



ABSTRACTS

2024

MSTAR

Icahn School of Medicine at Mount Sinai

Program

Medical Student Training in Aging Research



MSTAR



The **Medical Student Training in Aging Research (MSTAR) Program** at **The Icahn School of Medicine at Mount Sinai** is a T-32 program, generously funded by The National Institute on Aging (NIA). It proudly stands as one of the eight National Training Centers, an impressive group that includes Harvard Medical School, Johns Hopkins University School of Medicine, NYU, UCLA, UC San Diego, University of North Carolina, and Augusta University (Puerto Rico).

MSTAR is an intensive eight-week immersion into aging and palliative care research. Under the guidance of leading experts, students delve into a wide range of scientific investigations, encompassing basic sciences, clinical research, and health services studies.

The MSTAR program uniquely positions students early in their medical training to acquire hands-on experience and insights often only accessible in the later phases of academic training. The program offers an in-depth exploration of research methodologies, platforms for research presentations and opportunities for publications, real-world clinical geriatrics and palliative medicine exposure, comprehensive information on various medical career paths, and opportunities to network with peers and mentors.

Alumni of the MSTAR Program at ISMMS have carved out successful careers in diverse areas, contributing to the expanding pool of dedicated scientists, innovative thinkers, and adept physicians. Regardless of their specific field, MSTAR alumni are applying the fundamental principles of aging and palliative care, a foundation built during their time in the program, with escalating significance. This expertise is increasingly vital to meet the demands of our rapidly aging society.

MSTAR Program at ISMMS

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Rainier P. Soriano, MD
MSTAR Co-Program Director

Professor & Senior Associate Dean for
Curricular Affairs
The Leni & Peter May Department of
Medical Education
Icahn School of Medicine at Mount Sinai



Melissa Aldridge, PhD, MBA
MSTAR Co- Program Director

Professor & Vice Chair of Research
The Brookdale Department of Geriatrics
& Palliative Medicine
Icahn School of Medicine at Mount Sinai



Deborah Watman, MPH
MSTAR Program Manager

Research Program Manager
The Brookdale Department of Geriatrics
& Palliative Medicine
Icahn School of Medicine at Mount Sinai



Jahriah Philip Hill
MSTAR Program Coordinator

Department Coordinator
The Leni & Peter May Department of
Medical Education
Icahn School of Medicine at Mount Sinai

2024 MSTAR Program at ISMMS Scholars



Ryan Afreen

Icahn School of Medicine at
Mount Sinai

Project: Effect of COVID-19
Pandemic on the Clinical
Outcomes of Interhospital
Transfer of Intracerebral
Hemorrhage Patients
Undergoing Minimally Invasive
Surgery

Mentor: Christopher Kellner,
MD



Julia An

Icahn School of Medicine at
Mount Sinai

Project: Second Primary
Malignancy Risk in Geriatric
Patients Treated with
Radioactive Iodine for
Differentiated Thyroid Cancer:
A SEER Registry Study

Mentor: Maaïke Van Gerwen,
MD, PhD



Cole Brown

Icahn School of Medicine at
Mount Sinai

Project: Assessing the mFI-5
Frailty Score and Delirium in
Geriatric Patients
Undergoing Colectomy
Procedures

Mentor: Celia Divino, MD



Bradley Michael Caston

Wright State Boonshoft School of
Medicine

Project: Frailty's Impact on Vision
Recovery after Pituitary Apoplexy
Resolution

Mentor: Raj Shrivastava, MD

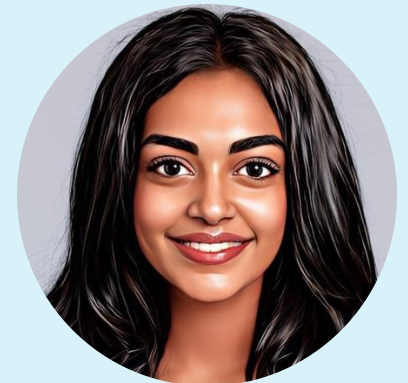


Diana Dangoor

University of Illinois College of
Medicine at Chicago

Project: Using Machine
Learning To Assess Region-
specific Accelerated Brain
Aging: A Modeling Study

Mentor: John F. Crary, MD,
PhD



Mehek Dedhia

Icahn School of Medicine at
Mount Sinai

Project: Patterns of Platelet
Dysfunction in Neurotrauma
Patients based on Clinical and
Demographic Characteristics

Mentor: Zachary Hickman,
MD

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Varun Devraj

Icahn School of Medicine at
Mount Sinai

Project: Associations Between
Social Support and Radiation
Outcomes in Older Adults
with Cancer Undergoing
Palliative Radiation Therapy

Mentor: Kavita Dharmarajan,
MD



Ryan Hoang

University of California, Irvine,
School of Medicine

Project: The Role of Different
Climates on Seasonal Factors
and Wound Infections
Following Spine Surgery in
Geriatric Patients

Mentor: Samuel Cho, MD



James Hong

Icahn School of Medicine at
Mount Sinai

Project: The Role of
Neutrophils in Aging and
Healing of the Intervertebral
Disc

Mentor: James Iatridis, MD



Benjamin Hu

Icahn School of Medicine at
Mount Sinai

Project: Serum Proteomic
Analysis of Cancer Patients
with Cutaneous Immune-
related Adverse Events

Mentor: Nicholas Gulati, MD,
PhD



Michael Lemonick

Icahn School of Medicine at
Mount Sinai

Project: Raloxifene Treatment
Increases Pain Tolerance In
Young Female Mice But Does
Not Protect From Injury-
Induced Pain Sensitivity

Mentor: Nilsson Holguin, PhD



Albert Li

USC Keck School of Medicine

Project: Call for Further
Investigation into Minimally
Invasive Foraminotomies as a
Non-Fusion Option After
Comparing Complication
Frequency of 1-Level
ACDF/TDA Compared with 1-
Level Foraminotomies

Mentor: Samuel Cho, MD

2024 MSTAR Program at ISMMS Scholars



Sela Marin

University of Maryland

Project: Enhancing Integrated Care: The Role of Community Health Workers (CHWs) in a Comprehensive Program for Older Adults

Mentor: Abigail Baim-Lance, PhD



Kareem Mohamed

Icahn School of Medicine at Mount Sinai

Project: Social Deprivation and Dual Eligibility Lead to Poorer Postoperative Outcomes in Older Adults Undergoing Shoulder Arthroplasty

Mentor: Paul Cagle Jr., PhD



Arvind Sommi

Icahn School of Medicine at Mount Sinai

Project: Systemic Risk Factors for Infectious Keratitis

Mentor: Sumayya Ahmad, MD



Taylor Rosalie Veschio

The University of Arizona
College of Medicine

Project: Impact of 2016 Opioid Guidelines: Reduced Opioid Prescriptions and Increased Anticonvulsant Use in Older Adults with Dementia

Mentor: Rebecca Rodin, MD



Alexander Yu

Icahn School of Medicine at Mount Sinai

Project: Impact of Spinal Fusion on Global Sagittal Alignment: The Role of Fusion Region in Predicting Postoperative Outcomes

Mentor: Samuel Cho, MD



Jennifer Yu

Icahn School of Medicine at Mount Sinai

Project: Analysis of Activity and Sleep Data from Wearable Accelerometers among Older Adults with a History of Knee and Hip Replacement.

Mentor: Brett L. Hayden, MD




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Abstracts and Posters

EFFECT OF COVID-19 PANDEMIC ON THE CLINICAL OUTCOMES OF INTERHOSPITAL TRANSFER OF INTRACEREBRAL HEMORRHAGE PATIENTS UNDERGOING MINIMALLY INVASIVE SURGERY

Ryan Afreen BA, Bahie Ezzat MS, Roshini Kalagara BA, Leslie Melo MPH, Masha Morozov MPH, Javin Bose BMus, J Mocco, MD MS, Joshua B. Bederson MD, Christopher P. Kellner MD, and Neha S. Dangayach MD MSCR



Effect of COVID-19 pandemic on the Clinical Outcomes of Interhospital Transfer of Intracerebral Hemorrhage Patients Undergoing Minimally Invasive Surgery

Ryan Afreen BA, Bahie Ezzat MS, Roshini Kalagara BA, Leslie Melo MPH, Masha Morozov MPH, Javin Bose BMus, J Mocco, MD MS, Joshua B. Bederson MD, Christopher P. Kellner MD, and Neha S. Dangayach MD MSCR on behalf of the Mount Sinai NEMAT Research Group

Department of Neurosurgery, Icahn School of Medicine at Mount Sinai

OBJECTIVE



Assess IHT impact on immediate (e.g., symptomatic postoperative rebleed, home discharge) and long-term outcomes (e.g., 30-day mortality, 6-month mRS scores) during COVID-19 phases.

RESULTS

INTRODUCTION

- **Intracerebral hemorrhage (ICH):** Stroke subtype with high morbidity and mortality.
- **Research Gap:** Limited data on interhospital transfer (IHT) safety and efficacy for ICH patients.

Figure 1 | Transfer Pathways and Frequencies of Intracerebral Hemorrhage Patients to the Central Hospital

• **Cohort:** 261 ICH patients (85% IHT, 15% ED)

• **Key Findings:**

- No significant demographic or clinical differences between IHT and ED groups.
- **Higher GCS in ED patients** (13 vs. 9, p=0.005).
- **Predictors of symptomatic rebleed:** Presence of spot sign (OR 4.35) and lower evacuation percentage (OR 0.96).
- **Predictors of non-home discharge:** Older age (OR 1.06/year) and longer ICU stay (OR 1.12/day).
- **Predictor of 30-day mortality:** Anticoagulant use (OR 4.35).
- **Predictors of poor 6-month outcome:** Age (OR 1.06/year) and lower GCS (OR 0.89/point).
- **IHT:** No significant effect on rebleed, discharge disposition, 30-day mortality, or functional outcome.

METHODS

- **Study Design:** Prospective registry of ICH patients undergoing minimally invasive surgery (March 2017–April 2023).
- **COVID-19 Phases:**
 - Pre-pandemic [Phase 1]: before 2/29/20
 - First wave [Phase 2]: 3/1/20–12/31/20
 - Second wave [Phase 3]: after 1/1/21
- **Groups:** IHT vs. direct ED admission
- **Primary Outcomes:**
 - Symptomatic postoperative rebleed.
 - Non-home discharge.
 - 30-day mortality.
 - Poor functional outcome (6-month mRS 4–6)

Variables significant on univariate analyses (p<0.05) were advanced to binary logistic regression models analyzing four primary outcomes

Table 1: Binary Logistic Regression of Symptomatic Postoperative Rebleed:

Variable	Total Cohort (N=261)		
	Odds Ratio	95% CI	p-value
Age	1.06	(1.01, 1.11)	0.03
Preoperative GCS	0.89	(0.84, 0.94)	0.0001
Preoperative mRS	1.12	(1.04, 1.21)	0.003
Preoperative Hematocrit	1.04	(0.99, 1.09)	0.08
Preoperative Hemoglobin	1.01	(0.99, 1.03)	0.0001

Table 2: Binary Logistic Regression of Suboptimal Discharge Disposition (SAR, SNF, Other Institution, Hospice, or Expertise):

Variable	Total Cohort (N=261)		
	Odds Ratio	95% CI	p-value
Age	1.06	(1.01, 1.11)	0.03
Preoperative GCS	0.89	(0.84, 0.94)	0.0001
Preoperative mRS	1.12	(1.04, 1.21)	0.003
Preoperative Hematocrit	1.04	(0.99, 1.09)	0.08
Preoperative Hemoglobin	1.01	(0.99, 1.03)	0.0001

Table 3: Binary Logistic Regression of 30-Day Mortality:

Variable	Total Cohort (N=261)		
	Odds Ratio	95% CI	p-value
Age	1.06	(1.01, 1.11)	0.03
Preoperative GCS	0.89	(0.84, 0.94)	0.0001
Preoperative mRS	1.12	(1.04, 1.21)	0.003
Preoperative Hematocrit	1.04	(0.99, 1.09)	0.08
Preoperative Hemoglobin	1.01	(0.99, 1.03)	0.0001

Table 4: Binary Logistic Regression of Poor Functional Outcome (6-month modified Rankin Scale score 4–6):

Variable	Total Cohort (N=261)		
	Odds Ratio	95% CI	p-value
Age	1.06	(1.01, 1.11)	0.03
Preoperative GCS	0.89	(0.84, 0.94)	0.0001
Preoperative mRS	1.12	(1.04, 1.21)	0.003
Preoperative Hematocrit	1.04	(0.99, 1.09)	0.08
Preoperative Hemoglobin	1.01	(0.99, 1.03)	0.0001

CONCLUSIONS

- **IHT is safe** for ICH patients, with no adverse effects on key outcomes.
- **Supports IHT as a viable management option** for acute ICH care.

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“The study supports the safety of interhospital transfer for intracerebral hemorrhage patients, showing no negative impact on key outcomes, making it a viable management option.”

EFFECT OF COVID-19 PANDEMIC ON THE CLINICAL OUTCOMES OF INTERHOSPITAL TRANSFER OF INTRACEREBRAL HEMORRHAGE PATIENTS UNDERGOING MINIMALLY INVASIVE SURGERY

Ryan Afreen BA, Bahie Ezzat MS, Roshini Kalagara BA, Leslie Melo MPH, Masha Morozov MPH, Javin Bose BMus, J Mocco, MD MS, Joshua B. Bederson MD, Christopher P. Kellner MD, and Neha S. Dangayach MD MSCR

BACKGROUND AND OBJECTIVES: Intracerebral hemorrhage (ICH) is a stroke subtype associated with significant morbidity and mortality. Despite the extensive literature on interhospital transfer (IHT) within the context of ischemic stroke, there remains a paucity of data on the safety and efficacy of IHT for ICH patients. The objective of this study is to assess the impact of IHT on immediate outcomes, such as symptomatic postoperative rebleed and home discharge disposition, and long-term outcomes, including 30-day mortality and 6-month modified Rankin Scale (mRS) scores, while also examining the interplay between different phases of the COVID-19 pandemic with these outcomes.

METHODS: A prospectively collected registry of ICH patients undergoing minimally invasive endoscopic evacuation at a large urban hospital between March 2017 and April 2023 were analyzed. Data collected include demographics, comorbidities, presenting clinical/radiographic characteristics, transfer data, procedural metrics, and clinical outcomes. The COVID-19 timeline were grouped into three phases: pre-pandemic (before 2/29/20) [Phase 1], first COVID-19 wave (3/1/20-12/31/20) [Phase 2], and second COVID-19 wave (after 1/1/21) [Phase 3]. The cohort was divided into two groups: direct emergency department (ED) admission and IHT. Variables significant on univariate analyses ($p < 0.05$) were advanced to binary logistic regression models analyzing four primary outcomes: symptomatic postoperative rebleed, suboptimal discharge disposition (nonhome discharge), 30-day mortality, and poor functional outcome (6-month modified Rankin Scale score 4-6).

