

Neurology Research Newsletter

Spring 2024 Newsletter

Farewell to Arms



Dr. Jeffrey Klingman

It is my pleasure to offer some parting wisdom as I ride off into the sunset of retirement from 35 years of full-time clinical practice. The last 35 years have seen amazing changes in medicine and in particularly Neurology. The old joke was that Neurologists admired diseases rather than treating them, but that has been changing rapidly. Involvement in clinical research has been critical to advances in treatment.

35 years ago, strokes were treated by pushing them in the back corner of the emergency room - now we have multiple acute treatments. Multiple sclerosis had no treatments other than supportive care - now we routinely stop nearly all attacks with anti CD20 drugs. It was inconceivable at the time that genetic diseases could be treated and yet now we have gene therapy for such horrific conditions as Spinal Muscular Atrophy.

All this innovation and improvement requires implementation. From reports of new treatments to widespread implementation it has been reported to take an average of 17 years. At Kaiser Permanente, we are uniquely positioned to facilitate and improve the speed to implementation and show the rest of the world in how to do so - but only when we publish and report our results. A great example is the Stroke EXPRESS program. In 2015 the seminal endovascular trials were reported. At the time we had 21 facilities barely meeting a 60-minute door to needle target and were only infrequently searching for large vessel occlusions. By the end of the year, more than half of patients were treated in less than 30 minutes. Everyone was being screened for endovascular therapy, and publication of our results was a guide for many other systems to improve their performance.

Another area where we can make unique contributions to advancing medical care is using big data. A lot of people talk about big data, but we have a unique advantage here - 4.6 million members, ethnically diverse, often with a long history of membership. Thus, we can investigate natural experiments, the real-world applicability of new treatments, and the possible expansion of therapies beyond the narrow clinical trial population. A great example is some of the work done in inpatient statin use in stroke, the effect of hypertension on cardiovascular outcomes and the risk of Guillan Barre after vaccinations.

Clinical trials are the backbone of medical care advances. TPMG Neurologists have been active in clinical trials including, for example, involvement in a randomized study of efficacy of carotid endarterectomy in asymptomatic stenosis (CREST-2) and the INTREPID trial for Parkinson's. Access to clinical trials can offer our patients access to new and innovative treatments and enhance our reputation in offering cutting edge treatments. We need to continue to support and facilitate the ability of our physicians to participate in clinical trials (rather than having to send our patients to the Universities).

Involvement in research is great for doctors as well. It can get grueling to spend your whole life doing nothing but straight clinical medicine - churning through patients and the never-ending inbox. I have found that variety - quality work, research, advocacy, etc. has kept me interested, motivated, and engaged. So, consider getting involved in research - it's good for the patient, the doctor, and the organization - and it can change the world.

Congratulations Dr. Klingman on your retirement!



A Deeper Look Inside This Update:

- Research Highlight
- Who's doing research
- Upcoming events & funding
- Active and recent research projects
- Recent peer reviewed publications

Research Highlight:

Determinants of Acute Kidney Injury in Exertional Rhabdomyolysis: A Large, Longitudinal Cohort Study in Diverse Population

Authors:

Amir H. Sabouri, MD, PhD, Brian Yurgionas, MD, MS, Sara Khorasani, MD, Edward Durant, MD, MPH, Jafar Kafaie, MD, PhD, Yun-Yi Hung, PhD, Jeffery G. Klingman, MD, Siamack Nemazie, MD

Author Affiliations:

Department of Neurology, The Permanente Medical Group, Walnut Creek, California (Sabouri, Khorasani, Klingman), Department of Neurology, The Permanente Medical Group, San Francisco, California (Yurgionas), Department of Emergency Medicine, The Permanente Medical Group, Manteca, California (Durant), Division of Research, Kaiser Permanente Northern California, Oakland, California (Hung), Department of Neurology, St Louis University, St Louis, MN (Kafaie) Department of Nephrology, The Permanente Medical Group, Santa Rosa, California (Nemazie)

ABSTRACT

IMPORTANCE: An association between serum CK levels and the risk of kidney failure in ERM has been suggested. However, the actual incidence of AKI in ERM within large, diverse community populations, along with the contributing cofactors that may increase the risk of AKI, has rarely been investigated.

OBJECTIVE: To determine the incidence of kidney injury in hospitalized patients with ERM and to identify additional cofactors that might contribute to the development of kidney injury in ERM patients.

