Artificial Intelligence for AKI: Is it Really Elementary, my Dear Watson?

September 14, 2021

Organized by the ASN AKI!Now Artificial Intelligence Workgroup
Welcome and Introductions

Jay L. Koyner, MD
AKI!Now
Artificial Intelligence Workgroup Chair
University of Chicago

Today’s Moderator
Shina Menon, MD
AKI!Now AI Workgroup Member
Seattle Children’s Hospital
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<td>Jay L. Koyner, MD AKI!Now AI Workgroup Chair</td>
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<td>Machine Learning and Data Science: Demystifying the Hype</td>
<td>Girish N. Nadkarni MD, MPH</td>
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<td>Panel Roundtable</td>
<td>Shina Menon, MD (Moderator) Erina Ghosh PhD Vitaly Herasevich, MD, PhD Parisa Rashidi, PhD Nicholas M. Selby, MD, MBBS Len A. Usvyat, PhD</td>
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This webinar is being recorded.

Following today’s webinar, the recording, slides, and speaker bio handout will be posted on the ASN AKI website at:

https://www.asn-online.org/aki!now/
This webinar, Artificial Intelligence for AKI: Is it Really Elementary, my Dear Watson?, is provided as information and education and should not be construed as medical advice or recommendations for patient care.

The information expressed is that of the speaker(s) and contributor(s) only. Clinicians are to use their own training, clinical observations, and judgment to make all diagnostic and treatment decisions. The ASN Alliance (including ASN) does not offer medical advice.
AKI!Now Objective

To promote excellence in the prevention and treatment of Acute Kidney Injury (AKI) by building a foundational program that transforms the delivery of AKI care, reduces morbidity and mortality, and improves long-term outcomes.

https://aki.asn-online.org/home
2021 AKI!Now Goals

- Explore and promote early AKI recognition and intervention
- Investigate challenges and opportunities to improve AKI recovery
- Develop and conduct an AKI public awareness campaign
2021 AKI!Now Workgroups

• AKI!Now Basic Science
• AKI!Now AI (Artificial Intelligence)
• AKI!Now Recovery Post AKI
• AKI!Now Education and Public Awareness
Artificial Intelligence (AI) Effort for Quality Improvement in Acute Kidney Injury

Gaps
- Many desired tools do not exist.
- AI tools may not be broadly validated.
- Current efforts are uncoordinated.
- AI tools can carry implicit bias if not carefully designed and evaluated.
- AI tools may not consistently provide evidence on improvements in care or cost savings.

Patients
- Design fair and equitable AI models
- Identify scenarios based on personal and caregiver experience that could be improved with AI
- Improve patient centered outcomes in AKI survivors

Clinicians
- Design fair and equitable AI models
- Identify areas of clinical uncertainty that may benefit from new AI tools
- Guide appropriate follow-up for AKI survivors

Researchers
- Evaluate current AI tools, with a focus on removing implicit bias
- Develop new AI tools to address gaps identified by patients and clinicians
- Develop AI methods to advance the science of AKI

Improve the quality, accessibility, affordability, and equity of care.
AI Workgroup Goals

• Complete 1-3 AKI!Now Webinars, which help define the current state of AI in AKI and sets the stage for future projects.
• Establish a web-based platform for ASN members to ask questions, communicate with “AI experts,” and utilize resources around AI tools.
• Utilize Patient Advocates to better understand which issues around the intersection of AI and AKI are important to patients and caregivers
• Provide content for ASN-Kidney Week and other Nephrology meetings in 2021 and 2022
• Establish a platform/collaborative network (academic and industry) to test and validate novel AKI models and other AI tools
• Develop AI tools w/ Industry partners to establish baseline quality and cost of care metrics around AKI and acute dialysis patient care
Jay L. Koyner MD (Chair)
University of Chicago
jkoyner@uchicago.edu