RESULTS: Among 261 ICH patients that underwent minimally invasive surgery, 221 (85%) were in the IHT group and 40 (15%) were in the ED group. The average transfer distance and duration were 17.3 km (SD 51) and 3.2 hours (SD 10.7), respectively. The average bleed-to-time-out time, door-in-door-out time, and transfer out time were 18.8 (SD 252.5), 19.7 (SD 34.9), and 2.2 (SD 1.3) hours respectively. The largest number of total transfers occurred on Thursdays (16.3%). Most patients from the study cohort originated from New York county (36.2%). There were no significant differences in demographics, comorbidities, including history of ICH or ischemic stroke, presenting radiographic characteristics, pre- or post-operative characteristics, or hospital course. Patients presenting directly to the ED had a higher Glasgow Coma Scale (GCS) score than the IHT group (13 vs. 9; $p = 0.005$). On binary logistic regression, the presence spot sign on computed tomography (OR 4.35, 95% CI [1.16-16.1], $p = 0.03$) and lower evacuation percentage (OR 0.96, 95% CI [0.94-0.99], $p = 0.01$) were associated with increased odds of symptomatic postoperative rebleed. Advanced age (OR 1.06 per year, 95% CI [1.03-1.09], $p < 0.001$), and longer stays in the intensive care unit (ICU) (OR 1.12 per day, 95% CI [1.06-1.19], $p < 0.001$) increased the likelihood of suboptimal discharge disposition. Only anticoagulant use significantly increased the risk of 30-day mortality (OR 4.35, 95% CI [1.25-15.2], $p = 0.02$). Additionally, each incremental year of age (OR 1.06, 95% CI [1.02-1.09], $p < 0.001$) and each point decrease in the GCS score (OR 0.89, 95% CI [0.79-0.99], $p = 0.04$) were associated with poorer functional outcome at 6 months. Conversely, IHT did not significantly impact Symptomatic Postoperative Rebleed (OR 1.00, 95% CI [0.99-1.01], $p = 0.99$), suboptimal discharge disposition (OR 0.92, 95% CI [0.33-2.54], $p = 0.87$), 30-day mortality (OR 2.18, 95% CI [0.27-17.4], $p = 0.46$) or 6-month functional outcome (OR 0.99, 95% CI [0.34-2.86], $p = 0.98$).

CONCLUSIONS: The study's findings support the safety of IHT for ICH patients, with data demonstrating no detrimental impact on key postoperative and long-term outcomes. Thus, this study suggests that IHT is a viable option in the strategic management of acute care for this high-risk patient population.

ASSOCIATION BETWEEN RADIOACTIVE IODINE TREATMENT FOR DIFFERENTIATED THYROID CANCER AND SECOND PRIMARY MALIGNANCIES AMONG GERIATRIC PATIENTS

Julia An, Mark Choi, MSE, Chen Yang, PhD, Maaïke van Gerwen, MD PhD

Second Primary Malignancy Risk in Geriatric Patients Treated with Radioactive Iodine for Differentiated Thyroid Cancer: A SEER Registry Study



Julia An¹, Mark Choi, MSE, Chen Yang, PhD^{2,3}, Maaïke van Gerwen, MD, PhD^{4,5}

¹ Department of Medical Education, Icahn School of Medicine at Mount Sinai, New York, NY, USA; ² Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai; ³ Institute for Health Care Delivery Science, Icahn School of Medicine at Mount Sinai; ⁴ Department of Otolaryngology-Head and Neck Surgery, Icahn School of Medicine at Mount Sinai; ⁵ Institute for Translational Epidemiology, Icahn School of Medicine at Mount Sinai

INTRODUCTION

- Radioactive iodine (RAI) is a common treatment for differentiated thyroid cancer (DTC) following thyroidectomy, particularly for higher-risk cases.^{1,2}
- RAI is significantly less frequently prescribed in the geriatric population, for reasons that remain unclear.^{1,2}
- In the general population, RAI has been linked to an increased risk of second primary malignancies (SPMs) (leukemia, uterine, stomach, lung, liver, breast, and bladder cancer).^{3,4}
- There is a lack of research on whether RAI treatment is associated with an increased risk of SPMs in the geriatric population.²

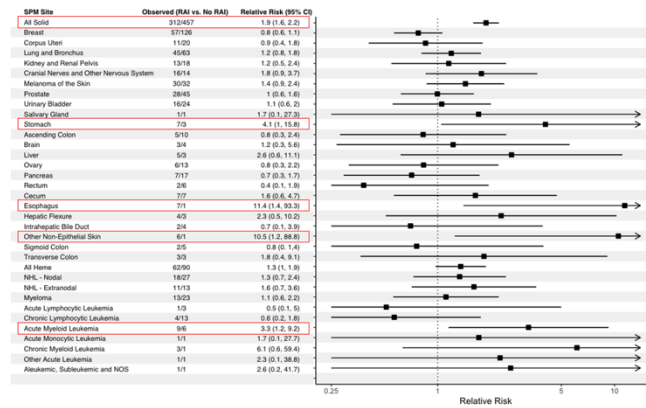
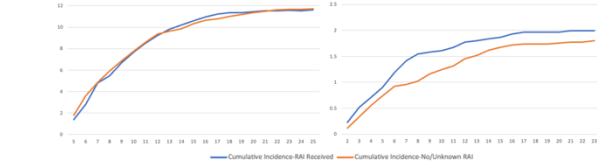
AIM: Investigate whether RAI treatment is associated with an increased risk of specific SPMs in geriatric patients

METHODS

- We identified 9,971 individuals 65+ diagnosed with a non-metastatic primary DTC from eight SEER Registries (1975-2021).⁵
- We stratified patients into two groups according to RAI treatment status: received (n = 3708) vs. not received/unknown (n = 6263). 69.6% were female.
- Follow-up for solid and hematologic SPMs began 5 and 2 years after DTC diagnosis, respectively, to account for the latency period of radiation carcinogenesis.^{3,6}
- 5098 patients were ≥ 5-year survivors, and 669 patients developed solid SPMs during follow-up.
- 8,115 patients were ≥ 2-year survivors, and 152 patients developed hematological SPMs during follow-up.
- We calculated relative risks (RRs) and 95% confidence intervals using Poisson regression models, adjusting for age at DTC diagnosis, sex, and latency.

RESULTS

Cumulative incidence of solid and hematological second primary malignancies among DTC survivors



*Adjusted for age at DTC diagnosis, sex, and latency. Prostate RR analysis was restricted to men only. Ovary and corpus uteri cancer analyses were restricted to women only.

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CONCLUSIONS

- In the geriatric population, RAI treatment is associated with a higher relative risk of acute myeloid leukemia and cancers of the stomach, esophagus, and non-epithelial skin.
- Given the low incidence of these cancers, (< 43 cases per 100,000 people), RAI benefits may outweigh the risks for most patients.⁷ The potential benefits of increasing RAI use in geriatric populations should be evaluated.
- Future research should focus on the relationship between RAI dose and risk of specific SPMs.

CLINICAL RELEVANCE

- RAI's association with rare cancers should not deter use given its value in improving DTC prognosis.
- Physicians may need to closely monitor geriatric DTC survivors who received RAI for acute myeloid leukemia, stomach, esophagus, and non-epithelial skin cancers, particularly if additional risk factors are present.

ACKNOWLEDGEMENTS



Disclosures: This study was supported by the National Institute for Aging (NIA) and the Medical Student Training in Aging Research (MSTAR) program at the Icahn School of Medicine at Mount Sinai. The investigators retained full independence in the conduct of this research.

Questions: julia.an@icahn.mssm.edu



"Radioactive iodine treatment in the elderly increases the risks of acute myeloid leukemia, stomach, esophageal, and non-epithelial skin cancers, suggesting the need for careful patient monitoring to balance treatment benefits."

ASSOCIATION BETWEEN RADIOACTIVE IODINE TREATMENT FOR DIFFERENTIATED THYROID CANCER AND SECOND PRIMARY MALIGNANCIES AMONG GERIATRIC PATIENTS

Julia An, Mark Choi, MSE, Chen Yang, PhD, Maaïke van Gerwen, MD PhD

INTRODUCTION: Radioactive iodine (RAI) is commonly used as a treatment for differentiated thyroid cancer (DTC) following thyroidectomy, particularly for higher-risk cases. However, it is significantly less frequently prescribed in the geriatric population, for reasons that remain unclear. In the general population, RAI has been linked to an increased risk of second primary malignancies (SPMs), which is often cited as a potential reason for its reduced use in older adults. To our knowledge, this association has not been specifically studied in the geriatric population. Therefore, this study aims to assess whether RAI treatment is associated with an increased risk of solid and hematological SPMs in the geriatric population.

METHODS: We identified 9,971 individuals aged 65 and older diagnosed with a non-metastatic primary DTC from eight SEER Registries (1975-2021). We further classified DTCs by size and lymph node involvement according to the TNM definitions of the American Joint Committee on Cancer (AJCC), 7th and 8th editions. We stratified patients into two groups according to RAI treatment status (received vs. not received/unknown). Follow-up for hematological and solid SPMs began two and five years after DTC diagnosis, respectively, to account for the latency period of radiation carcinogenesis. Follow-up ended at the date of SPM diagnosis, death, last follow-up, or December 31st, 2021, whichever occurred first. Using the SEER database, the observed and expected number of SPMs by cancer site were used to calculate relative risks (RRs), 95% confidence intervals (CI), and the excess number of SPMs attributable to RAI using Poisson regression models. All analyses were done in SEER*Stat and SAS (Statistical Analysis System, Version 9.4, Cary, NC).

RESULTS: The overall risk of solid SPMs was increased among RAI-treated geriatric patients (RR=1.88, 95% CI, 1.59 to 2.21). Risks were significantly increased for cancers of the stomach (RR=4.06, 95% CI, 1.05 to 15.81), esophagus (RR=11.42, 95% CI, 1.07 to 140) and non-epithelial skin (RR=10.52, 95% CI, 1.09 to 88.77). There was no increased risk of cancers of the corpus uteri, lung and bronchus, kidney and renal pelvis, cranial nerves and other nervous system, melanoma of the skin, prostate, bladder, salivary gland, colon, brain, liver, ovary, pancreas, rectum, hepatic flexure, and intrahepatic bile duct. We estimated that 6 excess stomach cancers, 6 excess esophageal cancers, and 5 excess non-epithelial skin cancers were attributable to RAI treatment. Among hematological SPMs, acute myeloid leukemia had a significantly increased risk among RAI-treated patients (RR=3.26, 95% CI, 1.15 to 9.24). There was no increased risk of other lymphomas, myelomas, or leukemias. We estimated that 9 excess acute myeloid leukemia cases were attributable to RAI treatment.

CONCLUSION: Increased risks of acute myeloid leukemia, stomach, esophageal, and non-epithelial skin cancer were found following RAI treatment in the geriatric population. As these cancers are relatively uncommon (<43 cases per 100,000 people), the benefits of RAI treatment may outweigh the risks for certain patients. Physicians may need to more closely monitor geriatric survivors of DTC who received RAI for cancers of the stomach, esophagus, and non-epithelial skin. Future research should focus on the impact of RAI dose on specific SPMs and evaluate the potential benefit of increasing use of RAI treatment in geriatric patients.

ASSESSING THE mFI-5 FRAILTY SCORE AND DELIRIUM IN GERIATRIC PATIENTS UNDERGOING COLECTOMY PROCEDURES

Cole Brown, BS, Alexandra Agathis, MD, Jeanne Wu, MS, and Celia Divino, MD



Assessing the mFI-5 Frailty Score and Delirium in Geriatric Patients Undergoing Colectomy Procedures

Cole Brown, BS; Alexandra Agathis, MD; Jeanne Wu, MS; Celia Divino, MD



BACKGROUND

- Frailty is a well-established predictor of poor postoperative outcomes in geriatric patients undergoing major abdominal surgery, such as colectomy.
- Early identification of frailty is essential for mitigating risks, such as postoperative delirium, a common complication in this population.
- The modified Frailty Index (mFI-5) is a simplified tool for assessing frailty in geriatric patients.

Objective: The objective of this study is to determine the predictive value of the mFI-5 for postoperative delirium in elderly patients undergoing colectomy, to provide clinical guidelines for high-risk geriatric patients

METHODS

- Using the National Surgical Quality Improvement Program Database from 2021 and 2022, all patients aged 75 years and older who underwent colectomy were included (N = 17,795).
- Preoperative mFI-5 scores were calculated by the sum of the 5 factors and patients were placed in non-frail, intermediate frailty, and high frailty groups.
- Logistic regressions models were implemented to analyze the association between mFI-5 score and postoperative delirium.

Factor	Score	Frailty Index Score	Categorization
Diabetes	+1	0	non-frail
Hypertension	+1		
Congestive Heart Failure	+1		
Chronic Obstructive Pulmonary Disease	+1	1	intermediate frailty
Non-Independent Functional Status	+1	≥ 2	high frailty

High frailty, smoking, emergent case status, and non-white race are all significantly associated with a higher incidence of postoperative delirium in elderly patients

RESULTS

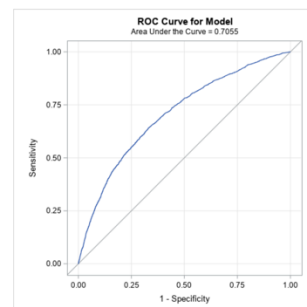
Table 1

Variable	mFI=0	mFI=1	mFI≥2	p-value
	[n=3767 (22.4%)]	[n=7595 (45.2%)]	[n=5408 (32.4%)]	
Age, years, mean (interquartile range)	80.55 (77-84)	81.23 (77-85)	81.28 (77-85)	
Sex				<.01
Female	2349 (13.20)	4884 (27.45)	3165 (17.79)	
Male	1635 (9.19)	3167 (17.80)	2595 (14.58)	
Race				<.01
White	2511 (14.11)	5313 (29.86)	3719 (21.90)	
Black	105 (0.59)	459 (2.58)	457 (2.57)	
Asian	134 (0.75)	253 (1.42)	219 (1.23)	
Other/Unknown	1234 (6.93)	2026 (11.39)	1365 (7.67)	
Body Mass Index (interquartile range)	23.7 (21.03-27.58)	25.46 (22.40-29.35)	27.01 (23.09-31.47)	0.46
Smoking Status				<.01
Non-Smoker	3767 (21.17)	7595 (42.68)	5408 (30.39)	
Smoker	217 (1.22)	456 (2.56)	352 (1.98)	
Case Type				<.01
Elective	2835 (15.93)	5696 (32.01)	3771 (21.19)	
Urgent	500 (2.81)	948 (5.33)	817 (4.59)	
Emergent	649 (3.65)	1407 (7.91)	1172 (6.59)	
Delirium				<.01
Yes	378 (2.12)	990 (5.56)	1003 (5.64)	
No	3606 (20.26)	7061 (45.78)	4757 (26.73)	

RESULTS

- The model is predictive of postoperative delirium with an area under the curve of 0.7055 in the receiver operating characteristic curve.
- High frailty patients had a 60.2% increased odds of developing postoperative complications (OR=1.602, CI 1.402-1.832).

Figure 1



CONCLUSIONS

- The mFI-5 is an effective tool for predicting postoperative delirium in geriatric patients undergoing colectomy.
- The mFI-5's application in the preoperative assessment in geriatric patients can help identify high-risk patients, allowing for targeted interventions to reduce the incidence of delirium and other postoperative complications.

FINANCIAL DISCLOSURE: This study was supported by the National Institute of Aging (NIA) and the Medical Student Training in Aging Research (MSTAR) program at the Icahn School of Medicine at Mount Sinai. Investigators retained full independence in the conduct of this research.



“The mFI-5 effectively predicts postoperative delirium in geriatric colectomy patients, allowing early identification of high-risk individuals and targeted interventions to reduce complications.”

ASSESSING THE MFI-5 FRAILITY SCORE AND DELIRIUM IN GERIATRIC PATIENTS UNDERGOING COLECTOMY PROCEDURES

Cole Brown, BS, Alexandra Agathis, MD, Jeanne Wu, MS, and Celia Divino, MD

BACKGROUND: Frailty is a well-established predictor of poor postoperative outcomes in geriatric patients undergoing major abdominal surgery, such as colectomy. Early identification of frailty is essential for mitigating risks, such as postoperative delirium, a common complication in this population. The modified Frailty Index (mFI-5) is a simplified tool for assessing frailty in geriatric patients. This study aims to evaluate the association between mFI-5 scores and the incidence of postoperative delirium in geriatric patients undergoing colectomy using data from the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) in 2021 and 2022.