DESIGN: This was a retrospective cohort study conducted in a diverse community population of patients aged 18 and over with ERM who presented in the emergency department and were subsequently admitted to hospitals across Kaiser Permanente Northern California between January 1, 2009, and December 31, 2019. Patients were initially identified through electronic screening for all-cause rhabdomyolysis admissions, followed by manual chart reviews to verify their eligibility for the study. The diagnosis of AKI and chronic kidney disease (CKD) was determined using KDIGO (Kidney Disease Improving Global Outcomes) criteria and confirmed by chart review. Patients with a prior history of CKD were excluded.

EXPOSURES: History of strenuous physical exercise prior to hospitalization for ERM.

MAIN OUTCOME AND MEASURES: Development of AKI, CKD, compartment syndrome, and death.

RESULTS: Among 3,790 patients admitted to 21 Kaiser Permanente Northern California hospitals following presentation at the emergency department between 2009 and 2019, 200 cases were confirmed with the diagnosis of exertional rhabdomyolysis (ERM), defined as when it was the primary diagnosis at ED admission, and further evaluation found definitive, unambiguous patient histories reporting strenuous exercise prior to admission and absence of any alternative explanation for elevated serum CK. The mean age of the patients was 30.9 years (SD: ± 8.8), with 27.5% female and 72.5% male. Among those hospitalized with ERM, 17 (8.5%; 95% Confidence Interval [CI], 5.0-13.3) developed AKI, and 1% (n=2)

developed CKD. One out of 200 patients (0.5%) developed compartment syndrome. There were no fatalities in the cohort. There was no association between serum CK levels and the risk of AKI. However, the risk of AKI was significantly higher in patients with ERM who used NSAIDs preadmission (64.7% vs 21.9%, $p < 0.001$) or experienced dehydration (52.9% vs 4.9%, $p < 0.001$). Given the observed frequency of preadmission NSAIDs use and dehydration, our analysis suggested that eliminating these 2 risk factors could reduce the risk of potential AKI in ERM patients by 92.6% (95% CI: 85.7-96.1) in our population.

CONCLUSION AND RELEVANCE: Results of this study suggest that serum CK elevation alone is insufficient to cause AKI in ERM. Furthermore, it provides evidence that concurrent risk factors, such as NSAIDs use or dehydration, may be associated with AKI development in ERM patients.

Upcoming Events

European Stroke Conference

Dates: May 15th - 17th, 2024

Location: Basel, Switzerland

<https://eso-stroke.org/esoc2024/>

Consortium of Multiple Sclerosis Centers Annual Meeting

Dates: May 29th - June 1st, 2024

Location: Nashville, TN

<https://cmscscholar.org/2024-annual-meeting/>

Alzheimer's Association International Conference

Dates: July 28th - July 1st, 2024

Location: Philadelphia, PA (and virtual)

<https://aaic.alz.org/>

International Congress of Parkinson's Disease and Movement Disorder

Dates: September 27th - October 1st, 2024

Location: Philadelphia, PA

<https://www.mdscongress.org/>

American Heart Association International Stroke Conference

Dates: February 5th - 7th, 2025

Location: Los Angeles, CA

<https://professional.heart.org/en/meetings/international-stroke-conference>

Kaiser Permanente Stroke Conference

Dates: 2025 TBD

Location: TBD

Muscular Dystrophy Association Clinical & Scientific Conference

Dates: March 16th - 19th, 2025

Location: Dallas, TX

<https://www.mdaconference.org/>

SFSN Annual Meeting

Dates: 2025 TBD

Location: TBD

American Academy of Neurology Annual Meeting

Dates: April 5th - 9th, 2025

Location: San Diego, CA (and virtual)

