Machine Learning Approaches to Reduce Economic Impact of Effective Interventions

Aniket A. Kawatkar, PhD MS[1]; Aileen S. Baecker, PhD[1]; Rita F. Redberg, MD MSc[2]; Ming-Sum Lee, MD PhD[3]; Maros Ferencik, MD PhD MCR[4]; Steve Goodacre, PhD[5]; Praveen Thokala, PhD[5]; Adam L. Sharp, MD MS[1]; Benjamin C. Sun, MD MPP[6]

1. Kaiser Permanente Southern California, Pasadena, CA, USA, 2. University of California, San Francisco, San Francisco, CA, USA, 3. Kaiser Permanente Southern California, Los Angeles, CA, USA, 4. Oregon Health and Science University, Portland, OR, USA, 5. University of Sheffield, Sheffield, South Yorkshire, UK, 6. University of Pennsylvania, Philadelphia, PA, USA

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Background

- Professional guidelines recommend non-invasive cardiac testing (NIT) within 72 hours after an emergency department (ED) evaluation for suspected acute coronary syndrome (ACS), after acute myocardial infarction (AMI) has been excluded
- Our economic evaluation found use of NIT to be cost-effective (<$6,000/QALY)
- However, even cost-effective interventions face challenges in terms of adoption if the upfront economic costs are high due to a large target population
- If early NIT is adopted as standard of care in the 8 million annual suspected ACS cases in the US, direct medical expenditure could increase by nearly $35 billion annually

Objective

- Hence, we explore if machine learning algorithms can be developed to identify features that classify patients most likely at risk of death or acute myocardial infarction (MI) especially in those with pre-test low-risk

Methods

- We used a retrospective cohort study design within the adult ED patient population in whom MI was ruled out, belonging to Kaiser Permanente Southern California integrated healthcare delivery system
- We included ED patients with pre-test low-risk based on HEART risk score and followed them up to 1-year post ED discharge

Methods (Continued)

- We compared the effectiveness of early NIT vs. no early testing, using confounder adjusted propensity score models and instrumental variables models to evaluate the marginal effect of early NIT
- The number needed to treat (NNT) was calculated as the inverse of the absolute composite risk reduction in death/AMI
- We used least absolute shrinkage and selection operator (LASSO) techniques to reduce the large number of baseline socio-demographic, cardiac and non-cardiac conditions that could be features classifying death/MI risk (Table 1)
- We then used k-fold Classification and Regression Tree Analysis (CART) to identify the most important factors that contribute to the risk of future MI/death

Results

- The cohort included 106,478 patients [mean age 53 (±15) years; female 58%]
- The unadjusted composite outcome of death/non-fatal MI was 2.8% vs 1.1% in the No-NIT and NIT arm respectively
- CART analysis (Fig. 1) identified age above 65 followed by elevated troponin as the most important factors for future MI/death. Peripheral vascular disease and female sex were identified as important features ahead of CAD and CHF

