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TITLE: Development and Validation of Predictive Models for Transition from Acute to Persistent Pain After Major Surgery

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The transition from acute to pathological persistent pain is complex and is dependent on multiple biological, psychological, and social-environmental factors that change across the surgical care continuum. Current approaches for predicting PPSP are primarily based on risk factors assessed at a single time point, most often - preoperatively. Moving beyond a one-time baseline assessment to a multifactorial and temporal measurement approach is a relatively unexplored research avenue that has a substantial potential. A temporal approach, accounting for multiple factors across the care continuum can afford opportunities for ascertaining the impact of time-varying patient and clinical events across the surgical care continuum. Our central hypothesis is that advanced machine learning models that account for individual biological, cognitive, and psychological factors across the surgical care continuum will allow personalized prediction of PPSP. In this context, pragmatic prediction models for precise PPSP prediction will allow appropriate resource allocation in mitigating PPSP and long-term disability in high-risk individuals. From a research standpoint, such models will allow the efficient testing of perioperative interventions or rehabilitation programs, by implementing appropriate risk stratification to improve assay sensitivity in future clinical trials. We have two specific aims:
Aim 1: Collect longitudinal prospective data for a comprehensive biological, psychological, cognitive, and psychophysical characterization of a surgical patient cohort.
Aim 2: Develop, validate, and test advanced machine learning models for predicting PPSP.

15. SUBJECT TERMS

Acute pain, persistent post-surgical pain, surgery, risk prediction, chronic pain, machine learning, prediction modeling

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1. Introduction

Persistent postsurgical pain (PPSP) is the most common long-term postoperative complication, affecting approximately one in eight patients undergoing surgery. PPSP substantially affects patients' functioning, quality of life, and ability to return to work or service. Associations between several individual or perioperative factors and increased risk of PPSP have been reported, but current methodological approaches are ill-equipped to predict an individual patient's risk. Our proposal will determine whether machine learning methods, applied to analyzing longitudinal multifactorial perioperative data, will result in robust prediction models, that will allow the identification of patients at risk for PPSP after major surgery. In this context, pragmatic prediction models for PPSP prediction will (a) allow appropriate resource allocation in mitigating PPSP and long-term disability in high-risk individuals, and (b) allow the efficient testing of perioperative interventions or rehabilitation programs, by implementing appropriate risk stratification in future clinical trials.

2. Keywords

Acute pain, persistent post-surgical pain, surgery, risk prediction, chronic pain, machine learning, prediction modeling

3. Accomplishments

What were the major goals of the project?

CY22 Goal – Prospective data collection and follow-up

- Obtaining all regulatory approvals, establishing recruitment and data collection framework, troubleshooting processes, initiating and maintaining recruitment and data collection.

CY23 Goals – Model training and feature engineering

CY24 Goal – Model validation and testing

CY25 Goal – Manuscript preparation

What was accomplished under these goals?

1. All preparations for enrollment and data collection completed, study underway
2. Study staff training is completed
3. Patient enrollment to the study ongoing, data collection under way. We have currently consented and enrolled 901 participants as of September 12, 2022, above the planned target. Our Q1 +Q2 target was 800 patients.
4. Follow-up data (3 months and 6 months postoperatively) are being collected.
5. We started developing pipelines for data synchronization (data collected to REDCap, EMAs, and data extracted from the electronic health record (Epic), and developing initial Machine Learning models

What opportunities for training and professional development has the project provided?

Nothing to report

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

1. Our recruitment is going according to the plan.
2. During the next reporting period, we will continue to enroll subjects prospectively, and collect perioperative and follow-up data.
3. We will continue collecting the 3 and 6-months outcomes data.
4. We expect to complete the pipelines for data synchronization (data collected to REDCap, EMAs, and data extracted from the electronic health record (Epic))

4. Impact

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?

Nothing to report

What was the impact on society beyond science and technology?

Nothing to report

5. Changes/Problems

Actual or anticipated problems or delays and actions or plans to resolve them:

Nothing to report

Changes that had a significant impact on expenditures

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. Products

Publications, conference papers, and presentations

Nothing to report

Journal publications

Nothing to report

Books or other non-periodical, one-time publications

Nothing to report

Other publications, conference papers and presentations

Nothing to report.

Website(s) or other Internet site(s)

Nothing to report

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other Products

Nothing to report

7. Participants & Other Collaborating Organizations

What individuals have worked on the project?

Simon Haroutounian, MSc. Pharm, PhD, Principal Investigator 1.44 calendar months. Dr. Haroutounian is responsible for the overall study design, and will provide general oversight and management of the project, ensuring timely progression to meet milestones.

Thomas Rodebaugh, **PhD.** Co-Investigator; 0.6 calendar months, Dr. Rodebaugh is responsible for incorporating EMA into the study protocol, and developing the platform for data collection, cleaning and harmonization, in preparation for modeling.

Chenyang Lu, PhD; Co-Investigator; 0.6 calendar months; Dr. Lou is responsible for development and validation of the advanced machine learning models for prediction clinical outcomes.

Denise Head, PhD; Co-Investigator; 0.36 calendar months, Dr. Head contributes to optimizing cognitive and psychological assessment in the proposed study, and will assist with cognitive and psychological data analysis and interpretation.

Thomas Kannampallil, PhD; Co-Investigator; 1.14 calendar months; Dr. Kannampallil contributes to study design, oversees electronic data collection, and contribute to data analysis and interpretations.

Liz Wilson, Research Coordinator; 2.4 calendar months; assists in patient recruitment, data collection, and maintaining the appropriate study documentation.

Alyssa Gonzales, Research Coordinator, no longer on study team as of 8/1/22. Assisted in patient recruitment and data collection.

Cristina Bowman, Research Coordinator; 6.0 calendar months; assists in patient recruitment, data collection, and maintaining the appropriate study documentation.

Bulenda Shayo; Research Coordinator; 12.0 calendar months; assists in patient recruitment, data collection, and maintaining the appropriate study documentation.

Preston Boyd; Student; 12 calendar months; Assists with study recruitment, consenting, blood processing, and remuneration.

Joel Hanns, Research Assistant 4 calendar months. Assists with study recruitment, consenting, blood processing, and remuneration.

Haley Bernstein; Research Assistant 1.0 calendar months. Assists with study recruitment, consenting, blood processing, and remuneration.

Melinda Xu, Student; 7.0 calendar months. Assists with study recruitment, consenting, blood processing, and remuneration.

Joel Brown, Research Nurse; 5.0 calendar months; Assists with study recruitment, consenting, blood processing, and remuneration.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Nothing to report

8. Special Reporting Requirements

Quad Report attached

9. Appendices

Nothing to report