<https://www.aan.com/events/annual-meeting>

Internal Funding & Research Resources



General Funding Opportunities



Delivery Science and Applied Research



Specialty Research Networks



Getting Started with Research



Division of Research

Active Research Projects and Collaborations

- **Acute Emergency Care and Outcomes for Stroke, Myocardial Infarction, and Surgery During the COVID-19 Pandemic in Kaiser Permanente Northern California: Implications for Care Delivery During COVID-19 Recovery Phase and Future Surges**
Mai Nguyen-Huynh, Matthew Solomon, David Vinson, Robert Chang | Other | Ongoing
- **Assessing adverse events and clinical outcomes in patients with multiple sclerosis on Rituximab versus biosimilar in a large racial-ethnically diverse community cohort**
Mai Nguyen-Huynh, Jeffrey Klingman | PRP | Ongoing
- **Blood Pressure Trajectories to Predict Hypertensive Disorders of Pregnancy and CV Health Outcomes (BEST IPO)**
Erica Gunderson | NIH | Ongoing
- **Contemporary Outcomes and Management of Asymptomatic Carotid Stenosis (COMACAS)**
Robert Chang | Other | Ongoing
- **Evaluation of Clinical Outcomes in Hospitalized Patients with Exertional Rhabdomyolysis (ERM).**
Amir Sabouri | CH | Ongoing
- **Extended window for thrombectomy: Have we extended our resources appropriately and effectively?**
Mai Nguyen-Huynh, Jeffrey Klingman | PRP | Ongoing

- **Extending Intravenous Tenecteplase Beyond 4.5-hour Window for Patients with Acute Ischemic Stroke**
Mai Nguyen-Huynh, Jeffrey Klingman | DSGP | Ongoing
- **Incidence of Cancer among Idiopathic Inflammatory Myopathy (IIM) Patients Compared with a Matched Group**
Sarah Ringsted, Raymond Liu | Other | Ongoing
- **Multiple Sclerosis Specialty Care: Effect on Patient Outcomes and Utilization Patterns**
Jessica Fan | TAP | Ongoing
- **Predicting Readmission after Stroke Study**
Mai Nguyen-Huynh | NIH | Ongoing
- **Predictors of CVD among breast cancer survivors in an integrated health system**
Marilyn Kwan | NIH | Ongoing
- **Remote assessment of cognitive function in MS patients**
Lisa Barcellos, Catherine Schaefer, Terrence Chin | NIH | Ongoing
- **Surgical Epilepsy Center Referral Time Within an Integrated Health Care Network**
Josiah Ambrose, Cynthia Campbell | RAU | Ongoing
- **To Walk-In or Not to Walk-In: Understanding Mode of Arrival Choices to the Emergency Department Among Acute Stroke Patients and Their Effects on Stroke Care Processes and Outcomes in Kaiser Permanente Northern and Southern California**
Mai Nguyen-Huynh. Co-Investigators: Navdeep Sangha, Dana Sax, Jeff Klingman, Molly Burnett, Patricia Zrelak, Stacey Alexeeff | Garfield Memorial Fund | Ongoing

Recent Peer Reviewed Neurology - Authored Publications in 2023

*KPNC authors listed in alphabetical order below. For details on author order, click on the link included to the PubMed Abstract.

1. **Stroke characteristics and outcomes in urban Tanzania: Data from the Prospective Lake Zone Stroke Registry** [[PubMed Abstract](#)] Nguyen-Huynh MN | 12/16/2023 | Int J Stroke.
2. **Comparative safety of Tenecteplase vs alteplase for acute ischemic stroke** [[PubMed Abstract](#)] Nguyen-Huynh MN | 11/30/2023 | J Stroke Cerebrovasc Dis.