Table 1. Descriptive Statistics of the Cohort by NIT

	No NIT (N=101347)	NIT (N=5131)
Age at ED, Mean (SD)	52.4 (15.58)	55.1 (11.37)
Female, n (%)	59509 (58.7%)	2730 (53.2%)
White Race, n (%)	54726 (54.0%)	2759 (53.8%)
Smoking Status, n (%)		
Active	6352 (6.3%)	291 (5.7%)
Never	65519 (64.6%)	3437 (67.0%)
Passive	584 (0.6%)	14 (0.3%)
Quit	23940 (23.6%)	1240 (24.2%)
Obese, n (%)	42028 (41.5%)	2234 (43.5%)
HEART History, n (%)		
Slightly suspicious	95627 (94.4%)	3916 (76.3%)
Moderately suspicious	5573 (5.5%)	1130 (22.0%)
Highly suspicious	147 (0.1%)	85 (1.7%)
HEART ECG, n (%)		
Normal	85035 (83.9%)	4126 (80.4%)
Non-specific repolarization changes	16225 (16.0%)	986 (19.2%)
Significant ST deviation	87 (0.1%)	19 (0.4%)
HEART Age, n (%)		
Less than 45 years	32080 (31.7%)	928 (18.1%)
Between 45 to 64 years	48749 (48.1%)	3347 (65.2%)
Age 65 and above	20518 (20.2%)	856 (16.7%)
HEART Risk, n (%)		
No Risk factors	33986 (33.5%)	1093 (21.3%)
1-2 Risk Factors	60777 (60.0%)	3551 (69.2%)
3 or More Risk factors or Atherosclerotic disease	6584 (6.5%)	487 (9.5%)
Initial Troponin, n (%)		
Normal	100260 (98.9%)	4986 (97.2%)
1-3 times Normal limit	990 (1.0%)	127 (2.5%)
More than 3-times normal limit or higher	97 (0.1%)	18 (0.4%)
Clinical Characteristics and Comorbidities		
CAD, n (%)	5468 (5.4%)	283 (5.5%)
Stroke, n (%)	2342 (2.3%)	56 (1.1%)
CABG in year prior to ED admission, n (%)	87 (0.1%)	5 (0.1%)
PTCA in year prior to ED admission, n (%)	223 (0.2%)	16 (0.3%)
Family history of CAD, n (%)	32712 (32.3%)	1881 (36.7%)
Family history of stroke, n (%)	21413 (21.1%)	1058 (20.6%)
Elixhauser Comorbidity Index, Mean (SD)	2.8 (2.49)	2.4 (2.13)

Table 2. Difference in Risk Associated with Early NIT and Number Needed to Treat

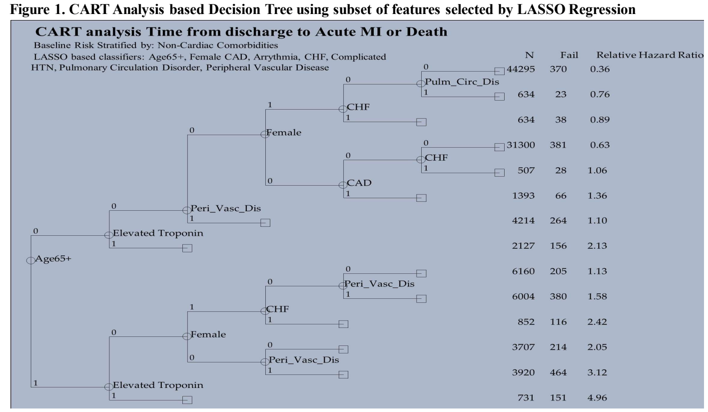
Statistical Model*	Risk Difference Mean (95% CI)	Number Needed to Treat NNT
IPW	-1.54% (-1.95% to -1.12%)	65
Multivariable Logistic Regression	-1.62% (-2.30% to -0.95%)	62
Multivariable Probit Regression	-1.32% (-1.92% to -0.72%)	76
IPWRA	-1.38% (-1.81% to -0.95%)	72
AIPW	-1.36% (-1.82% to -0.90%)	73
GMM IV^	-5.17% (-6.86% to -3.47%)	19

IPW: Inverse Probability of Weighting; IPWRA: IPW with regression adjustment (doubly robust); AIPW: IPW with an augmentation term (doubly robust); GMM IV: Generalized method of moment instrument variables

*Multivariate model estimates are adjusted using the following covariates: based on inverse of treatment probability models where receipt of early NIT was modelled as a logit function of age, sex, race, Hispanic ethnicity, income quintiles, insurance type, BMI categories, smoking status, cardiac comorbidities (CAD, stroke, past history of CABG or PCI, family history of CAD, family history of stroke, arrythmia, CHF, complicated hypertension, uncomplicated hypertension, valvular disease, pulmonary circulation disorders, and peripheral vascular disorders) and non-cardiac comorbid condition based on the Elixhauser comorbidity index

^ Excluded instruments (1) each KPSC medical center's historical practice pattern for early NIT based on HEART risk strata and (2) day of the week of the ED encounter

Figure 1. CART Analysis based Decision Tree using subset of features selected by LASSO Regression



Conclusion

- We implemented machine learning techniques to further classify low-risk patients using smaller set of clinical features & created a decision tree. Our findings may help improve economic and clinical efficiency of use of NIT