OBJECTIVE: The objective of this study is to determine the predictive value of the mFI-5 for postoperative delirium in elderly patients undergoing colectomy, to provide clinical guidelines for high-risk geriatric patients, and to further explore the utility of the mFI-5 in improving perioperative care.

METHODS: A retrospective cohort study was conducted using the 2021 and 2022 NSQIP databases, including all patients aged 75 years and older who underwent colectomy. Preoperative mFI-5 scores were calculated by the sum of the presentation of hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), diabetes, and non-independent functional status. Delirium is a new variable that was added to the NSQIP database in 2021 and was tracked postoperatively in all patients of 75 years of age and older. Using Statistical Analysis Software, logistic regressions models were implemented to analyze the association between mFI-5 scores and the incidence of delirium, adjusting for potential confounders.

RESULTS: The study included 17,795 patients consisting of 22.46% mFI = 0, 45.29% mFI = 1, and 32.25% mFI \geq 2. The mean age of the cohort was 81.09 years (SD = 4.65) with an average body mass index of 25.57 (SD = 8.06). The cohort was 58.4% female and 41.57% male. 69.13% of cases were elective, 12.73% were urgent, and 18.14% were emergent. The overall incidence of postoperative delirium was 13.32%. The model is predictive of postoperative delirium with an area under the curve (AUC) of 0.71 in the receiver operating characteristic curve (ROC). Frail (mFI \geq 2) patients were significantly more likely to develop postoperative delirium than non-frail (mFI = 0) patients (OR=1.602, CI 1.402-1.832). Other factors, such as smoking ($p = 0.001$), non-white race ($p = 0.0007$), and urgent/emergent case ($p < 0.001$), were also significantly associated with higher rates of postoperative delirium.

CONCLUSIONS: The mFI-5 is an effective tool for predicting postoperative delirium in geriatric patients undergoing colectomy. The mFI-5's application in the preoperative assessment in geriatric patients can help identify high-risk patients, allowing for targeted interventions to reduce the incidence of delirium and other postoperative complications.

PATTERNS OF PLATELET DYSFUNCTION IN NEUROTRAUMA PATIENTS BASED ON CLINICAL AND DEMOGRAPHIC CHARACTERISTICS

Mehek Dedhia, Daniel Cummins MD, Jueria Rahman, and Zachary Hickman MD

Patterns of Platelet Dysfunction in Neurotrauma Patients based on Clinical and Demographic Characteristics

Mehek Dedhia¹, Daniel Cummins MD², Jueria Rahman³, Zachary Hickman MD^{2,3}

¹. Icahn School of Medicine at Mount Sinai; ². Department of Neurosurgery, ISMMMS; ³. Department of Neurosurgery, NYC Health + Hospitals/Elmhurst



BACKGROUND

Platelet dysfunction in neurotrauma patients is a significant concern as it can negatively impact recovery by impairing clotting or promoting hemorrhage. Platelet dysfunction often arises due to the direct impact of traumatic brain injury on platelet activation and aggregation processes; however, the precise mechanisms and how they may differ between patients are still unclear. This study uses thromboelastography with platelet mapping (TEG-PM) data from trauma patients, the majority with neurotrauma, to investigate the incidence and association of platelet dysfunction in this patient population with demographic and clinical characteristics.

METHODS

- A retrospective chart review was conducted of trauma patients admitted to NYC Health + Hospitals/Elmhurst between 7/1/2021 and 6/30/2023, age 18-100, and having at least one TEG-PM data point within 48 hours of admission
- Demographic data and clinical data, such as trauma type, TBI, chronic alcohol use, blood alcohol levels, and anticoagulant (AC)/antiplatelet (AP) use were collected and descriptive statistics were used to characterize the cohort
- Platelet dysfunction was defined as having inhibition of the arachidonic acid (AA) or adenosine diphosphate (ADP) pathway of 20% or more
- Fischer's test was used to compare incidence of platelet dysfunction between groups and the Mann Whitney U test was used to compare TEG-PM marker means between groups based on age

RESULTS

A total of 247 patients were included in the cohort. The mean age was 54.0 years (SD= 20.9) and 27.1% were female (Table 1). Clinically, 85.0% (n=210) were patients with head or neck trauma, 9.7% had thrombocytopenia on admission, while 8.9% had thrombocythemia on admission, and a majority of patients (68.6%) had platelet dysfunction.

Table 1. Demographic and Clinical Characteristics

Variable	N=247
Demographic Characteristics	
Age, years (SD)	54.0 (20.9)
Female, % (n)	27.1% (67)
White, % (n)	16.6% (41)
Black, % (n)	7.3% (18)
Asian, % (n)	17.0% (42)
Other, % (n)	8.5% (21)
Hispanic, % (n)	50.6% (125)
Clinical Characteristics	
%Head or neck trauma	85.0% (210)
%Thrombocytopenia	9.7% (24)
%Thrombocythemia	8.9% (22)
%with platelet dysfunction	68.6% (169)
Initial GCS, mean (SD)	13.4 (SD=3.03)
Injury Severity Score, mean (SD)	17.3 (SD=9.28)

The incidence of platelet dysfunction was not significantly different across clinical and demographic groups (Table 2). MA Kaolin, MA ActF, MA ADP, and ADP aggregation were significantly increased in patients above 65 years of age (Table 3). ADP inhibition and AA aggregation were significantly decreased in patients above 65 years of age (Table 3).

Table 2. Incidence of Platelet Dysfunction by Demographic and Clinical Characteristics

Category	Groups	Incidence	P-value
Trauma type	Head trauma	0.833	0.92
	Non-head trauma	0.811	
Age	<65 years	0.834	0.94
	>65 years	0.821	
Acute alcohol intoxication	Yes	0.816	0.89
	No	0.833	
Chronic alcohol usage	Yes	0.880	0.16
	No	0.804	
Chronic AC/AP Usage	Yes	0.857	0.76
	No	0.823	

Table 3. TEG-PM Markers Based on Age

TEG-PM Marker	>65 years (Median)	< 65 years (Median)	P-value
MA Kaolin	60.6	58	0.002
MA ActF	15	9.9	<0.001
MA ADP	43.80	31.35	<0.001
MA AA	41	41.75	0.46
Inhibition ADP%	30.20	47.45	0.005
Inhibition AA%	44.6	28.5	0.069
Aggregation ADP%	69	51.95	0.007
Aggregation AA%	53.4	72.1	0.046

CONCLUSIONS

- A significant proportion (83%) of trauma patients had platelet dysfunction on admission
- Platelet dysfunction incidence did not differ significantly between groups
- However, platelet function markers did significantly differ between older and younger patients
- This indicates a potential benefit to targeted interventions for groups based on demographic and clinical characteristics to reverse platelet dysfunction and improve trauma outcomes

FUTURE DIRECTIONS

- Compare association of platelet dysfunction with additional patient characteristics, such as those with/without acute alcohol intoxication, severity of injury, etc.
- Investigate if defects in the AA or ADP pathway are associated with deviations in other coagulation markers and with worse clinical outcomes.

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I would like to thank Dr. Hickman and Dr. Cummins for their mentorship and the MSTAR program for their support.



“83% of neurotrauma patients showed platelet dysfunction on admission, with age-related differences indicating the potential for targeted interventions to improve outcomes.”

PATTERNS OF PLATELET DYSFUNCTION IN NEUROTRAUMA PATIENTS BASED ON CLINICAL AND DEMOGRAPHIC CHARACTERISTICS

Mehek Dedhia, Daniel Cummins MD, Jueria Rahman, and Zachary Hickman MD

INTRODUCTION: Platelet dysfunction in neurotrauma patients is a significant concern as it can negatively impact recovery by impairing clotting or promoting hemorrhage. Platelet dysfunction often arises due to the direct impact of traumatic brain injury on platelet activation and aggregation processes; however, the precise mechanisms and how they may differ between patients are still unclear. This study uses thromboelastography with platelet mapping (TEG-PM) data from trauma patients, the majority with neurotrauma, to investigate the incidence and association of platelet dysfunction in this patient population with demographic and clinical characteristics.

METHODS: A retrospective chart review was conducted of trauma patients admitted to NYC Health + Hospitals/Elmhurst between 7/1/2021 and 6/30/2023, age 18-100, and having at least one TEG-PM data point within 48 hours of admission. Demographic data and clinical data, such as trauma type, TBI, chronic alcohol use, blood alcohol levels, and anticoagulant (AC)/antiplatelet (AP) use were collected and descriptive statistics were used to characterize the cohort. Platelet dysfunction was defined as having inhibition of the arachidonic acid (AA) or adenosine diphosphate (ADP) pathway of 20% or more. Chi-square test was used to compare incidence of platelet dysfunction between groups and the Mann Whitney U test was used to compare TEG-PM marker means between groups based on age

RESULTS: A total of 247 patients were included in the cohort. The mean age was 54.0 years (SD= 20.86), and 27.1% were female (Table 1). Clinically, 85.0% (n=210) experienced some form of head/neck trauma, 9.7% had thrombocytopenia on admission and 8.9% had thrombocythemia on admission and 83.0% had platelet dysfunction. The incidence of platelet dysfunction was not significantly different across clinical and demographic groups (Table 2). MA Kaolin, MA ActF, MA ADP, and ADP aggregation were significantly increased in patients above 65 years of age (Table 3). ADP inhibition and AA aggregation were significantly decreased in patients above 65 years of age (Table 3). MA Kaolin, MA ActF, MA ADP, and ADP aggregation were significantly increased in patients above 65 years of age. ADP inhibition and AA aggregation were significantly decreased in patients above 65 years of age.

FUTURE DIRECTIONS: We will compare the markers of coagulation pathways for more clinically and demographically defined patient groups, such as based on acute alcohol intoxication, extent of injury etc. Furthermore, we will investigate if defects in the AA or ADP pathway are associated with deviations in other coagulation markers and with worse clinical outcomes.

CONCLUSIONS: A significant proportion (83%) of trauma patients had platelet dysfunction on admission. Platelet dysfunction incidence did not differ significantly between groups. However, platelet function markers did significantly differ between older and younger patients. This indicates a potential benefit to targeted interventions for groups based on demographic and clinical characteristics to reverse platelet dysfunction and improve trauma outcomes

ASSOCIATIONS BETWEEN SOCIAL SUPPORT AND RADIATION OUTCOMES IN OLDER ADULTS WITH CANCER UNDERGOING PALLIATIVE RADIATION THERAPY

Varun Devraj, Mayuri Jain, Laura Jonsson, Erin Moshier, MS3, and Kavita Dharmarajan, MD, MSc

Associations Between Social Support and Radiation Outcomes in Older Adults with Cancer Undergoing Palliative Radiation Therapy

Varun Devraj¹, Mayuri Jain^{1,2}, Laura Jonsson¹, Erin Moshier, MS³, Kavita Dharmarajan, MD, MSc¹

INTRODUCTION

- Social support is an important factor in older patients' health, especially in those undergoing treatment for cancer
- Tools measuring social support have been recommended for standard of care screening in older patients undergoing chemotherapy
- Relationship between social support and radiation outcomes such as motor/cognitive functioning and post-radiation toxicities is not understood

OBJECTIVE

- To examine associations between pre-radiation therapy (RT) social support and post-RT changes in cognitive function, motor ability, and RT-caused toxicities in older patients with metastatic disease

METHODS

- Prospective cohort study of patients 65 years and older with metastatic disease receiving palliative RT at Mount Sinai Hospital
- Social support measured using the Medical Outcomes Study (MOS) Social Support Survey, where a score of 3 or lower indicated a lack of social support
- Cognitive function assessed using the BOMC
- Motor function assessed using TUG test and SPPB
- Post treatment toxicities assessed using PRO-CTCAE scale based on treatment site
- Associations analyzed with mixed model ANOVAs fitted separately for each outcome measure of interest

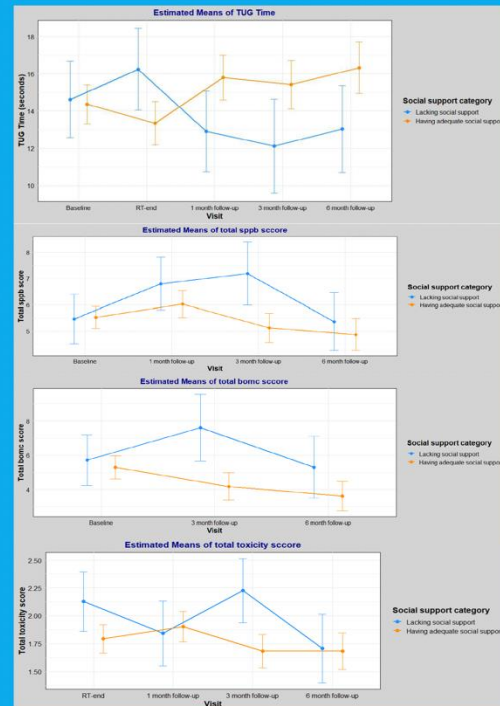
RESULTS

- Accessed data from 58 survey participants that had completed RT and answered the MOS Social Support Survey; 10 lacking social support and 48 with adequate social support
- Between RT-end and 6 months post-RT, TUG time significantly increased in patients with adequate social support ($p = 0.0206$) and showed a decreasing trend in patients lacking social support; difference of the mean changes was also significant ($p = 0.032$)
- SPPB score decreased significantly (indicating worsening motor functioning) between 1 month and 6 months post-RT ($p = 0.0495$) in patients with adequate social support, but the mean difference between the two groups was not significant
- BOMC scores significantly decreased (indicating better cognitive functioning) between baseline (before radiation) and 6 months post-RT in patients with adequate social support
- Toxicities did not show any trend in patients lacking and with adequate social support

AFFILIATIONS

¹ Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai
² Biostatistics and Clinical Informatics, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai
³ Department of Population Health Science and Delivery, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai

Motor functioning worsens and cognitive functioning improves 6 months after radiation in patients with adequate social support.