Azra Bihorac, MD, MS, FASN
University of Florida
abihorac@ufl.edu

Stuart Goldstein MD, FASN
Cincinnati Children's Hospital Medical Center
stuart.goldstein@cchmc.org

Kianoush Kashani MD, MS, FASN
Mayo Clinic
kashani.kianoush@mayo.edu

Shina Menon MD
Seattle Children's Hospital
shina.menon@seattlechildrens.org

Girish N. Nadkarni MD, MPH
Icahn School of Medicine
girish.nadkarni@mountsinai.org

Javier A. Neyra, MD, MS, FASN
University of Kentucky Medical Center
javier.neyra@uky.edu

Neesh I. Pannu MD, MS
University of Alberta
npannu@ualberta.ca

Karandeep Singh MD, MS
University of Michigan
kdpsingh@med.umich.edu

Danielle Soranno, MD
Children’s Hospital Colorado
danielle.soranno@childrenscolorado.org
“Artificial Intelligence and Machine Learning: A 30,000-foot view
-Girish Nadkarni

@girish_nadkarni
www.nadkarnilab.com
<table>
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<tr>
<th>Entity</th>
<th>Type(s) of relationship(s)</th>
<th>Product name(s)</th>
<th>Relevant disease(s) or condition(s)</th>
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<tbody>
<tr>
<td>RenalytixAI</td>
<td>Scientific Co-founder, SAB member, Co-inventor</td>
<td>KidneyIntelX™</td>
<td>Biomarkers for CKD Progression</td>
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<td>Pensieve Health</td>
<td>Co-Founder, SAB member</td>
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<td>Genomics</td>
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<tr>
<td>Reata, AstraZeneca, BioVie, GLG Consulting, Variant Bio, Siemens</td>
<td>Consultant</td>
<td></td>
<td>CKD, ESRD, Genomics</td>
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The Hype Cycle

- Peak of Inflated Expectations
- Innovation Trigger
- Trough of Disillusionment
- Slope of Enlightenment
- Plateau of Productivity

 ASN
American Society of Nephrology
Not Really New Though

- 1950: Alan Turing develops the "Turing Test"
- 1956: John McCarthy coins the term "AI"
- 1961: Unimate, the first industrial robot, joins the assembly line at GM
- 1964: First chatbot: Eliza
- 1966: Shakey, "first electronic person"
- 1971: Research Resources on Computers in Biomedicine was founded; Saul Amarel at Rutgers University
- 1972: MYCIN was developed
- 1973: SUMEX-AIM was created
- 1975: The first NIH-sponsored AIM Workshop held
- 1976: CASNET was demonstrated at the Academy of Ophthalmology meeting
- 1980: Development of EMYCIN: expert rule-based system
- 1986: Release of Explain: a decision support system
- 1990s: Second AI Winter
- 2000: Deep learning
- 2007: IBM began development of DeepQA technology (Watson)
- 2010: CAD applied to endoscopy
- 2014: Amazon's virtual assistant, Alexa is released
- 2015: Pharmabot was built
- 2017: Arterys: First FDA-approved cloud-based DL application in healthcare
- 2018-2020: AI trials in Gastroenterology
- 2017: Chatbot Mandy: automated patient intake
- 2011: Apple's virtual assistant, Siri, is integrated into iPhones

Kaul et al; GIE
So, What’s Changed?
A part of our daily life
STRONG OR GENERAL AI
Computers thinking at a level that meets or surpasses people at multiple tasks
Computers engaging in abstract reasoning & thinking

WEAK OR SPECIFIC AI
Computers solve problems by detecting useful patterns

ARTIFICIAL INTELLIGENCE
Programs with the ability to learn and reason like humans

MACHINE LEARNING
Algorithms with the ability to learn without being explicitly programmed

DEEP LEARNING
Subset of machine learning in which artificial neural networks adapt and learn from vast amounts of data
Formal definition.
A computer program is said to learn from experience $E$ with respect to some class of tasks $T$ and performance measure $P$, if its performance at tasks in $T$, as measured by $P$, improves with experience $E$.
- Tom Mitchell (1996)

