Machine Learning-based Prediction of Unplanned Readmission due to Major Adverse Cardiovascular Events (MACE) among Hospitalized Patients with Blood Cancers

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BACKGROUND

- Cardiovascular diseases (CVD) and cancers are the two major causes of death worldwide.[1]
- Cancer patients have a higher risk of unplanned readmissions than non-cancer patients.[2]
- These unplanned readmissions are associated with worse mortality in cancer patients.[3]
- Survivors of blood cancers had significantly increased risks of developing all types of CVD[4]
- Blood cancer survivors may face an elevated risk of developing subsequent CVD after being exposed to cardiotoxic cancer therapies.[4]

OBJECTIVE

- Developing a machine learning (ML) model predicting 90-day unplanned readmission due to major adverse cardiovascular events (MACE) among hospitalized patients with blood cancers

METHODS

DATA SOURCE

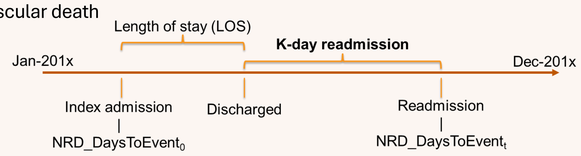
- The 2017-2019 Healthcare Cost and Utilization Project-Nationwide Readmission Database (HCUP)

POPULATION

- Patients hospitalized with a primary diagnosis of blood cancers, including (1) leukemia, (2) lymphoma, (3) myelodysplastic syndromes, (4) myeloproliferative disorder, (5) multiple myeloma:
- Aged 18 years or older and whose transfers and/or same-day stays that were not combined
- Patients whose index admission was discharged by November and who survived the index admission

OUTCOME

- An unplanned readmission due to MACE within 90 days after the index hospitalization
- **MACE:** acute myocardial infarction; acute coronary syndrome/ischemic heart disease; stroke and transient ischemic attack; heart failure; revascularization procedures; cardiovascular death



90-day readmission = if(NRD_DaysToEvent$_t$ - NRD_DaysToEvent$_0$ - LOS) ≤ 90

FEATURES

- **Demographic:** Age, sex, median household income level, primary payer, urban-rural, resident of the state in which patient received hospital care
- **Admission-Discharge:** Weekend index admission, month and quarter of index admission, elective/non-elective admission, length of stay
- **Clinical:** Clinical classifications software refined (CCSR) for diagnoses and procedures

MACHINE LEARNING ALGORITHM

- **Training set:** HCUP data from 2017 to 2018
- **Test set:** HCUP data in 2019
- **Algorithm:** Tree-based gradient boost framework (LightGBM)
- **Feature selection:** L1 penalty
- **Hyperparameter tuning:** Learning rate, number of leaves, minimum sum of instance weight (Hessian), frequency of subsample, subsample ratio of columns, L1 penalty, and the scale of positive and negative weight.
- The hyperparameters were first screened with random search and optimized using Bayesian search.
- **Imbalance classification:** Cost-sensitive learning
- **Cross-validation:** A 5-fold stratified cross-validation
- **Thresholding:** Youden's J statistic
- **Classification performance metrics:** Balance accuracy; F2 score; Area under the receiver operating curves (AUROC); Area under precision-recall curves (AUPRC)

RESULTS

Figure 1. Patient selection process

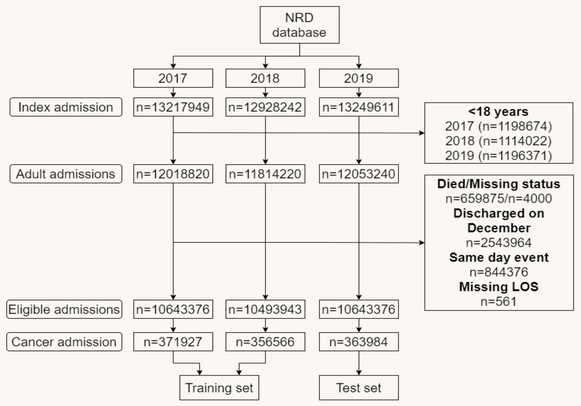
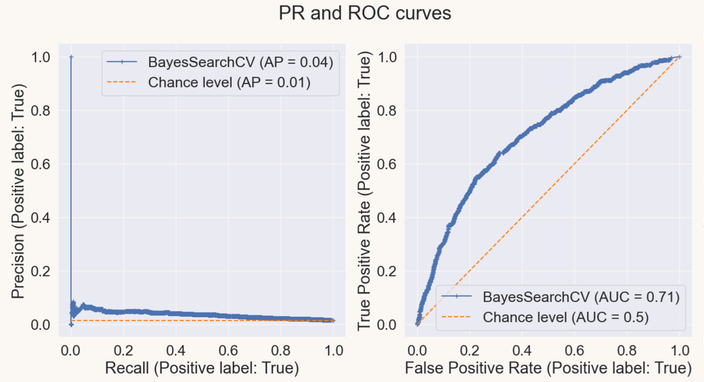