DISCUSSION

- Adequate social support may be associated with worse motor function and lack of social support may be associated with better motor function 6 months post RT, significantly as measured by the TUG screening tool
- Conversely, cognitive function significantly improves 6 months post RT in patients with adequate social support
- Elucidating the relationship between social support and radiation outcomes will be important to help clinicians tailor treatment for geriatric patients undergoing palliative RT
- Due to a small sample size, especially in the lacking social support group, additional analysis is required with a larger sample population
- Further exploratory analysis will divide social support into "physical" and "emotional" categories to understand associations based on types of social support; additional analysis will also be done into associations between social support and other quality of life markers

Study Timepoint	Lacking Adequate Support (n = 10)				P-value	Adequate Support (n = 48)				Difference in Mean Change (95% CI)	P-value
	Unadjusted Mean (95% CI)	Adjusted Mean (95% CI)	Adjusted Mean Change From Baseline (95% CI)	Reference		Unadjusted Mean (95% CI)	Adjusted Mean (95% CI)	Adjusted Mean Change From Baseline (95% CI)	Reference		
TUG Time (s)											
Pre-RT	15.46 (10.94-19.98)	14.51 (10.44-18.59)	Reference	Reference		12.91 (12.13-14.46)	14.97 (12.27-16.67)	Reference	Reference	Reference	Reference
Post-RT	17.16 (12.34-21.97)	16.06 (11.73-20.39)	1.54 (2.95-0.85)	0.4895		12.00 (9.84-14.17)	13.38 (11.07-15.70)	-0.98 (2.95-0.99)	0.3252	2.52 (2.34-2.69)	0.3062
1 month follow-up	13.18 (8.34-17.98)	12.41 (8.15-16.67)	-1.76 (4.12-0.70)	0.4522		14.54 (12.38-16.70)	15.86 (13.86-17.86)	1.49 (0.46-2.52)	0.1325	-3.19 (1.07-1.60)	0.1064
3 month follow-up	12.28 (8.52-17.96)	12.78 (8.75-16.81)	-0.50 (1.98-0.98)	0.3896		15.10 (13.09-17.10)	16.51 (14.24-18.77)	1.13 (0.69-1.57)	0.2195	-1.17 (1.26-2.27)	0.3732
6 month follow-up	13.56 (8.36-17.96)	12.89 (8.23-16.55)	-1.24 (3.52-1.04)	0.5122		14.81 (12.25-17.46)	16.41 (13.66-19.16)	2.01 (0.90-3.12)	0.0873	-0.69 (0.98-1.76)	0.1839
BOMC Score											
Pre-RT	5.79 (3.63-7.95)	5.49 (3.63-7.35)	Reference	Reference		6.58 (3.74-9.42)	5.52 (3.66-7.38)	Reference	Reference	Reference	Reference
1 month follow-up	7.38 (5.12-9.64)	6.81 (4.80-8.82)	1.32 (0.78-1.87)	0.2162		7.13 (5.34-8.92)	6.00 (4.64-7.36)	0.43 (0.64-0.82)	0.3027	0.81 (1.45-0.82)	0.4701
3 month follow-up	7.09 (5.00-9.18)	7.17 (4.75-9.59)	1.42 (1.40-1.44)	0.1886		6.13 (5.04-7.17)	5.09 (3.90-6.28)	-0.42 (0.40-0.56)	0.3983	1.01 (0.36-1.66)	0.1281
6 month follow-up	6.89 (3.49-10.29)	5.39 (3.12-7.66)	-0.99 (2.40-0.42)	0.9349		5.91 (4.74-7.08)	4.89 (3.68-6.10)	-0.68 (1.74-0.40)	0.2274	1.28 (1.95-0.39)	0.6489
SPPB Score											
Pre-RT	4.44 (2.49-6.39)	5.47 (2.72-8.22)	Reference	Reference		5.12 (3.90-6.34)	5.31 (3.99-6.63)	Reference	Reference	Reference	Reference
1 month follow-up	7.24 (3.52-10.96)	7.93 (3.88-11.98)	1.89 (1.40-2.38)	0.2340		5.98 (3.24-8.72)	4.71 (2.42-6.99)	-1.14 (1.24-0.97)	0.0643	3.01 (0.48-5.55)	0.0204
3 month follow-up	6.91 (3.53-10.29)	5.91 (3.84-7.98)	-0.48 (1.38-0.42)	0.7604		5.82 (3.09-8.55)	4.93 (3.76-6.10)	-0.89 (1.20-0.42)	0.0097	1.61 (1.40-1.82)	0.1783
6 month follow-up	6.15 (3.12-9.18)	6.84 (4.41-9.27)	0.69 (1.40-0.01)	0.7604		5.82 (3.09-8.55)	4.93 (3.76-6.10)	-0.89 (1.20-0.42)	0.0097	1.61 (1.40-1.82)	0.1783
Toxicity Score											
Pre-RT	2.24 (1.76-2.72)	2.12 (1.65-2.59)	Reference	Reference		1.76 (1.38-2.15)	1.79 (1.34-2.25)	Reference	Reference	Reference	Reference
1 month follow-up	1.93 (1.40-2.46)	1.84 (1.29-2.41)	-0.28 (0.48-0.92)	0.3458		1.81 (1.44-2.18)	1.93 (1.44-2.42)	0.12 (0.34-0.50)	0.3803	0.41 (1.05-0.23)	0.2212
3 month follow-up	1.93 (1.40-2.46)	1.84 (1.29-2.41)	-0.28 (0.48-0.92)	0.3458		1.81 (1.44-2.18)	1.93 (1.44-2.42)	0.12 (0.34-0.50)	0.3803	0.41 (1.05-0.23)	0.2212
6 month follow-up	1.80 (1.34-2.26)	1.71 (1.15-2.27)	-0.42 (0.63-0.79)	0.137		1.83 (1.36-2.30)	1.88 (1.36-2.40)	-0.10 (0.41-0.20)	0.4818	-0.11 (1.05-0.83)	0.1839



FINANCIAL DISCLOSURE

- This study was supported by the National Institute for Aging (NIA) and the Medical Student Training in Aging Research (MSTAR) Program at the Icahn School of Medicine at Mount Sinai. The investigators retained full independence in the conduct of this research.



“Preliminary data suggests that older cancer patients with adequate social support show improved cognitive but worsened motor functioning six months after radiation therapy, emphasizing the need for tailored treatments.”

ASSOCIATIONS BETWEEN SOCIAL SUPPORT AND RADIATION OUTCOMES IN OLDER ADULTS WITH CANCER UNDERGOING PALLIATIVE RADIATION THERAPY

Varun Devraj, Mayuri Jain, Laura Jonsson, Erin Moshier,MS3, and Kavita Dharmarajan, MD, MSc

BACKGROUND: Social support is an important dimension of the cancer experience among older adults. While social support, as measured by various tools, has already been included in standard of care screening for older patients undergoing chemotherapy, the relationship between social support and post-RT outcomes, such as cognitive function, motor ability, and radiation toxicities, is not well studied. The objective of this study is to examine associations between pre-RT social support and post-RT changes in cognitive function, motor ability, and RT-caused toxicities in older patients with metastatic disease.

METHODS: This is a prospective cohort study of patients 65 years and older with metastatic cancer undergoing palliative RT at Mount Sinai Hospital, a large academic center in New York City. This study is part of a larger, ongoing study aiming to improve outcomes and quality of life for older patients undergoing palliative RT. Social support was measured using the Medical Outcomes Study (MOS) Social Support Survey, where a score of 3 or lower indicated a lack of social support. We assessed cognitive function using the Blessed Orientation-Memory-Concentration Assessment (BOMC) before radiation and 1, 3, and 6 months post-RT. Mobility was assessed using two tools: the Timed Up and Go (TUG) test conducted before radiation, at RT-end, and at 1, 3, and 6 months post-RT; and the Short Physical Performance Battery (SPPB), conducted before radiation and at 1, 3, and 6 months post-RT. We assessed radiation toxicities using the Patient-Reported Outcomes Version of Common Terminology Criteria for Adverse Events (PRO-CTCAE) scale based on treatment site at RT-end and at 1, 3, and 6 months post-RT. Mixed model ANOVAs were fitted separately for each outcome to assess differences in scores between baseline and post-RT assessments in patients grouped by social support category (lacking social support or having adequate social support). Demographic characteristics were compared using descriptive statistics.

RESULTS: We accessed survey responses from 58 survey participants that had completed RT and answered the MOS Social Support Survey, 10 of whom lacked social support and 48 of whom had adequate social support. Between RT-end and 6 months post-RT, TUG time significantly increased in patients with adequate social support ($p = 0.0206$) and showed a decreasing trend in patients lacking social support. The difference of the mean changes between RT-end and 6 months post-RT in the two groups was also significant ($p = 0.032$). In patients with adequate social support, SPPB score decreased significantly (indicating worse motor functioning) between 1 month and 6 months post-RT ($p = 0.0495$), although the mean difference between the two groups was not significant. BOMC scores significantly decreased (indicating better cognitive functioning) between baseline (before RT) and 6 months post-RT in patients with adequate social support. We did not find any significant mean difference between the two groups for BOMC scores. Toxicities did not show any trend in patients with adequate social support and those lacking social support.

CONCLUSIONS: This preliminary data demonstrates that among patients self-reporting adequate social support, motor functioning, measured by two different screening tools, significantly worsened and cognitive functioning significantly improved 6 months after radiation in older individuals undergoing RT. Further analysis grouped by subscales within larger screening tools and with a larger study population is required to better understand the association between social support and cognitive functioning, motor functioning, self-reported toxicities, and other measures of quality of life in older patients with metastatic disease undergoing RT. This will eventually help clinicians tailor treatment for geriatric patients that are more at risk for poor outcomes from RT.

THE ROLE OF NEUTROPHILS IN AGING AND HEALING OF THE INTERVERTEBRAL DISC

James Hong, BS, Timothy Jacobsen, PhD, and James Iatridis, PhD



The Role of Neutrophils in Aging and Healing of the Intervertebral Disc



James Hong, BS, Timothy Jacobsen, PhD, James Iatridis, PhD
Icahn School of Medicine at Mount Sinai

INTRODUCTION

- Back pain is a leading cause of disability worldwide, with over 80% of adults over 50 experiencing intervertebral disc (IVD) degeneration due to diminished healing capacity.
- Chronic IVD degeneration involves persistent inflammation and elevated pro-inflammatory cytokines, leading to tissue breakdown and pain.
- Neonatal mice exhibit regenerative IVD healing, unlike adult and aged mice, with immune cell involvement potentially playing a key role.
- No studies have characterized the effects of aging on IVD healing or the role of immune cell involvement in age-specific models with a high prevalence of back pain.

The objectives of this study are to determine the effects of age on:

1. Immune cell populations in naïve IVDs
2. Responses of IVD immune cells to injury

METHODS

- C57BL/6 mice were used at three ages: **Neonatal** (14 days; regenerative), **Adult** (4 months; skeletal maturity), and **Aged** (1 year; equivalent to human peak back pain disability).
- AF-hermiation injury was created in coccygeal IVDs using 26- or 30-gauge needle to produce an injury ~80% of IVD height.
- Single-Cell RNA Sequencing (scRNA-Seq) was performed on cells pooled from whole naïve IVDs of 6 mice (10X Genomics Chromium 3' kit, Illumina S1 NovaSeq chip). Cell clusters were visualized with uniform manifold approximation and projection (UMAP). Differential gene expression analysis of canonical markers facilitated annotation.
- IVD segments were collected 14 days post-injury, fixed, decalcified, resin embedded, and sectioned for histology. Immunohistochemistry for Ly6G assessed neutrophil presence.



FINANCIAL DISCLOSURE: This study was supported by the National Institute of Aging (NIA) and the Medical Student Training in Aging Research (MSTAR) program at the Icahn School of Medicine at Mount Sinai. Investigators retained full independence in the conduct of this research.

RESULTS

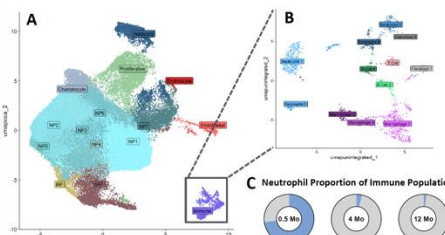


Figure 1: (A) Single Cell RNA Sequencing of mouse IVDs revealed distinct populations of IVD cells and immune cells. (B) Sub clustering analysis of immune cells further revealed populations of Macrophages, Neutrophils, T Cells, and B Cells within naïve IVDs. (C) Neutrophils were found to distinctly decrease with age in naïve mouse discs.

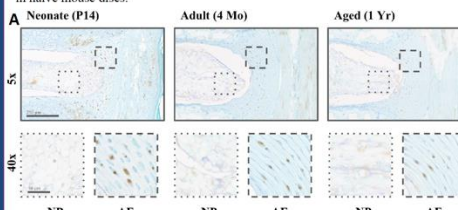
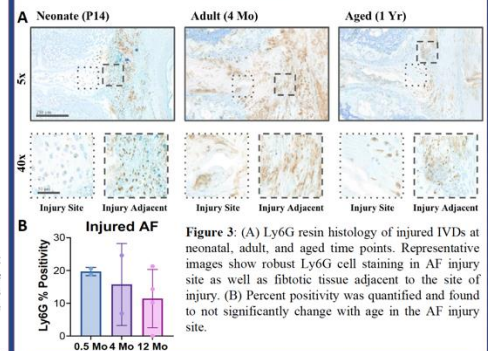


Figure 2: (A) Ly6G resin histology of uninjured IVDs at neonatal, adult, and aged time points. Representative images show minimal Ly6G cell staining in NP, with most cellular staining being present in the AF tissue. (B) Percent positivity was quantified and found to significantly decrease with age in the AF.

RESULTS



DISCUSSION & CONCLUSION

- Neonatal mice IVDs had a large population of resident neutrophils observed with sc-RNASeq in naïve IVDs that was notably absent at older age points. Ly6G staining similarly showed decreased presence of neutrophils with aging. These results suggest that neutrophils could play a role in the distinct neonatal mouse IVD healing responses.
- No difference in Ly6G percent positivity in injured AFs was observed with age indicating it may be the initial presence of neutrophils in naïve neonatal IVDs and not infiltrating neutrophils that drive the regenerative response in neonates.
- Ongoing work will utilize intraperitoneal injections of a Ly6G/Ly6C antibody to systematically deplete neutrophils to mechanistically observe their role in neonatal IVD healing.
- This research implicates resident neutrophils as important mediators of regenerative healing in neonatal mice and points to the potential of future neutrophil modulating immunotherapies for enhancing IVD repair in advanced age patients.



“Resident neutrophils are key mediators of regenerative healing in neonatal mice, suggesting potential for neutrophil-modulating therapies to improve intervertebral disc repair in aging patients.”

THE ROLE OF NEUTROPHILS IN AGING AND HEALING OF THE INTERVERTEBRAL DISC

James Hong, BS, Timothy Jacobsen, PhD, and James Iatridis, PhD

INTRODUCTION: Back pain is a leading cause of disability worldwide, with over 80% of adults over 50 experiencing intervertebral disc (IVD) degeneration due to diminished healing capacity. Chronic IVD degeneration involves persistent inflammation and elevated pro-inflammatory cytokines, leading to tissue breakdown and pain. Neonatal mice exhibit regenerative IVD healing, unlike adult and aged mice, with immune cell involvement potentially playing a key role. No studies have characterized the effects of aging on IVD healing or the role of immune cell involvement in age-specific models with a high prevalence of back pain. The objectives of this study are to determine the effects of age on: 1. Immune cell populations in naïve IVDs and 2. Responses of IVD immune cells to injury.

METHODS: C57BL/6 mice were used at three ages: Neonatal (14 days; regenerative), Adult (4 months; skeletal maturity), and Aged (1 year; equivalent to human peak back pain disability). AF-herniation injury was created in coccygeal IVDs using 26- or 30-gauge needle to produce an injury ~80% of IVD height. Single cell RNA sequencing (scRNA-Seq) was performed on cells pooled from whole naïve IVDs of 6 mice (10X Genomics Chromium 3' kit, Illumina S1 NovaSeq chip). Cell clusters were visualized with uniform manifold approximation and projection (UMAP). Differential gene expression analysis of canonical markers facilitated annotation. IVD segments were collected 14 days post-injury, fixed, decalcified, resin embedded, and sectioned for histology. Immunohistochemistry for Ly6G assessed neutrophil presence.

RESULTS: Single cell RNA sequencing of mouse IVDs revealed distinct populations of IVD cells and immune cells. Sub-clustering analysis of immune cells further revealed populations of macrophages, neutrophils, T-cells, and B-cells within naïve mouse IVDs. Neutrophils were found to distinctly decrease with age in naïve mouse discs.

Ly6G resin histology of uninjured IVDs at neonatal, adult, and aged time points found minimal staining in the nucleus pulposus (NP) with most cellular staining being present in the annulus fibrosus (AF). Percent positivity was quantified and also found to significantly decrease with age in the AF.

Ly6G resin histology of injured IVDs at neonatal, adult, and aged time points found robust Ly6G staining in the AF injury site as well as fibrotic tissue that had formed adjacent to the site of injury. Percent positivity was quantified, but found to not significantly change with age in the AF injury site.

DISCUSSION: Neonatal mice IVDs had a large population of resident neutrophils observed with scRNASeq in naïve IVDs that were notably absent at older age points. Ly6G staining similarly showed decreased presence of neutrophils with aging. These results suggest that neutrophils could play a role in distinct neonatal mouse IVD healing responses. No difference in Ly6G percent positivity in injured AFs was observed with age, indicating it may be the initial presence of neutrophils in naïve neonatal IVDs and not infiltrating neutrophils that drive the regenerative response in neonates. This research implicates that resident neutrophils are important mediators of regenerative healing in neonatal mice and points to the potential of future neutrophil modulating immunotherapies for enhancing IVD repair in advanced age patients.