Functional Definition.
Algorithms get better at tasks with experience and more data without being explicitly programmed
Types of Machine Learning

**Supervised**
- The algorithm is given an idea of right/wrong or yes/no (a label)
- Classification / Regression / Prediction

**Unsupervised**
- The algorithm tries to find patterns within unlabeled data
- Clustering

**Reinforcement learning**
- The algorithm learns a series of actions to perform within an environment
- Q Learning
Supervised Machine Learning

Classification/Prediction

• Is this a cat or a chimney?
• Is this a person who has a disease state or not?
• Is this disease state likely to end in an adverse outcome?

Regression

• Given this description of a house – what’s the approximate price
• Given a patient’s age, gender, race, and drug history – what’s their approximate BP?
Unsupervised Machine Learning

Clustering

- Discover similarities in undifferentiated data
- Hypothesis generating
- Does not require knowledge of labels
Prototype of Pipeline for Machine Learning

Data collection/sourcing/access

Data preprocessing

Feature engineering/Selection

Training

Evaluation
Prototype of Pipeline for Machine Learning

Data collection/sourcing/access

Collection from various sources
- Electronic Healthcare Record data
- Imaging
- Notes

Data preprocessing

Feature engineering/Selection

Training

Evaluation
Prototype of Pipeline for Machine Learning

Data collection/sourcing/access

Data preprocessing

Feature engineering/Selection

Training

Evaluation

Process of converting the raw data into features that better represent the underlying problem
Prototype of Pipeline for Machine Learning

- Data collection/sourcing/access
- Data preprocessing
- Feature engineering
- Training
- Evaluation

Process of converting the raw data into features that better represent the underlying problem.
Algorithm Selection

- **Tabular data**
  - Linear models
  - Tree based models
  - Support Vector Machines

- **Imaging or multimodal data**
  - Deep Neural Networks (can be used for tabular data too)
Training and Testing

• Models are trained on a subset of data (Training data)

• Some data is separated out at the beginning – trained models are then asked to make predictions on this data (Testing data)
  • Performance on this data is usually reported

Validation in a completely independent dataset is desired for generalizability but depends on use case
Evaluation Metrics

• Threshold independent
  • Receiver Operating Characteristic curve
  • Precision Recall curve
Evaluation Metrics

- Threshold Dependent
  - Sensitivity
  - Specificity
- Positive Predictive Value
- Negative Predictive Value
Deep Learning
Why Deep Learning

• Deep neural networks scale
  • More data = More performance

• Models suited to tabular data can’t deal with images / notes / audio data
Deep Neural Networks are Similar to How Neurons Process data to find Patterns

A Multipolar Neuron

A Neural Network
Gradient Descent

• How all learning happens
• Cost function – How wrong are we right now?
  • Compare labels between predictions and available truth
  • If prediction is incorrect > adjust model > decrease in cost function
• Lowest level of cost function > best performance
Selected Relevant Examples in Kidney Disease
The Development of a Machine Learning Inpatient Acute Kidney Injury Prediction Model*

Jay L. Koyner, MD; Kyle A. Carey, MPH; Dana P. Edelson, MD, MS; Matthew M. Churmek, MD, MPH, PhD

was 0.96 (0.96–0.96) for receipt of renal replacement therapy (n = 821) in the next 48 hours. Accuracy was similar across hospital settings (ICU, wards, and emergency department) and admitting serum creatinine groupings. At a probability threshold of greater than or equal to 0.022, the algorithm had a sensitivity of 84% and a specificity of 85% for stage 2 acute kidney injury and predicted the development of stage 2 a median of 41 hours (interquartile range, 12–141 hr) prior to the development of stage 2 acute kidney injury.

