, M.D., D.M.Sc., Frederik Persson, M.D., Julia B. Lewis, M.D., Edmund J. Lewis, M.D., Norman K. Hollenberg, M.D., Ph.D., for the AVOID Study Investigators

Aliskiren Combined with Losartan in Type 2 Diabetes and Nephropathy

N Engl J Med, Volume 358(23):2433-2446. June 5, 2008

PATIENTS	INTERVENTION
599 pts with type 2 DM, HTN and nephropathy, multiple countries and centers **1892 pts screened** **Exclusion criteria**: GFR<30, K>5.1	Direct Renin Inhibitor (**Aliskiren** 150mg x 3 months, then 300mg) vs Placebo Both groups on **Losartan** 100mg Qday
METHODS	**OUTCOMES**
Randomized (table of random numbers) **Allocation concealed** **Masking: Double Blind, placebo used** **Analysis:** Intention to Treat, Last Observation Carried forward **Follow up**: 6 months, Drop-outs < 10%	**Primary outcome**: Change in urinary albumin to creatinine ratio **Secondary outcomes**: GFR, Blood pressure, Hyperkalemia

	Aliskiren+Losartan	Placebo+Losartan	P value or Risk reduction with CI
Urinary albumin to creatinine ratio	?	?	p < 0.001 RRR 20% (9-30%)
Mean GFR decline	2.4 ml/min	3.8 ml/min	p 0.07
Blood pressure reduction	Mean BP 2/1 mmHg lower than placebo		p 0.07 (SBP) and 0.08 (DBP)
Severe hyperkalemia (>6.0)	4.7%	1.7%	p 0.06

JADAD SCALE TO ASSESS VALIDITY OF RCTs	YES	NO
Was the study described as randomized?	**1**	0
Was the study described as double blind?	**1**	0
Was there a description of withdrawals and dropouts (number and reason for withdrawals)?	**1**	0
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated etc)?	**1**	-1
Was the method of double blinding described and appropriate (identical placebo, double dummy etc)?	**1**	-1

Discussion:

High quality RCT (5/5 score on Jadad scale).

Methodological limitations include short follow up, use of ARB as comparator and not ACE inhibitors and use of surrogate outcomes compared to patient oriented outcomes like mortality, hospitalization and need for dialysis.

Risk of hyperkalemia may be quite high with combination use, although not statistically significant in this study.

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