SERUM PROTEOMIC ANALYSIS OF CANCER PATIENTS WITH CUTANEOUS IMMUNE-RELATED ADVERSE EVENTS

Benjamin D. Hu, BS; Jacob Glickman, MD; Camille M. Powers, BA; Yeriell D. Estrada, BS; Daniel Lozano-Ojalvo, PhD; Emma Guttman-Yassky, MD, PhD; Nicholas Gulati, MD, PhD

Serum Proteomic Analysis of Cancer Patients with Cutaneous Immune-related Adverse Events



Benjamin D. Hu, BS¹; Jacob Glickman, MD¹; Camille M. Powers, BA¹; Yeriell Estrada, BS¹; Daniel Lozano-Ojalvo, PhD¹; Emma Guttman-Yassky, MD, PhD¹; Nicholas Gulati, MD, PhD¹

¹ Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA

BACKGROUND

Cutaneous reactions contribute significantly to the morbidity of patients receiving anti-cancer therapies, often appearing within weeks of the first treatment, and sometimes causing a delay or discontinuation of treatment.¹ One group of such side-effects are cutaneous immune-related adverse events (irAEs) – inflammatory adverse reactions resulting from immune checkpoint inhibitor (ICI) use. irAEs can occur in over 40% of patients taking ICIs.²

As cancer risk increases with age, many irAE patients are from the geriatric population. Immunocompromised elderly cancer patients are particularly vulnerable to the mortality of irAEs, given disrupted skin barriers that potentially increase the risk of infection and side effects associated with commonly used treatments by clinicians (e.g. systemic steroids). Little research has investigated the similarities and differences between irAEs and the spontaneous versions of these skin conditions, and not much is known about the pathomechanisms underlying these ICI-induced cutaneous reactions, thus limiting options for treatment.³ To our knowledge, there is currently no proteomic data published on irAEs.

METHODS

Serum samples were collected from 14 patients with irAEs, 21 patients with general inflammatory dermatologic conditions (atopic dermatitis [AD] and lichen planus [LP]), and 5 healthy controls. The raw proteomic data was extracted from the samples using the high-throughput OLINK Proximity Extension Assay, an assay utilizing oligonucleotide-labeled antibody probe pairs. 4 panels with 96 proteins each were measured during the OLINK Assay: inflammation, neurology, cardiovascular II, and cardiovascular III. Correlation and differential protein expression pipelines were executed comparing the three patient groups. Statistical analyses were performed using R software and the Bioconductor packages.

RESULTS

Our irAE patients, AD/LP controls, and healthy controls have an average age of 70.4, 64.5, 59.6 years, respectively, with no significant differences amongst patient groups in terms of age, race, or sex.

Compared to healthy controls (HCs), patients with ICI-induced eczematous reactions (ICI-Ecz) demonstrated dysregulation of proteins involved in inflammatory pathways. There was upregulation of interferon gamma, TNF, CCL19 (all related to the Th1 pathway), ARTN, and IL10R- α , along with downregulation of IL4, a cytokine associated with the Th2 pathway. When compared to general AD, ICI-Ecz showed upregulation of interferon gamma as well as downregulation of IL4, IL13, and IL4R- α (all involved in the Th2 pathway). Additionally, between ICI-Ecz and ICI-induced lichenoid reactions (ICI-LP), ICI-Ecz displayed increased expression of proteins involved in inflammatory processes. Comparing serum proteomic data and skin RNA expression in ICI-Ecz, we saw a statistically significant moderate positive correlation, indicating some consistency in dysregulation of certain proteins/genes in these patients.

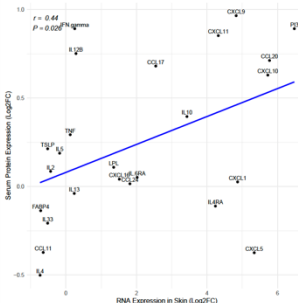


Figure 1. Scatterplot comparing the log₂ fold change (Log₂FC) in RNA expression in the skin with corresponding protein change in serum in patients with ICI-induced eczematous reactions.

Subject	irAE Diagnosis	Age	Sex	Race + Ethnicity	Cancer Type	Cancer Therapy	Treatment for irAE (if pre-sample)
1	Eczematous	45	Female	White, NH	Breast Cancer	Pembrolizumab	NA
2	Eczematous	64	Male	Black, NH	Bladder Cancer	Pembrolizumab	NA
3A	Eczematous	63	Male	Other, H	Multiple Myeloma	Lenalidomide	NA
3B	Eczematous	63	Male	Other, H	Multiple Myeloma	Lenalidomide	Dupilumab
4	Eczematous	85	Female	White, NH	Non-Small Cell Lung Cancer	Pembrolizumab	NA
5	Prurigo Nodulatus	82	Male	Other, H	Urothelial Cancer	Pembrolizumab	NA
6	Bullous Pemphigoid	89	Male	Other, H	Renal Cell Carcinoma	Nivolumab	NA
7	Bullous Pemphigoid	71	Male	White, NH	Lung Adenocarcinoma	Pembrolizumab	NA
8	Bullous Pemphigoid	67	Male	White, NH	Urothelial Cancer	Pembrolizumab	Dupilumab
9	Lichen Planus	78	Male	White, NH	Non-Small Cell Lung Cancer	Darvadumab	NA
10	Lichen Planus	72	Female	White, NH	Breast Cancer	Pembrolizumab	NA
10A	Lichen Planus	72	Female	White, NH	Breast Cancer	Pembrolizumab	Dupilumab
11	Lichen Planus	81	Female	White, NH	Colon Adenocarcinoma	Pembrolizumab	NA
12	Morbiform Drug Eruption	54	Male	White, NH	AML, MRC	Azacitidine	NA

Table 1. Demographics table for irAE patients. NH = Non-Hispanic and H = Hispanic.

Protein	FC in ICI-Ecz vs. HC	Protein	FC in ICI-Ecz vs. AD	Protein	FC in ICI-Ecz vs. ICI-LP
PRTN3	2.93	IFN- γ	1.39	FGF21	36.00
SRC	2.77	KM1	-2.380924	CXCL5	30.48
CCL19	1.96	SERPINA12	-2.727273	IL12B	16.45
MPO	1.93	FABP2	-1.8518519	CXCL9	15.24
IFN- γ	1.85	CSTB	-1.7241379	TNFRSF9	11.71
IL10R- α	1.74	ADM	-1.666667	CCL19	9.06
COL1A1	1.54	IL4R- α	-1.492573	CXCL11	8.46
BLM Hydrolase	1.49	IL4	-1.4285714	CCL11	7.73
ARTN	1.22	SPPS1	-1.388889	CD5	7.26
TNF	1.22	ALCAM	-1.3197895	OSM	5.58
IL4	-1.25	IL13	-1.2345679	CCL28	2.30

Table 2. Top differentially expressed proteins comparing patients with ICI-induced eczematous reactions (ICI-Ecz) vs. healthy controls (HC), ICI-Ecz vs. general AD patients, and ICI-Ecz vs. patients with ICI-induced lichen planus (ICI-LP) based on unadjusted p-values and ordered by fold change (FC). Proteins listed for ICI-Ecz vs. ICI-LP are from the inflammation panel only. Bolded proteins are downregulated.

CONCLUSIONS AND NEXT STEPS

Our serum proteomic data demonstrated protein dysregulation in patients with ICI-induced eczematous reactions compared to healthy controls and general AD, with potential upregulation of proteins involved in the Th1 pathway and downregulation of some proteins involved in the Th2 pathway. There also seem to be differences in serum protein expression amongst the various types of irAEs, with ICI-Ecz having higher expression of inflammation-related proteins compared to ICI-LP. Consistencies between serum protein expression and skin RNA expression in ICI-Ecz patients have also been noted.

Next steps include running correlations on disease severity and serum protein expression levels in irAE patients, analyzing differential protein expression in more types of irAEs, and downstream analyses to determine what biological pathways these proteins are involved in. We also hope to obtain more serum irAE data and more control data from an older age group.

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Thank you to the patients and their referring providers for their participation. Thank you as well to the MSTAR program and the NIA for their support this summer.



“Our findings show distinct inflammatory protein dysregulation in ICI-induced eczematous reactions, suggesting unique immune pathways and potential targets for future therapeutic interventions.”

SERUM PROTEOMIC ANALYSIS OF CANCER PATIENTS WITH CUTANEOUS IMMUNE-RELATED ADVERSE EVENTS

Benjamin D. Hu, BS; Jacob Glickman, MD; Camille M. Powers, BA; Yeriel D. Estrada, BS; Daniel Lozano-Ojalvo, PhD; Emma Guttman-Yassky, MD, PhD; Nicholas Gulati, MD, PhD

BACKGROUND: With the increasing use of anti-cancer treatments such as cytotoxic agents, targeted therapies, and immunotherapies to fight malignancies, there has been an unprecedented incidence of associated toxic cutaneous reactions, which are the most common adverse events. These reactions contribute significantly to the morbidity of patients receiving these therapies, often appearing within weeks of the first treatment, and sometimes causing a delay or discontinuation of treatment. One group of such side-effects are cutaneous immune-related adverse events (cirAEs) – inflammatory adverse reactions resulting from immune checkpoint inhibitor (ICI) use. CirAEs occur in up to 30-60% of patients taking ICIs. Reported cirAEs include morbilliform rash, pruritus, vitiligo, and the development of inflammatory skin diseases such as eczema, psoriasis, bullous pemphigoid, and lichen planus. Notably, development of these reactions has been associated with increased progression-free and overall survival.

As cancer risk increases exponentially with age, many cirAE patients in our cohort are part of the geriatric population. These immunocompromised elderly cancer patients are particularly vulnerable to the mortality of cirAEs, given disrupted skin barriers that potentially increase the risk of infection and side effects associated with commonly used treatments by clinicians (e.g. systemic steroids). Little research has directly investigated the similarities and differences between cirAEs and the spontaneous versions of these skin pathologies. Results from the few studies that have explored this topic seem to suggest that ICI-induced cutaneous reactions and their spontaneous analogues may have different immunopathogenic mechanisms. To better define changes in protein expression arising from cirAE patients, we are analyzing proteomic data from skin and blood samples in patients with adverse skin reactions to antineoplastic agents, patients with inflammatory skin diseases not arising from anti-cancer treatment, and healthy controls. To our knowledge, there is currently no proteomic data published on cirAEs.

METHODS: Serum samples were collected from 14 patients with cirAEs, 21 patients with de novo inflammatory dermatologic conditions (atopic dermatitis [AD] and lichen planus [LP]), and 5 healthy controls. The raw proteomic data was extracted from the samples using the high-throughput OLINK Proximity Extension Assay, an assay utilizing oligonucleotide-labeled antibody probe pairs. 4 panels with 96 proteins each were measured during the OLINK Assay: inflammation, neurology, cardiovascular II, and cardiovascular III. Baseline characteristic analysis was conducted to ensure there were no significant differences in age, race, and sex between the three patient groups. Correlation and differential protein expression pipelines were also executed. All statistical analyses were performed using R software and the Bioconductor packages.

CURRENT RESULTS: Our 14 cirAE patients had an average age of 70.4 years with a standard deviation of 12.2 years, our AD and LP controls had an average age of 64.5 years old and a standard deviation of 8.0 years, and our healthy controls had an average age of 59.6 years and a standard deviation of 6.5 years. There were no statistically significant differences amongst patient groups in terms of age, race, or sex.

Patients with ICI-induced eczematous reactions (ICI-Ecz) exhibited dysregulation of proteins involved in inflammatory pathways. Specifically, there was upregulation of interferon gamma, TNF, CCL19 (all related to the Th1 pathway), ARTN, and IL10R- α , along with downregulation of IL-4, a cytokine associated with the Th2 pathway. When compared to general atopic dermatitis (AD), ICI-Ecz showed increased levels of interferon gamma and reduced levels of IL4, IL13, and IL4R- α , all linked to the Th2 pathway. Additionally, comparisons between ICI-Ecz and ICI-induced lichenoid reactions (ICI-LP) revealed upregulation of inflammatory proteins in ICI-Ecz, including Th1-related proteins such as IL12-B, CXCL5/9/11, and CCL19.

Additionally, our serum proteomic data for ICI-Ecz was compared to skin RNA expression that was previously analyzed in our lab. Looking at overlapping gene-protein pairs, we saw a significant moderately positive correlation, with a correlation coefficient of 0.44 and a p-value of 0.026. Thus, our findings indicated some consistency in dysregulation of certain proteins/genes between serum protein and skin RNA in ICI-Ecz patients.

FUTURE STUDY DESIGN: Future steps include running correlations on disease severity and expression levels of the OLINK panel proteins, as well as analyzing differential protein expression in the other types of cirAEs observed. More downstream analyses are also required to determine what biological pathways these DEPs are involved in. Additionally, we hope to recruit more cirAE patients and obtain more serum data from healthy controls with ages closer to our cirAE patients, as we could only include 5 healthy controls without having a statistically significant difference in age.

RALOXIFENE TREATMENT INCREASES PAIN TOLERANCE IN YOUNG FEMALE MICE BUT DOES NOT PROTECT FROM INJURY-INDUCED PAIN SENSITIVITY

Michael Lemonick, Neharika Bhadouria, Joana L. Almeida, Tori Kroon, Janai Augustin, Nilsson Holguin



Raloxifene Treatment Increases Pain Tolerance In Young Female Mice But Does Not Protect From Injury-Induced Pain Sensitivity

Michael Lemonick, Neharika Bhadouria, Joana L. Almeida, Tori Kroon, Janai Augustin, Nilsson Holguin
Department of Orthopedics, Icahn School of Medicine at Mount Sinai, New York, NY



INTRODUCTION

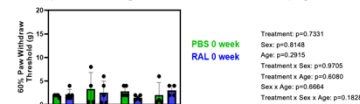
- 70-85% of the American population will experience lower back pain in their lives.¹
- Intervertebral disc (IVD) degeneration is a common factor in back pain.¹
- There are few non-surgical treatments for IVD degeneration and resultant pain: NSAIDs, corticosteroids, icing, and physical therapy
- Raloxifene (RAL) is an FDA-approved selective estrogen receptor modulator used to treat and prevent osteoporosis in postmenopausal women. It exhibits estrogen-agonistic effects on bone receptors and negatively modulates osteoclasts, indicating antiresorptive effects in bone.^{2,3,4}
- RAL may help maintain IVD height and resist degeneration, especially in postmenopausal women.⁵
- RAL has also shown to reduce the expression of Substance P.^{6,7}
- Hypothesis:** Raloxifene injection increases pain tolerance in mice

METHODS

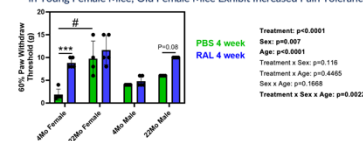
- Male and female C57Bl/6J mice, ages 4Mo and 22Mo, were treated with RAL or PBS for one month via tail vein injection (5X/week; 0.1 ml / 20 gram mouse).
- Mice underwent one week of tail compression (2.25N at CC7-CC9) to simulate IVD degeneration.
- Behavioral data (grip strength, Von Frey Test, and gait data) were collected at the following time points:
 - Baseline, before treatment with RAL or PBS
 - After drug treatment
 - After one week of tail compression plus three weeks rest

RESULTS

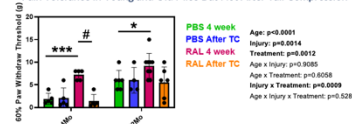
Von Frey Baseline Testing - Pain Tolerance Not Different by Age or Sex



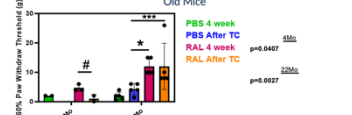
Von Frey Testing After 4 Weeks RAL Injection - RAL Increases Pain Tolerance in Young Female Mice; Old Female Mice Exhibit Increased Pain Tolerance



Von Frey Testing after Tail Compression (Female Group) - RAL Increases Pain Tolerance in Young and Old Mice But Not After Tail Compression



Von Frey Testing after Tail Compression (Male Group) - RAL Increases Pain Tolerance in Young and Old Mice and After Tail Compression in Old Mice



VON FREY TESTING

- Method to determine the pain threshold that elicits a withdrawal response. Plastic filaments of increasing gauges (grams) are applied to the plantar surface of the hind right paw until stimulation elicits 60% (3/5) hind paw withdrawal.