3. **A comparative effectiveness study of carotid intervention for long-term stroke prevention in patients with severe asymptomatic stenosis from a large integrated health system** [[PubMed Abstract](#)] Nguyen-Huynh MN | 11/30/2023 | J Vasc Surg.
4. **Anti-CD20 monoclonal antibody therapy in postpartum women with neurological conditions** [[PubMed Abstract](#)] Marcus, Jacqueline F | 11/1/2023 | Annals Of Clinical And Translational Neurology
5. **An Unusual Case of LGI1 (Leucine-Rich Glioma-Inactivated Protein 1) Limbic Encephalitis With Anti-acetylcholine Receptor and Anti-striational Autoantibodies** [[PubMed Abstract](#)] Zhong, Ning | 10/1/2023 | Cureus
6. **Characteristics of multiple sclerosis and demyelinating disease in an Asian American population** [[PubMed Abstract](#)] Fan, Jessica | 9/1/2023 | Multiple Sclerosis (Houndmills, Basingstoke, England)
7. **An Uncommon Presentation of Cervical Myelopathy** [[PubMed Abstract](#)] Lai, Neuzil | 9/1/2023 | Cureus
8. **Development of cardiometabolic risk factors following endocrine therapy in women with breast Cancer** [[PubMed Abstract](#)] Iribarren, Carlos; Kwan, Marilyn L; Kushi, Larry; Laurent, Cecile A; Lee, Valerie S; Neugebauer, Romain S; Nguyen-Huynh, Mai N; Rana, Jamal S; Roh, Janise M | 8/1/2023 | Breast Cancer Research And Treatment
9. **Development of cardiometabolic risk factors following endocrine therapy in women with breast cancer** [[PubMed Abstract](#)] Nguyen-Huynh M | 8/1/2023 | Breast Cancer Res Treat.
10. **In Memory of Gary Heit: Pioneer and Humanitarian** [[PubMed Abstract](#)] Sedrak, Mark F | 7/15/2023 | Neuromodulation : Journal Of The International Neuromodulation Society
11. **Early Pregnancy Systolic Blood Pressure Patterns Predict Early- and Later-Onset Preeclampsia and Gestational Hypertension Among Ostensibly Low-to-Moderate Risk Groups** [[PubMed Abstract](#)] Nguyen-Huynh MN | 7/12/2023 | J Am Heart Assoc.
12. **Lateral Mass Screws Versus Pedicle Screws at C7 - Reoperation Rates for Adjacent Segment Disease (Operative ASD) and Nonunions (Operative Nonunions) in Posterior Cervical Fusions** [[PubMed Abstract](#)] Fennessy, Jacob H; Guppy, Kern H | 7/1/2023 | Spine
13. **Undiagnosed Cognitive Impairment and Impact on Instrumental Activities of Daily Living Among People With HIV Infection in Primary Care** [[PubMed Abstract](#)] Gilsanz, Paola; Hou, Craig E; Lam, Jennifer; Lea, Alexandra N A; Lee, Catherine; Silverberg, Michael J | 6/1/2023 | Open Forum Infectious Diseases
14. **Bradykinesia and Its Progression Are Related to Interhemispheric Beta Coherence** [[PubMed Abstract](#)] Anderson, Ross W | 5/1/2023 | Annals Of Neurology
15. **Clinical Spectrum, Diagnosis, and Treatment Outcome in Individuals With Intravascular Large B-cell Lymphoma Affecting the Nervous System: A Case Series** [[PubMed Abstract](#)] Zhong, Ning | 4/1/2023 | Cureus
16. **Hospital EEG Capability and Associations With Interhospital Transfer in Status Epilepticus** [[PubMed Abstract](#)] Betjemann, John P | 4/1/2023 | Neurology. Clinical Practice
17. **A Cross-Trait, Mendelian Randomization Study to Investigate Whether Migraine Is a Risk Factor for Multiple Sclerosis** [[PubMed Abstract](#)] Bakshi, Nandini; Barcellos, Lisa F; Bellesis, Kalliope H; Chinn, Terrence A; Choudhary, Vidhu; Dorin, Pete S; Marcus, Jacqueline F; Mei, Jin; Meyers, Travis; Schaefer, Catherine | 3/28/2023 | Neurology

18. **Sex differences in Parkinson disease-associated episodic memory and processing speed deficits** [[PubMed Abstract](#)] Wheelock, Vicki L | 3/27/2023 | Journal Of The International Neuropsychological Society : Jins
19. **Familial Epilepsy Associated With Concurrent CHRN2 Mutation and RBFOX1 Exon Deletion: A Case Report** [[PubMed Abstract](#)] Luong, Dorris D; Zhong, Ning | 3/1/2023 | Cureus
20. **Increased Intracranial Pressure Due to Transverse Sinus Compression by a Meningioma En Plaque** [[PubMed Abstract](#)] Lai, Neuzil | 1/1/2023 | Cureus
21. **Isolated Hypoglossal Nerve Palsy Secondary to Oligosecretory Multiple Myeloma** [[PubMed Abstract](#)] Chang, Jason S | 1/1/2023 | Cureus
22. **Multiple sclerosis: Exploring the limits and implications of genetic and environmental susceptibility** [[PubMed Abstract](#)] Khankhanian, Pouya | 1/1/2023 | Plos One
23. **Pathogenesis of cerebral amyloid angiopathy caused by chaotic glymphatics-Mini-review** [[PubMed Abstract](#)] Zhong, Ning | 1/1/2023 | Frontiers In Neuroscience
24. **External carotid artery-radial artery-vertebral artery bypass for surgical treatment of radiculopathy caused by an extracranial vertebral artery aneurysm: A case report and review of the literature** [[PubMed Abstract](#)] Duong, Huy T | 1/1/2023 | Surgical Neurology International