Development and validation of models for dialysis and death at various time points following hospital admission

<table>
<thead>
<tr>
<th>Model</th>
<th>Internal Validation</th>
<th>External Validation</th>
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<tr>
<td>XGBoost without imputation</td>
<td>0.93-0.98 AUROC</td>
<td>0.78-0.82 AUPRC</td>
</tr>
<tr>
<td>XGBoost without imputation</td>
<td>0.85-0.87 AUROC</td>
<td>0.27-0.54 AUPRC</td>
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Conclusions: An XGBoost model without imputation for prediction of a composite outcome of death or dialysis in COVID positive patients had the best performance compared to standard and other machine learning models.

Can AI predict future AKI?

Retrospective cohort

US VA dataset
Inpatient + Outpatient

Deep learning algorithm
Recurrence neural network

Dataset randomized

703,782 patients 94%

Model performance
Lead time: up to 48 hours

- 56% Inpatient AKI
- 84% AKI needing dialysis within 30d
- 90% AKI needing dialysis within 90d

True positive False positive
1:2

Conclusions: Deep learning prediction models may help identify patients at risk of AKI within a time window that enables early treatment.


Visual abstract by @BetterCalSieth
Utilization of deep learning for subphenotype identification in sepsis-associated AKI

<table>
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<th>Methods and Cohort</th>
<th>Results</th>
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<tr>
<td>EHR data from ICUs in a tertiary care hospital</td>
<td>Patients with sepsis and AKI N=4001</td>
</tr>
<tr>
<td>Adult patients with sepsis and AKI within 48h of ICU admission</td>
<td>Mortality 28d post AKI</td>
</tr>
<tr>
<td>Deep learning utilizing all available vital signs, labs, and comorbidities</td>
<td>Subphenotype 1 N=1443</td>
</tr>
<tr>
<td>K Means clustering to identify subphenotypes</td>
<td>Subphenotype 2 N=1898</td>
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<td>Subphenotype 3 N=660</td>
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<tr>
<td>Mortality 28d post AKI</td>
<td>Dialysis requirement</td>
</tr>
<tr>
<td>23%</td>
<td>4%</td>
</tr>
<tr>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>35%</td>
<td>7%</td>
</tr>
<tr>
<td>aOR 1.4 (1.2-1.6)</td>
<td>NS</td>
</tr>
<tr>
<td>49%</td>
<td>26%</td>
</tr>
<tr>
<td>aOR 1.9 (1.5-2.4)</td>
<td>aOR 3.6 (2.5-5.4)</td>
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Conclusion: Utilizing routinely collected laboratory variables, vital signs, and comorbidities, we were able to identify three distinct subphenotypes of sepsis-associated AKI with differing outcomes.

## Computational Segmentation and Classification of Diabetic Glomerulosclerosis

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<th>Glomerular classification pipeline</th>
<th>Agreement with renal pathologists</th>
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<tr>
<td>1. Glomerular detection</td>
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<td>2. Compartamentalization</td>
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<td>3. Feature extraction</td>
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<tr>
<td>4. Recurrent glomerular classification</td>
<td>$G_i \Rightarrow G_2 \Rightarrow G_3 \Rightarrow \cdots \Rightarrow G_n = \text{Stage III}$</td>
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CONCLUSION

Digital, quantitative, structural analysis can enhance diagnostic objectivity.

doi: 10.1681/ASN.2018121259
Thank You
@girish_nadkarni
Panel Discussion

Erina Ghosh, PhD  
*Phillips*

Vitaly Herasevich,  
MD, PhD  
*Mayo Clinic*

Parisa Rashidi,  
PhD  
*University of Florida*

Nicholas M.  
Selby, MD, MBBS  
*University of Nottingham*

Len A. Usvyat,  
PhD  
*Fresenius Medical Care North America*
Thank you.

For more information or to get involved, please reach out to EPC@asn-online.org or via https://www.asn-online.org/aki!now/.