DISCUSSION

- Aged mice are less sensitive to mechanical stimuli than young mice. *Braz et al.* corroborates these findings while noting that mice exhibit hypersensitivity and decreased pain thresholds after nerve injury.⁸
- Relevant literature shows mixed results regarding the correlation between age and pain in mice.^{9,10, 11}

CONCLUSIONS

- RAL appears to increase pain thresholds in young female mice; RAL does not appear to increase pain thresholds in a model of IVD degeneration through tail compression.

ACKNOWLEDGEMENTS

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“Raloxifene increases pain tolerance in mice but does not protect against injury-induced pain, suggesting its potential use in pain management strategies for age-related conditions.”

RALOXIFENE TREATMENT INCREASES PAIN TOLERANCE IN YOUNG FEMALE MICE BUT DOES NOT PROTECT FROM INJURY-INDUCED PAIN SENSITIVITY

Michael Lemonick MA, Neharika Bhadouria, PhD, Joana I. Almeida, PhD, Tori Kroon, MS, Janai Augustin, BS, Nilsson Holguin, PhD

BACKGROUND: Lower back pain is a significant public health issue, affecting 70-85% of the American population, with intervertebral disc (IVD) degeneration being a major contributor. Older adults are particularly vulnerable to chronic pain conditions due to age-related musculoskeletal changes and degeneration. Current non-surgical treatment options for IVD degeneration are limited to NSAIDs, corticosteroids, and physical therapy, which may be insufficient or poorly tolerated in older individuals. Raloxifene (RAL), a selective estrogen receptor modulator approved for osteoporosis in postmenopausal women, has shown potential for modulating pain through estrogen-agonistic effects on bone receptors and reduced expression of Substance P, a neuropeptide involved in pain signaling.

AIM: To investigate whether RAL treatment increases pain tolerance in mice and assess its effectiveness in protecting against injury-induced pain following tail compression—a model for IVD degeneration. We hypothesize that RAL provides neuroprotective benefit to mice.

Methods: Male and female C57Bl/6J mice, aged 4 months (young) and 22 months (aged), were treated with RAL or phosphate buffered saline (PBS) for one month prior to one week of tail compression (2.25N applied at CC7-CC9) to simulate IVD degeneration. Von Frey tactile sensitivity testing occurred at baseline, after RAL or PBS treatment, and three weeks after removal of tail compression apparatus. The Von Frey test measured pain thresholds based on mechanical stimulation and paw withdrawal response.

RESULTS: At baseline, pain tolerance did not differ significantly by age or sex. After 4 weeks of RAL injection, young female mice in both groups and aged male mice in the second group only exhibited significantly increased pain tolerance compared to controls ($p < 0.001$ for both). RAL treatment in young male and old female mice did not significantly increase pain tolerance as compared to respective control groups. After application of tail compression apparatus, only aged female mice treated with RAL showed a significant increase in pain sensitivity as compared to controls. These data indicate that while RAL may help modulate pain thresholds, especially in young female mice, it does not prevent degeneration-related pain.

DISCUSSION: These findings are relevant for older adults, as chronic pain due to IVD degeneration is highly prevalent in this population. While RAL increased pain tolerance in both young and aged mice, its lack of protective effect against injury-induced pain suggests it may have limited use as a standalone therapy for chronic degenerative conditions. Nonetheless, RAL's impact on pain modulation following IVD injury, particularly in aged female mice, highlights its potential as a component of multi-modal pain management strategies for older adults, where preserving quality of life and reducing chronic pain are key goals while avoiding invasive treatments.

CONCLUSIONS: Injection of RAL may offer neuroprotective benefits both prophylactically and after the induction of IVD degeneration. This finding opens a potential avenue of further research to investigate the neurological and pain-moderating effects of raloxifene in the event of injury to the structure of the spinal column.

SOCIAL DEPRIVATION AND DUAL ELIGIBILITY LEAD TO POORER POSTOPERATIVE OUTCOMES IN OLDER ADULTS UNDERGOING SHOULDER ARTHROPLASTY

Kareem S. Mohamed; Christoph A. Schroen; Grace Van Hyfte; Brocha Z. Stern PHD; Eric D. Haunschild MD; William A. Ranson MD; Paul J. Cagle MD

Social Deprivation and Dual Eligibility Lead to Poorer Postoperative Outcomes in Older Adults Undergoing Shoulder Arthroplasty

Kareem S. Mohamed BS¹, Christoph A. Schroen BS¹, Grace Van Hyfte MSc^{1,2}, Brocha Z. Stern PHD^{1,2}, Eric D. Haunschild MD¹, William A. Ranson MD¹, Paul J. Cagle MD¹



BACKGROUND

- There has been an increasing incidence of anatomic total shoulder arthroplasty (aTSA) and reverse TSA (rTSA) in the older adult population, reflecting its growing role in addressing shoulder pathologies.
- While several studies have explored outcomes and complications associated with these procedures within the Medicare population, there remains a notable gap regarding the influence of social deprivation.
- Our study aims to use an area-level indicator, the social deprivation index, and a person-level indicator, dual eligibility for Medicare and Medicaid benefits, to examine how social deprivation impacts TSA outcomes on a national scale.
- This approach aims to provide a more comprehensive view of how socioeconomic factors influence postoperative outcomes in TSA patients on a national scale.

METHODS

- Using Medicare fee-for-service claims for 2016 to 2021, 10th revision International Classification of Diseases (ICD-10) procedure codes for aTSA and rTSA were indexed to find patients >65 years old presenting for elective shoulder arthroplasty with inpatient admission. Inclusion criteria included continuous enrollment in Part A+B (without Part C) for 12 months preoperatively and postoperatively, and a diagnosis of osteoarthritis, rotator cuff arthropathy or tear, and shoulder instability.
- The Social Deprivation Index (SDI), which quantifies socioeconomic status based on several county-level factors such as poverty, education, and employment, was binned into three groups (low 20%, middle 60%, top 20%). Patients who were dual eligible for Medicare and Medicaid benefits were also identified.
- Postoperative outcomes were evaluated through extended length of stay (LOS), discharge to institutional post-acute care (PAC), 30 and 90 day hospital return, medical complications within 30 days, and postoperative complications within 1 year.
- 30 day medical complications analyzed include pneumonia, myocardial infarction, cardiovascular incident, sepsis/septic shock, deep vein thrombosis, pulmonary embolism, hematoma, urinary tract infection, and pneumothorax.

RESULTS

- In total, 162,100 patients, 42.64% male and 57.36% female, were included in this study (Table 1).
- 30.63% of patients underwent aTSA and 69.37% rTSA. 5.09% of patients were eligible for Medicaid benefits (Table 1).
- Compared to those in the most deprived group per county-level SDI, patients in the least deprived group had lower odds of an extended length of stay (OR: 0.88, P= 0.019), 30-day hospital return (OR: 0.94, P= 0.036) and 90-day hospital return (OR: 0.93, P= 0.004), and developing 30-day medical complications (OR: 0.83, P= 0.002) (Table 2).
- Compared to those with moderate county-level social deprivation, patients in the most deprived group were more likely to develop 30-day medical complications (OR: 1.14, P= 0.003), and patients in the least deprived group were less likely to experience a 30-day or 90-day hospital return (OR: 0.95, P=0.046; OR: 0.95, P=0.020) (Table 2).
- Dual eligibility for Medicaid and Medicare benefits was associated with higher likelihood of an extended hospital length of stay (OR: 1.87, P<.0001), 5 day PAC discharge (OR: 2.62, P<.0001), 30-day and 90-day hospital return (OR: 1.51, P<.0001 and OR: 1.59, P<.0001, respectively), 30-day medical complications (OR: 1.34, P<.0001), and postoperative complications within 1 year (OR: 1.38, P<.0001) (Table 2).

Table 1. Patient Demographics

	Overall, N=162100	
	N	%
Age		
65-74	89159	55.00
≥75	72941	45.00
Male	69125	42.64
Female	92975	57.36
aTSA	49651	30.63
rTSA	112449	69.37
SDI Tertile		
Low 20th Percentile	32421	20
Middle 60th Percentile	98401	60.7
High 20th Percentile	31278	19.3
Dual Eligibility For Medicaid		
No	153851	94.91
Yes	8249	5.09

Table 2. Multivariable associations between county-level social deprivation (low 20%, middle 60%, top 20%) and dual eligibility and postoperative outcomes

		Deprivation Level			Dual Eligibility for Medicaid Yes vs No
		Low vs Moderate	High vs Moderate	Low vs High	
Extended LOS	Odds Ratio (95% CI)	0.95 (0.87-1.03)	1.08 (0.99-1.17)	0.88 (0.79-0.98)	1.87 (1.70-2.06)
	P-Value	0.211	0.09	0.019	<.0001
5 Day PAC Discharge	Odds Ratio (95% CI)	1.01 (0.95-1.07)	0.98 (0.91-1.04)	1.03 (0.96-1.12)	2.62 (2.44-2.81)
	P-Value	0.803	0.456	0.419	<.0001
30 Day Hospital Return	Odds Ratio (95% CI)	0.95 (0.91-1.0)	1.02 (0.97-1.07)	0.94 (0.88-1.0)	1.50 (1.40-1.61)
	P-Value	0.046	0.506	0.036	<.0001
90 Day Hospital Return	Odds Ratio (95% CI)	0.96 (0.92-0.99)	1.03 (0.99-1.07)	0.93 (0.89-0.98)	1.60 (1.51-1.68)
	P-Value	0.02	0.177	0.004	<.0001
30 Day Complications	Odds Ratio (95% CI)	0.95 (0.87-1.04)	1.14 (1.05-1.24)	0.84 (0.75-0.94)	1.34 (1.19-1.52)
	P-Value	0.311	0.003	0.002	<.0001
1 Year Complications	Odds Ratio (95% CI)	0.99 (0.94-1.05)	1.04 (0.99-1.1)	0.95 (0.89-1.02)	1.38 (1.28-1.49)
	P-Value	0.767	0.106	0.133	<.0001

METHODS CONTINUED

- 1-year complications included postoperative infection, non-infectious wound complication, wound dehiscence, humeral fracture, fracture of scapula, fracture of glenoid cavity, nerve injury, mechanical complication, prosthetic complication, and instability/dislocation.
- Mixed-effect generalized linear models modeled adjusted associations between SDI categories and outcomes; adjusted odds ratios (ORs) and 95% confidence intervals (CIs) are reported. The same models were repeated using dual eligibility status as the primary exposure.

Discussion

- Our findings suggest that increasing levels of county-level social deprivation and dual eligibility for Medicaid are associated with poorer outcomes in older adults undergoing TSA.
- Increased associations between dual eligibility versus county-level deprivation and adverse postoperative outcomes highlights the importance of considering patient-level indicators of social deprivation.
- Future research should aim to explore these patient-level factors on a more granular level.
- With recent Medicare approval, there is a growing trend toward same-day discharge for TSA procedures. Prolonged hospital stays due to social deprivation highlight the increased need for surgeons to place greater emphasis on discharge planning and perioperative care coordination for at-risk patients.

CLINICAL RELEVANCE

- The study underscores the importance of incorporating social determinants of health into surgical care planning for older adults undergoing shoulder arthroplasty, in order to address disparities and improve postoperative outcomes across diverse socioeconomic groups.



“Increased social deprivation and dual Medicaid eligibility are linked to poorer postoperative outcomes in older adults undergoing shoulder arthroplasty, highlighting the importance of addressing social determinants in surgical care.”

SOCIAL DEPRIVATION AND DUAL ELIGIBILITY LEAD TO POORER POSTOPERATIVE OUTCOMES IN OLDER ADULTS UNDERGOING SHOULDER ARTHROPLASTY

Kareem S. Mohamed; Christoph A. Schroen; Grace Van Hyfte; Brocha Z. Stern PHD; Eric D. Haunschild MD; William A. Ranson MD; Paul J. Cagle MD

BACKGROUND: There has been an increasing incidence of anatomic total shoulder arthroplasty (aTSA) and reverse TSA (rTSA) in the older adult population, reflecting its growing role in addressing shoulder pathologies. While several studies have explored outcomes and complications associated with these procedures within the Medicare population, there remains a notable gap regarding the influence of social deprivation. Our study aims to address these limitations by using an area-level indicator, the social deprivation index, and a person-level indicator, dual eligibility for Medicare and Medicaid benefits, to examine how social deprivation impacts TSA outcomes on a national scale. This approach aims to provide a more comprehensive view of how socioeconomic factors influence postoperative outcomes in TSA patients on a national scale.

METHODS: Using Medicare fee-for-service claims for 2016 to 2021, 10th revision International Classification of Diseases (ICD-10) procedure codes for aTSA and rTSA were indexed to find patients >65 years old presenting for elective shoulder arthroplasty with inpatient admission. Inclusion criteria included continuous enrollment in Part A+B (without Part C) for 12 months preoperatively and postoperatively, and a diagnosis of osteoarthritis, rotator cuff arthropathy or tear, and shoulder instability. The Social Deprivation Index (SDI), which quantifies socio-economic status based on several county-level factors such as poverty, education, and employment, was binned into three groups (low 20%, middle 60%, top 20%). Patients who were dual eligible for Medicare and Medicaid benefits were also identified. Postoperative outcomes were evaluated through extended length of stay (LOS), discharge to institutional post-acute care (PAC), 30 and 90 day hospital return, medical complications within 30 days, and postoperative complications within 1 year. 30 day medical complications analyzed include pneumonia, myocardial infarction, cardiovascular incident, sepsis/septic shock, deep vein thrombosis, pulmonary embolism, hematoma, urinary tract infection, and pneumothorax. 1-year complications included postoperative infection, non-infectious wound complication, wound dehiscence, humeral fracture, fracture of scapula, fracture of glenoid cavity, nerve injury, mechanical complication, prosthetic complication, and instability/dislocation. Mixed-effect generalized linear models modeled adjusted associations between SDI categories and outcomes; adjusted odds ratios (ORs) and 95% confidence intervals (CIs) are reported. The same models were repeated using dual eligibility status as the primary exposure.

RESULTS: In total, 162,100 patients, 42.64% male and 57.36% female, were included in this study. 30.63% of patients underwent aTSA and 69.37% rTSA. 5.09% of patients were eligible for Medicaid benefits. Compared to those in the most deprived group per county-level SDI, patients in the least deprived group had lower odds of an extended length of stay (OR: 0.88, P= 0.019), 30-day hospital return (OR: 0.94, P= 0.036) and 90-day hospital return (OR: 0.93, P= 0.004), and developing 30-day medical complications (OR: 0.83, P= 0.002). Compared to those with moderate county-level social deprivation, patients in the most deprived group were more likely to develop 30-day medical complications (OR: 1.14, P= 0.003), and patients in the least deprived group were less likely to experience a 30-day or 90-day hospital return (OR: 0.95, P=0.046; OR: 0.95, P=0.020). Dual eligibility for Medicaid and Medicare benefits was associated with higher likelihood of an extended hospital length of stay (OR: 1.87, P<.0001), 5 day PAC discharge (OR: 2.62, P<.0001), 30-day and 90-day hospital return (OR: 1.51, P<.0001 and OR: 1.59, P<.0001, respectively), 30-day medical complications (OR: 1.34, P<.0001), and postoperative complications within 1 year (OR: 1.38, P<.0001).