Table 1. Patient characteristics

Characteristics	MACE readmission (n=641)	Non-MACE readmission (n=49815)	Test set (n=26415)
Age years, mean (SD)	70.8 (13.5)	62.9 (16.2)	63.5 (16.1)
Female, n (%)	265 (49.6)	21648 (43.4)	11401 (43.2)
LOS, median (Q1-Q3)	7 (4-15)	9 (4-18)	9 (4-18)
Elective admission	74 (11.5)	11835 (23.8)	6056 (22.9)
Discharge quarter			
First (Jan-Mar)	264 (41.2)	17063 (34.3)	9142 (34.6)
Second (Apr-Jun)	159 (24.8)	13263 (26.6)	7096 (26.9)
Third (Jul-Sep)	155 (24.2)	11913 (23.9)	6172 (23.4)
Fourth (Oct-Nov)	63 (9.8)	7576 (15.2)	4005 (15.2)
Diseases of the circulatory system			
Hypertension with complications	221 (35.1)	8434 (16.9)	4981 (18.9)
Essential hypertension	225 (34.5)	18521 (37.2)	9723 (36.8)
Coronary atherosclerosis/other heart disease	200 (31.2)	6787 (13.6)	3725 (14.1)
Heart failure	185 (28.8)	4505 (9.0)	2707 (10.3)
Cardiac dysrhythmias	180 (28.0)	6887 (13.8)	3871 (14.7)
Procedure			
Bone marrow biopsy	263 (41.0)	18614 (37.4)	10152 (38.4)
Chemotherapy	164 (25.6)	17969 (36.1)	9010 (34.1)
Venous and arterial catheter placement	170 (26.5)	15910 (31.9)	8475 (32.1)
Transfusion of blood and blood products	248 (38.7)	14963 (30.0)	7501 (28.4)
Administration/transfusion of bone marrow, stem cells, pancreatic islet cells, and t-cells	39 (6.1)	8284 (16.6)	4180 (15.8)

Notes: top five common diagnoses (related to the circulatory system) and procedures were reported; results were reported as frequency (%) unless stated otherwise

Figure 2. AUPRC and AUROC



Classification performance
- Balanced accuracy: 0.657
- Recall: 0.563
- Precision: 0.033
- F2: 0.133

Optimum threshold: 0.021

SHAP feature importance (top 5)
- Age
- Heart failure
- Elective admission
- Coronary atherosclerosis/other heart disease
- Type 2 Diabetes

Figure 3. SHAP feature importance

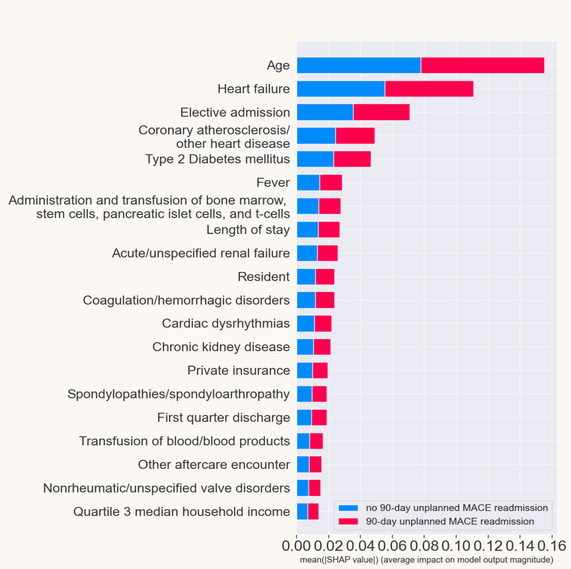
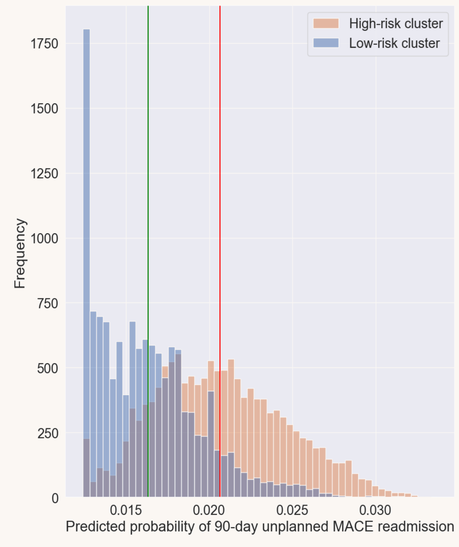


Figure 4. Predicted risk of two clusters



CONCLUSION

LIMITATIONS

- The small number of outcomes may affect the predictive performance and prevent us from developing a model for predicting shorter periods of unplanned readmission (e.g., 30-day unplanned readmission due to MACE)
- We are unable to obtain critical information that could serve as potential predictive variables, such as previous readmission events, the length of time between previous cardiovascular events and index admission, and clinical characteristics (e.g., cancer stage), due to the limitations of the variables in the NRD data.

CONCLUSION

- The tuned tree-based gradient boost framework model reliably identifies hospitalized patients with blood cancers at risk for unplanned MACE readmission, offering implications for improving discharge management to prevent unplanned readmission for MACE among older patients with blood cancers.

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