CONCLUSION: The study underscores the importance of incorporating social determinants of health into surgical care planning for older adults undergoing shoulder arthroplasty, in order to address disparities and improve postoperative outcomes across diverse socioeconomic groups. Our findings suggest that increasing levels of county-level social deprivation and dual eligibility for Medicaid are associated with poorer outcomes in older adults undergoing TSA. Increased associations between dual eligibility versus county-level deprivation and adverse postoperative outcomes highlights the importance of considering patient-level indicators of social deprivation. Future research should aim to explore these patient-level factors on a more granular level.

SYSTEMIC RISK FACTORS FOR INFECTIOUS KERATITIS

Arvind Sommi and Sumayya Ahmad, MD

Systemic Risk Factors for Infectious Keratitis

Arvind Sommi, BS¹, Sumayya Ahmad, MD¹

¹Icahn School of Medicine at Mount Sinai, New York, NY



BACKGROUND

- There are a variety of general risk factors for infectious keratitis such as contact lens wear and ocular trauma. Additionally, some studies have shown a connection between cars in the household, segregation, malnutrition, and socioeconomic status with the risk of developing infectious keratitis.
- Notably, the elderly represent a distinct clinical group within the realm of microbial keratitis, exhibiting unique risk profiles including worse visual outcomes, delayed corneal healing, increased complications, and a generally poorer prognosis compared to younger patients.

METHODS

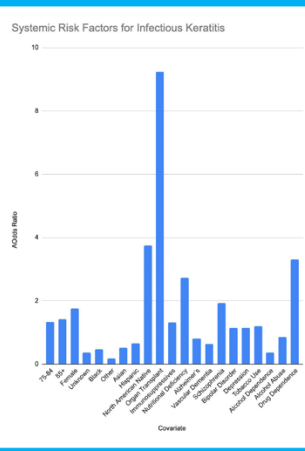
- This study analyzed a random 5% sample of national Medicare beneficiaries from 2011-2015 and included inpatient, emergency, and outpatient claims for those aged 65+ with infectious keratitis (n = 2,688,114).
- A multivariable logistic regression model assessed the outcome of infectious keratitis, considering factors such as age cohort, sex, race, and systemic risk factors, such as organ transplant and nutritional deficiency, as exposure variables.

Older age, female gender, Native American race, organ transplants, nutritional deficiency, and drug dependence were all associated with increased odds of developing infectious keratitis.

Association between systemic risk factors and infectious keratitis

Covariate	Odds Ratio	95% CI
Age		
65-74	Reference	
75-84	1.34**	1.11-1.61
85+	1.41**	1.13-1.75
Gender		
Male	Reference	
Female	1.76***	1.48-2.11
Race/Ethnicity		
White	Reference	
Unknown	0.96	0.06-1.10
Black	0.47***	0.31-0.68
Other	0.17*	0.03-0.53
Asian	0.52	0.24-0.98
Hispanic	0.65	0.33-1.15
North American Native	3.74***	1.79-9.80
Diagnoses		
Organ Transplant	0.24***	0.07-0.84
Immunosuppressives	1.31	0.07-2.22
Nutritional Deficiency	2.72***	2.29-3.21
Alzheimer's	0.80	0.49-1.24
Vascular Dementia	0.64	0.22-1.40
Other Persistent Mental Disorders	0.46*	0.24-0.81
Schizophrenia	1.92	0.47-7.15
Bipolar Disorder	1.15	0.51-2.22
Depression	1.15	0.78-1.63
Tobacco Use	1.20	0.41-3.09
Alcohol Dependence	0.36	0.02-1.67
Alcohol Abuse	0.86	0.21-2.28
Drug Dependence	3.31***	1.79-5.56
Headless	0.60*	0.05-6.00
HIV/AIDS	0.00	0.00-0.00
Laceration Repair	37.11***	5.80-131.23

*Adjusted for all listed covariates. *p < 0.05. **p < 0.01. ***p < 0.001



CONCLUSIONS

- These findings are significant for clinical practice and public health, as they provide insight into vulnerable populations and can inform personalized treatment strategies, resource allocation, and future research to reduce the incidence of infectious keratitis in high-risk groups, such as older populations.

Demographic Details of Patients

Characteristic	N=2,688,114
Male, n (%)	1,192,093 (44.3%)
Age, mean (SD)	75.5 (8.3)
Race, n (%)	
Unknown	31,530 (1.2%)
White	2,232,439 (83%)
Black	234,670 (8.7%)
Other	52,609 (2.0%)
Asian	62,856 (2.3%)
Hispanic	63,910 (2.4%)
North American Native	10,100 (0.4%)
Diagnoses, n (%)	
Organ Transplant	14,269 (0.53%)
Immunosuppressives	698 (0.03%)
Nutritional Deficiency	454,321 (16.90%)
Alzheimer's	97,087 (3.61%)
Vascular Dementia	29,924 (1.11%)
Other Persistent Mental Disorders	83,519 (3.11%)
Schizophrenia	6,986 (0.26%)
Bipolar Disorder	22,187 (0.83%)
Depression	87,848 (3.27%)
Tobacco Use	86,113 (3.20%)
Alcohol Dependence	10,376 (0.39%)
Alcohol Abuse	100,359 (3.75%)
Drug Dependence	13,223 (0.49%)
Headless	278 (0.01%)
HIV/AIDS	2,388 (0.09%)
Laceration Repair	62 (0.002%)



“Older age, female sex, Native American background, organ transplants, nutritional deficiency, and drug dependence increase the risk of infectious keratitis, while Black individuals and those with mental health conditions have lower odds, emphasizing the need for targeted prevention and treatment.”

SYSTEMIC RISK FACTORS FOR INFECTIOUS KERATITIS

Arvind Sommi and Sumayya Ahmad, MD

OBJECTIVE: To evaluate the extent to which systemic risk factors influence rates of infectious keratitis.

DESIGN: Retrospective cohort study

METHODS: This study analyzed a random 5% sample of national Medicare beneficiaries from 2011-2015 and included inpatient, emergency, and outpatient claims for those aged 65+ with infectious keratitis (n= 2,688,114). Data were retrieved from the Denominator and Physician Supplier Part B file from the Center for Medicare and Medicaid Services. A multivariable logistic regression model assessed the outcome of infectious keratitis, considering factors such as age cohort, sex, race, and systemic risk factors, such as organ transplant and nutritional deficiency, as exposure variables. Analyses were performed using R studio, with significance set at p-values ≤ 0.05 . The main outcome was the association between demographic characteristics (e.g. age, sex, race/ethnicity) and the presence of systemic risk factors on the incidence of infectious keratitis.

RESULTS: Compared to 65-74 year old patients, those aged 75-84 [Odds Ratio (OR) 1.34], [95% Confidence Interval (CI)=1.11-1.61] and 85+ (OR 1.41, 95% CI=1.13-1.75) had increased odds of developing infectious keratitis. Compared to Males, Females had an increased risk of infectious keratitis (OR 1.76, 95% CI=1.48-2.11). Compared to White patients, Black patients had significantly lower odds of infectious keratitis (OR 0.47, 95% CI=0.31-0.68) while Native American patients had higher odds (OR 3.74, 95% CI=1.79-9.80). Patients with organ transplants (OR 9.24, 95% CI=6.37-12.94), nutritional deficiency (OR 2.72, 95% CI=2.29-3.21), and drug dependence (OR 3.31, 95% CI=1.79-5.56) had significantly higher odds of infectious keratitis. Inversely, those with persistent mental disorders had lower odds of infectious keratitis (OR 0.46, 95% CI=0.24-0.81).

CONCLUSIONS: Older age, female gender, Native American race, organ transplants, nutritional deficiency, and drug dependence were all associated with increased odds of developing infectious keratitis. Black patients and those with persistent mental disorders had lower odds of infectious keratitis. These findings are significant for clinical practice and public health, as they provide insight into vulnerable populations and can inform personalized treatment strategies, resource allocation, and future research to reduce the incidence of infectious keratitis in high-risk groups, such as older populations.

IMPACT OF SPINAL FUSION ON GLOBAL SAGITTAL ALIGNMENT: THE ROLE OF FUSION REGION IN PREDICTING POSTOPERATIVE OUTCOMES

Alexander Yu, BS, Ryan Hoang, BS, Mark Kurapatti, BS, Kareem Mohamed, BS, Yash Lahoti, MSE, Akiro H. Duey, BS, Timothy Hoang, BS, Albert Li, BS, Justin Tiao, BS, Samuel K. Cho, MD

Impact of Spinal Fusion on Global Sagittal Alignment: The Role of Fusion Region in Predicting Postoperative Outcomes

Alexander Yu, BS, Ryan Hoang, BS, Mark Kurapatti, BS, Kareem Mohamed, BS, Yash Lahoti, MSE, Akiro Duey, BS, Timothy Hoang, BS, Albert Li, BS, Justin Tiao, BS, Samuel K. Cho, MD



BACKGROUND

Advances in Spine Imaging:
The introduction of biplanar X-ray systems now allows for full-body spine imaging, leading to the development of global sagittal alignment parameters

Global Sagittal Alignment:
Global sagittal alignment parameters have shown a stronger correlation with patient outcomes than traditional methods. These parameters are effective predictors of postoperative outcomes in deformity surgeries and may also prove useful in spinal fusion surgery

Spinal Fusion Surgery and Sagittal Alignment:
Spinal fusion surgery, the most common spinal procedure in elderly patients, has seen significant growth. However, the impact of these surgeries on global sagittal alignment remains insufficiently defined

Study Objective:
This study aims to evaluate how fusion status, the number of fused spinal levels, and the region of the spine fused influence global sagittal alignment in the elderly population

METHODS

Study Design:
A retrospective chart review was conducted on 1,128 patients at a single institution, collecting data on age, sex, prior spine surgery, adult spinal deformity, and spine surgery outcomes.

Radiographic Parameters:
Global spinal alignment measurements:
 • Cranial sagittal vertical axis to the sacrum (CrSVA-S)
 • Cranial sagittal vertical axis to the hip (CrSVA-H)
 • Cranial sagittal vertical axis to the knee (CrSVA-K)
 • Cranial sagittal vertical axis to the ankle (CrSVA-A)
 • Cranium-hip-sacrum angle (CrHS)
 • Cranium-knee-sacrum angle (CrKS)
 • Cranium-ankle-sacrum angle (CrAS)

Analysis:
Multivariable logistic regression models were developed to identify predictors for all radiographic parameters related to global spinal alignment.

Population:
395 patients with normal spine pathology and 167 with spinal fusion.

RESULTS

Table 1. Demographic characteristics and radiographic parameters of fusion patients

Sample Characteristics	Fusion Patients (n=167)	Healthy Patients (n=395)	P-value (2-tailed)
Mean Age (Years)	60.60 ± 13.52	49.0 ± 11.3	<0.001
Age Category			
<50	8 (4.8%)	57 (14.3%)	
50-59	13 (7.8%)	81 (20.5%)	
60-69	12 (7.2%)	44 (11.2%)	
70-79	24 (14.4%)	65 (16.5%)	
80-89	56 (33.5%)	72 (18.2%)	
>90	46 (27.5%)	43 (10.9%)	
>80	8 (4.8%)	11 (2.8%)	
Sex			<0.001
Male	48 (28.7%)	191 (48.1%)	
Female	119 (71.3%)	204 (51.9%)	

Mean Radiographic Parameters	Fusion Patients (n=167)	Healthy Patients (n=395)	P-value (2-tailed)
CrSVA-S (cm)	4.29 ± 4.21	3.1 ± 3.5	<0.001
CrSVA-H (cm)	0.26 ± 3.93	-1.3 ± 3.4	<0.001
CrSVA-K (cm)	1.81 ± 3.28	1.3 ± 3.4	0.376
CrSVA-A (cm)	3.38 ± 3.63	2.9 ± 3.2	0.116
CrHS (°)	23.26 ± 11.78	20.6 ± 8.0	<0.001
CrKS (°)	3.81 ± 4.46	2.4 ± 3.2	<0.001
CrAS (°)	1.27 ± 2.75	0.8 ± 2.3	0.015

Table 3. Multivariable Linear Regression Models for Radiographic Parameters among Fusion and Healthy

Parameter	Age	Beta Coefficient (95% CI)	Variable P-value
CrSVA-S (cm)	Age	0.063 (0.045, 0.080)	<0.001
	Male Sex	1.350 (0.748, 1.952)	<0.001
	Fusion	0.707 (0.026, 1.388)	0.042
CrSVA-H (cm)	Age	0.028 (0.010, 0.045)	0.002
	Male Sex	1.510 (0.919, 2.101)	<0.001
	Fusion	1.302 (0.633, 1.971)	<0.001
CrSVA-K (cm)	Age	-0.036 (-0.053, -0.020)	<0.001
	Male Sex	0.598 (0.035, 1.162)	0.038
	Fusion	0.262 (-0.375, 0.900)	0.420
CrSVA-A (cm)	Age	-0.099 (-0.025, 0.087)	0.278
	Male Sex	1.653 (0.997, 2.309)	<0.001
	Fusion	0.911 (0.283, 1.539)	0.005
CrHS (°)	Age	0.236 (0.194, 0.277)	<0.001
	Male Sex	0.422 (-1.010, 1.853)	0.563
	Fusion	0.044 (-1.575, 1.663)	0.957
CrKS (°)	Age	0.098 (0.082, 0.114)	<0.001
	Male Sex	0.937 (0.388, 1.487)	<0.001
	Fusion	0.505 (-0.116, 1.127)	0.111
CrAS (°)	Age	0.040 (0.029, 0.051)	<0.001
	Male Sex	0.010 (-0.346, 0.429)	0.835
	Fusion	-0.019 (-0.439, 0.401)	0.930

Table 2. Multivariable Linear Regression Models for Radiographic Parameters among Fusion Patients

Parameter	Age	Beta Coefficient (95% CI)	Variable P-value
CrSVA-S (cm)	Age	0.078 (0.038, 0.118)	<0.001
	Male Sex	2.241 (0.869, 3.614)	0.002
	Levels Fused	0.287 (0.093, 0.480)	0.004
	Cervical	-0.238 (-2.289, 1.813)	0.819
	Thoracic	-2.145 (-3.995, -0.294)	0.023
	Lumbar	-0.061 (-2.128, 2.005)	0.953
CrSVA-H (cm)	Age	0.019 (-0.019, 0.057)	0.314
	Male Sex	2.698 (1.386, 4.009)	<0.001
	Levels Fused	0.154 (-0.031, 0.339)	0.103
	Cervical	-0.117 (-2.076, 1.843)	0.907
	Thoracic	-1.533 (-3.300, 0.235)	0.089
	Lumbar	-0.775 (-2.750, 1.199)	0.439
CrSVA-K (cm)	Age	-0.057 (-0.088, -0.025)	<0.001
	Male Sex	1.368 (0.270, 2.467)	0.015
	Levels Fused	-0.114 (-0.269, 0.041)	0.147
	Cervical	1.024 (-0.617, 2.666)	0.220
	Thoracic	0.441 (-1.040, 1.922)	0.557
	Lumbar	0.299 (-1.355, 1.953)	0.722
CrSVA-A (cm)	Age	-0.10 (-0.045, 0.025)	0.566
	Male Sex	2.845 (1.636, 4.054)	<0.001
	Levels Fused	-0.031 (-0.201, 0.140)	0.722
	Cervical	-0.154 (-1.652, 1.960)	0.866
	Thoracic	0.151 (-1.479, 1.780)	0.855
	Lumbar	-0.053 (-1.873, 1.767)	0.954
CrHS (°)	Age	0.378 (0.278, 0.479)	<0.001
	Male Sex	0.092 (-3.375, 3.558)	0.958
	Levels Fused	0.776 (0.287, 1.266)	0.002
	Cervical	-0.661 (-5.840, 4.517)	0.801
	Thoracic	-4.002 (-8.674, 0.671)	0.093
	Lumbar	3.116 (-2.103, 8.334)	0.240
CrKS (°)	Age	0.130 (0.091, 0.169)	<0.001
	Male Sex	1.668 (-0.276, 2.412)	0.119
	Levels Fused	0.420 (0.210, 0.609)	<0.001
	Cervical	-1.334 (-3.343, 0.674)	0.191
	Thoracic	-3.174 (-4.986, -1.362)	<0.001
	Lumbar	-0.538 (-2.562, 1.486)	0.600
CrAS (°)	Age	0.052 (0.027, 0.078)	<0.001
	Male Sex	-0.602 (-1.491, 0.288)	0.183
	Levels Fused	0.209 (0.083, 0.334)	0.001
	Cervical	0.072 (-1.256, 1.401)	0.915
	Thoracic	-1.765 (-2.964, -0.566)	0.004
	Lumbar	-0.477 (-1.816, 0.862)	0.483

DISCUSSION

Impact of Spinal Fusion on Sagittal Alignment
 • Spinal fusion significantly alters global sagittal alignment, with increasing fusion levels resulting in notable changes in CrSVA and related parameters.

• These findings support previous research showing substantial sagittal alignment shifts due to spinal fusion, influencing postoperative outcomes.

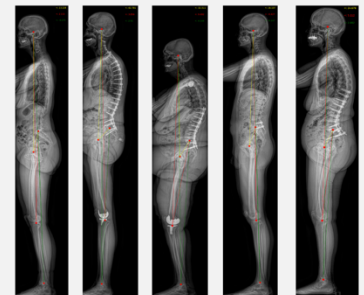
Cranial Sagittal Vertical Alignment (CrSVA) Parameters
 • Incorporating CrSVA offers a comprehensive assessment by including cranial alignment in the analysis.

Influence of Age and Sex
 • Age and sex significantly affect alignment changes after spinal fusion.

• Older patients and males exhibit greater deviations in CrSVA, likely due to age-related degeneration and anatomical differences.

Role of Fusion Region
 • Thoracic fusion is associated with decreases in CrSVA, potentially counteracting alignment shifts seen with more extensive fusions.

• Cervical and lumbar fusions have a less pronounced effect on CrSVA.



“Spinal fusion alters global sagittal alignment, with fused levels, thoracic fusion, age, and sex influencing changes, highlighting the need for careful preoperative planning in elderly patients.”

IMPACT OF SPINAL FUSION ON GLOBAL SAGITTAL ALIGNMENT: THE ROLE OF FUSION REGION IN PREDICTING POSTOPERATIVE OUTCOMES

Alexander Yu, BS, Ryan Hoang, BS, Mark Kurapatti, BS, Kareem Mohamed, BS, Yash Lahoti, MSE, Akiro H. Duey, BS, Timothy Hoang, BS, Albert Li, BS, Justin Tiao, BS, Samuel K. Cho, MD

INTRODUCTION: As the population ages, the number of elderly patients needing surgical intervention for spinal issues is expected to increase. The recent introduction of biplanar X-ray systems, which enable full-body spine imaging, has led to the development of global sagittal alignment parameters. Previous studies have introduced cranial sagittal vertical alignment (CrSVA) parameters, showing a stronger correlation with patient outcomes than traditional methods. These parameters have proven to be effective predictors of postoperative outcomes following deformity surgery and may also be valuable for assessing outcomes in spinal fusion surgery—the most common spinal procedure in elderly patients. However, the impact of spinal fusion surgery on global sagittal alignment remains insufficiently defined. With the rising prevalence of spinal fusion, this study aims to evaluate how fusion status, the number of spinal levels fused, and the region of the spine fused affect global sagittal alignment in elderly patients.

METHODS: A retrospective chart review was performed on 1128 patients at a single institution to collect data including age, sex, prior spine surgery, adult spinal deformity, and spine surgery outcomes. Radiographic parameters of global spinal alignment will be measured from biplanar full-body X-rays, including cranial sagittal vertical axis to the sacrum (CrSVA-S), to the hip (CrSVA-H), to the knee (CrSVA-K), to the ankle (CrSVA-A), cranium-hip-sacrum angle (CrHS), cranium-knee-sacrum (CrKS), and cranium-ankle-sacrum (CrAS). These parameters will be collected retrospectively from patients undergoing EOS biplanar X-ray imaging from November 2022 to May 2024. Multivariable logistic regression models were developed to identify predictors of all radiographic parameters related to global spine alignment.

RESULTS: The study included a total of 395 patients with normal spine pathology and 167 patients who underwent spinal fusion. The normal pathology group had a mean age of 49.0 years, with 48.1% being men, while the fusion group was significantly older, with a mean age of 60.6 years, and consisted of 28.7% men. Radiographic parameters significantly differed between the fusion and normal cohorts. Specifically, the fusion group had significantly higher CrSVA-S (4.29 cm vs. 3.1 cm), CrSVA-H (0.26 cm vs. -1.1 cm), CrHS (23.26° vs. 20.6°), CrKS (3.81° vs. 2.4°), and CrAS (1.27° vs. 0.8°) compared to the normal group (Table 1). In the spinal fusion cohort, age was linked to significant changes in CrSVA-S, CrSVA-K, CrHS, CrKS, and CrAS. Male sex was associated with significant increases in CrSVA-S, CrSVA-H, CrSVA-K, and CrSVA-A. The number of levels fused correlated with significant increases in CrSVA-S, CrHS, CrKS, and CrAS. Thoracic fusion significantly decreased CrSVA-S, CrKS, and CrAS, while cervical and lumbar fusion showed no association with the radiographic parameters. (Table 2). When considering the entire study population, including both fusion and normal pathology groups, spinal fusion was independently associated with significant increases in CrSVA-S, CrSVA-H, and CrSVA-A, regardless of age and sex (Table 3).

DISCUSSION: This study demonstrates that spinal fusion significantly impacts global sagittal alignment, particularly as the number of fused spinal levels increases, leading to notable changes in CrSVA and associated parameters. These findings align with previous research indicating that spinal fusion can cause substantial alterations in sagittal alignment, which may subsequently influence postoperative outcomes. The inclusion of CrSVA parameters provides a more comprehensive assessment by incorporating cranial alignment into the analysis. Age and sex significantly influenced alignment changes following spinal fusion, with older patients and males exhibiting greater deviations in CrSVA parameters. These results likely reflect age-related spinal degeneration and anatomical differences between sexes, underscoring the importance of considering these factors in preoperative planning. The region of the spinal fusion plays a crucial role in post-operative sagittal alignment. Thoracic fusion was associated with decreases in CrSVA values, potentially counteracting the alignment shifts observed with more extensive fusions. In contrast, cervical and lumbar fusions appeared to have a less pronounced effect on these parameters.

EVALUATING ORTHOPEDIC INJURY RISK IN ELDERLY POPULATIONS THROUGH SLEEP PATTERNS: INSIGHTS FROM WEARABLE DATA IN THE ALL OF US RESEARCH PROGRAM

Jennifer Yu BS and Brett L. Hayden MD

Evaluating Orthopedic Injury Risk in Elderly Populations Through Sleep Patterns: Insights from Wearable Data in the All of Us Research Program

Jennifer Yu BS, Brett L. Hayden MD

BACKGROUND

- Sleep health has emerged as a critical factor in understanding mortality and disease, with a growing body of evidence linking poor sleep quality to adverse health outcomes.
- Despite this, many epidemiological studies continue to rely heavily on self-reported sleep data, which can be subject to bias and inaccuracies.
- This issue is particularly pronounced in elderly populations, which have been historically underrepresented in epidemiological research.
- Consequently, the associations between sleep patterns and disease within these populations remain poorly understood.
- To address this gap, our study utilizes long-term, objectively monitored sleep data to explore how sleep affects the orthopedic health of elderly patients, offering new insights into the role of sleep in disease risk within this group.

METHODS

- The study utilized registered tier data from the All of Us Research Program, which includes consenting adults (≥18 years) from across the United States.
- 4,318 participants aged 60+ were included in the study. Demographic information, including age, sex, and ethnicity, was derived from survey data. Participants with inconsistent sleep data, defined as less than 4 hours of sleep for more than 30% of their monitored nights, were excluded.
- This dataset was analyzed using Phenome-wide association studies (PheWAS) through multiple logistic regression models. For each disease of interest, participants with any prior diagnosis of that disease before Fitbit monitoring were excluded. PheWAS analyses were adjusted for age and sex over the entire monitoring period. To account for the smaller dataset size and rare events, Firth's Logistic Regression Correction with inverse probability weighting was applied.

RESULTS

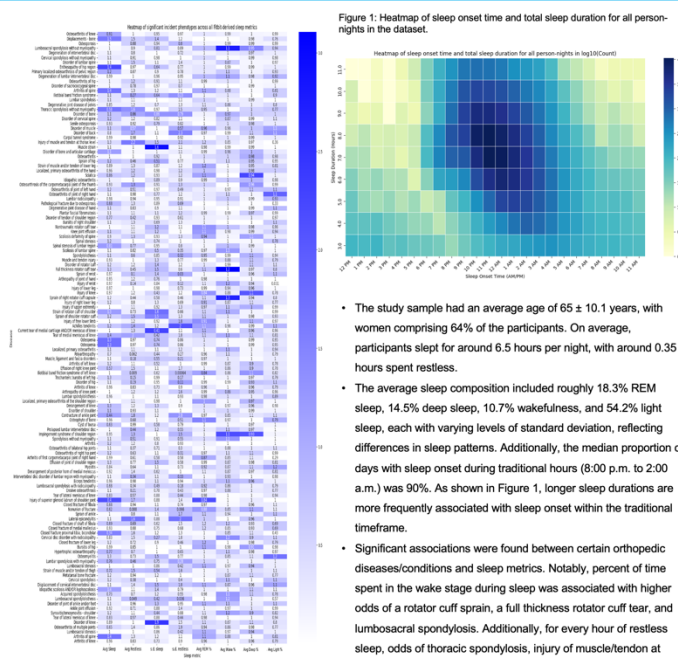
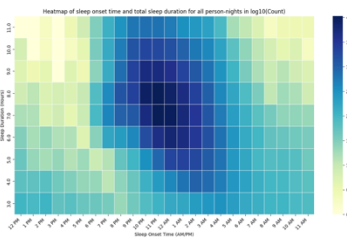


Figure 2: Heatmap of significant incident phenotypes across all Fitbit-derived sleep metrics.

Figure 1: Heatmap of sleep onset time and total sleep duration for all person-nights in the dataset.



- The study sample had an average age of 65 ± 10.1 years, with women comprising 64% of the participants. On average, participants slept for around 6.5 hours per night, with around 0.35 hours spent restless.
- The average sleep composition included roughly 18.3% REM sleep, 14.5% deep sleep, 10.7% wakefulness, and 54.2% light sleep, each with varying levels of standard deviation, reflecting differences in sleep patterns. Additionally, the median proportion of days with sleep onset during traditional hours (8:00 p.m. to 2:00 a.m.) was 90%. As shown in Figure 1, longer sleep durations are more frequently associated with sleep onset within the traditional timeframe.
- Significant associations were found between certain orthopedic diseases/conditions and sleep metrics. Notably, percent of time spent in the wake stage during sleep was associated with higher odds of a rotator cuff sprain, a full thickness rotator cuff tear, and lumbosacral spondylosis. Additionally, for every hour of restless sleep, odds of thoracic spondylosis, injury of muscle/tendon at thorax level and lateral epicondylitis were significantly increased as well.



DISCUSSION

- This study highlights the critical role of objectively monitored sleep data in understanding orthopedic disease/injury risks among elderly people, a historically underrepresented population in epidemiological studies.
- The findings reveal significant associations between poor sleep quality—such as increased restless sleep and irregular sleep patterns—and higher risks of certain orthopedic conditions and injuries.
- Future research with larger, more diverse samples is essential to confirm these findings and develop targeted interventions to improve sleep health and reduce disease risk in this group.

FUTURE WORK

- Future work involves building a more complex model to assess for various considerations, such as socioeconomic status, the presence of a home aid, and other sociodemographic considerations that may affect a person's health and care.
- Unsupervised machine learning can be utilized to categorize different groups of elderly adults into different strata of disease risk and thus help tailor better interventions for improving orthopedic health.
- Utilizing this data and data from a more controlled, prospective trial, we can expand on machine learning applications to provide a projection of disease risk based on sociodemographic variables to ensure preventative care.



“Objectively monitored sleep data links poor sleep quality, like restless sleep, to higher risks of orthopedic conditions in the elderly, highlighting the need for targeted interventions to improve sleep health and reduce disease risk.”

EVALUATING ORTHOPEDIC INJURY RISK IN ELDERLY POPULATIONS THROUGH SLEEP PATTERNS: INSIGHTS FROM WEARABLE DATA IN THE ALL OF US RESEARCH PROGRAM

Jennifer Yu BS and Brett L. Hayden MD

INTRODUCTION: Sleep health has emerged as a critical factor in understanding mortality and disease, with a growing body of evidence linking poor sleep quality to adverse health outcomes. Despite this, many epidemiological studies continue to rely heavily on self-reported sleep data, which can be subject to bias and inaccuracies. This issue is particularly pronounced in elderly populations, which have been historically underrepresented in epidemiological research. Consequently, the associations between sleep patterns and disease within these populations remain poorly understood. To address this gap, our study utilizes long-term, objectively monitored sleep data to explore how sleep affects the orthopedic health of elderly patients, offering new insights into the role of sleep in disease risk within this group.

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DISCUSSION/CONCLUSION: This study highlights the critical role of objectively monitored sleep data in understanding orthopedic disease/injury risks among elderly people, a historically underrepresented population in epidemiological studies. The findings reveal significant associations between poor sleep quality—such as increased restless sleep and irregular sleep patterns—and higher risks of certain orthopedic conditions and injuries. Future research with larger, more diverse samples is essential to confirm these findings and develop targeted interventions to improve sleep health and reduce disease risk in this group.

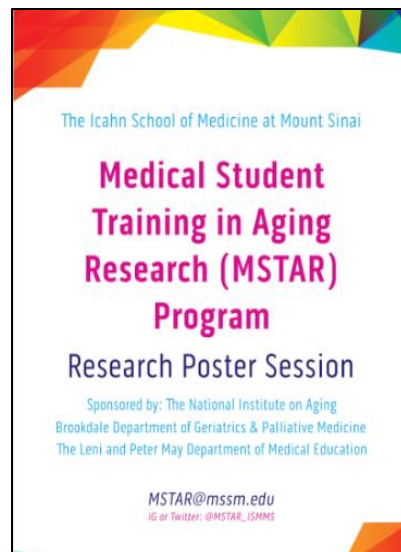
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2024 MSTAR Program RESEARCH FACULTY MENTORS

Sumayya Ahmad, MD
Abigail Baim-Lance, PhD
Paul Cagle, Jr, MD
Samuel Cho, MD
John Crary, PhD
Kavita Dharmarajan, MD
Celia Divino, MD
Nicholas Gulati, MD, PhD
Brett L. Hayden, MD
Zachary Hickman, MD
Nilsson Holguin, PhD
James Iatridis, PhD
Christopher Kellner, MD
Rebecca Rodin, MD
Raj Srivastava, MD
Maaïke Van Gerwen, MD PhD

2024 MSTAR Program Faculty

Melissa Aldridge, PhD, MBA
Claire Ankuda, MD MPH
Helen Fernandez, MD, MPH
Emily Franzosa, DrPH
Rosanne Leipzig, MD, PhD
Diane Meier, MD
R. Sean Morrison, MD
Albert Siu, MD, MSPH
Cardinale Smith, MD, PhD
Rainier P. Soriano, MD





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