Machine Learning as a New Frontier in Mitral Valve Surgical Strategy

Rashmi Nedadur[1], Bo Wang[2], and Wendy Tsang [2]

[1]University of Toronto
[2]Affiliation not available

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Abstract

One of the surgical options available for ischemic mitral regurgitation is mitral valve repair but is limited by recurrent regurgitation as it is experienced by a significant percent of patients and has a negative impact on patient outcomes. Efforts to model and identify predictors of recurrent MR rely on complicated echocardiographic and clinical measurements that are subjective and not routinely collected. Kachroo et. al. approached this problem in a unique way by using the STS database and Machine Learning to develop models that predict recurrent MR or death at one year. The STS database contains many routinely collected demographic and clinical parameters but requires a methodology, such as Machine Learning, that will accommodate collinearity and the unknown significance of many predictors. Kachroo et. al. developed three good Machine Learning models with AUC 0.72-0.75. Data- driven selection of important predictors showed that three revascularization targets, peripheral vascular disease and use of beta blockers are most predictive of recurrent mitral regurgitation. We applaud the authors in pioneering a novel methodology and paving the way for a bright future in Machine Learning which includes integrating medical imaging, waveform, and genomic data to practice personalized medicine for our patients.

Machine Learning as a New Frontier in Mitral Valve Surgical Strategy

Rashmi Nedadur, MD[1], Bo Wang, PhD[2], Wendy Tsang, MD[3]

[1]Division of Cardiovascular Surgery, University of Toronto, Toronto, Canada

[2]Vector Institute, University of Toronto, Toronto, Canada

[3]Division of Cardiology, Toronto General Hospital, University Health Network, University of Toronto, Toronto, Canada

Address for Correspondence

Rashmi Nedadur, MD

200 Elizabeth Street,

Toronto, ON, M5G 2C4

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Abstract (195 words)

One of the surgical options available for ischemic mitral regurgitation is mitral valve repair but is limited by recurrent regurgitation as it is experienced by a significant percent of patients and has a negative impact on patient outcomes. Efforts to model and identify predictors of recurrent MR rely on complicated echocardiographic and clinical measurements that are subjective and not routinely collected. Kachroo *et.*

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The Achilles heel of mitral valve repair

Mitral valve repair is the ideal surgical option for patients with mitral valve regurgitation. When performed by expert surgeons, it provides excellent long term outcomes with lower mortality and reduced operative risk, compared with mitral valve replacement [1][2]. One notable exception is in ischemic mitral regurgitation where recurrent regurgitation post repair is a significant limitation of surgery as it is experienced by a large percentage of patients and has significant clinical impact. For example, in the Cardiothoracic Surgical Trials Network (CTSN) randomized controlled trial of repair versus replacement for ischemic mitral regurgitation (MR), at 2 years, 35% of patients experienced recurrent moderate or greater MR as compared to 2% for mitral replacement [3, 4]. In fact, long term follow-up demonstrates that nearly 30% of patients undergoing repair for ischemic MR will have recurrent regurgitation [5] which is associated with a three times greater risk of death at 10 years and increased risk of hospital readmission for CHF and reoperation [5]. Patients with recurrent MR post repair also have less cardiac reverse remodelling with smaller improvements in body-surface area indexed left ventricular end-systolic volumes, compared to those without recurrent MR [4]. At the patient level, those with recurrent MR have a lower quality of life scores as measured by the Minnesota Living with Heart Failure questionnaire compared with those who do not [4]. Overall, patients with recurrent MR after mitral valve repair for ischemic regurgitation unfortunately do not benefit from the surgical undertaking. Thus, identifying differences between those with and without a durable repair is crucial to improve the outcomes of this surgery.

In this issue of the Journal, Kachroo *et al.* address this issue by using the STS database to identify features that would predict an unsuccessful repair for ischemic mitral regurgitation. The authors applied Machine Learning (ML) methods to data from 173 patients to predict recurrent MR ($>$ Grade 2) or death versus non-recurrence at one year. They trained three different ML algorithms (Support Vector Machine, Logistic Regression and Deep Neural network) and included 53 preoperative predictors relating to demographics, comorbidities, coronary artery disease architecture and bypass targeted vessels. They found that all three models performed well with AUC values between 0.72 -0.75. Important predictors for recurrent significant regurgitation identified by the models included the necessity of bypass to the ramus or the second obtuse marginal or the second diagonal coronary arteries, the presence of peripheral vascular disease, and the use of beta blockers. Through this paper, the authors have successfully sowed the seeds for the use of ML with structured, nationally collected STS data. The combination of the use of the STS database with ML methods will also allowed for effective use of data for modelling and identification of predictors of recurrent MR using a data-driven methodology.

Previous Models to Identify Predictors

Other investigators have attempted to identify predictors of recurrent MR. Some studies have been limited by performing only univariate analysis to identify specific echocardiographic measurements and clinical features associated with recurrent MR (Table). Others, using traditional statistical modelling, have been able to predict recurrent MR with AUC values of 0.82, sensitivity of 0.86 and specificity of 0.70. [3] but were limited to the inclusion of only 10 clinical and echocardiographic variables (Table). Though the above modelling of recurrent MR have been successful in provided us with mechanistic and clinical insights, they have not been reproducible and sometimes require extremely complicated measurements that are not routinely performed in echocardiography or collected in clinical practice. As such, a tool built on data that is easily and ubiquitously collected and available from all patients becomes important to inform all surgeons on the best surgical plan.

Univariate Predictors of Recurrent MR [3-6])
Clinical: Female gender History of ST elevation myocardial infarction *Echocardiographic*: Tenting area Coaptation distance

Table. Previously studied predictors of recurrent MR

Kachroo *et. al.* , in using the STS database, have developed a model that has these qualities, allowing it to be easily validated and deployed universally. While numerous, the included predictors are simpler to collect and therefore, increases the applicability of the model to all patients.

Machine Learning as a Method

ML is a tool that is increasing in popularity in data science as it identifies patterns in the data in order to predict outcomes. The use of ML in medicine is rapidly expanding with the development of large, scale, digitized medical data that could be used with ML for clinical prediction. ML is a well-suited option for this STS-based study for many reasons. First, ML is considered ”data-driven knowledge discovery” and as such, no prior knowledge is needed of a predictor's weight. The STS database contains numerous low-granularity predictors that have unclear significance. Using ML allowed the authors to use any variable that exists within the database knowing that modelling will be able to exclude those that are not significant for prediction. While, with traditional statistical methods, the addition of numerous predictors introduces collinearity, this is managed by ML as modelling is not based on linear relationships. As such, in this study, 53 predictors of unknown significance were used with 3 ML models to predict recurrent MR and death with great success.

Study results in context

A criticism of ML models in the past has been their lack of interpretability as the predictors that drive model output are unknown. Kachroo *et. al.* have addressed this limitation by providing analysis of the important model predictors, thus providing novel mechanistic and clinical insights. In this study, the authors' feature importance analysis reinforces the notion that each predictor on its own may not contain much predictive power, but, the combination of predictors, and the use of a powerful tool, like ML, can generate predictive power. When each predictor in this study is placed in order of importance, up to 20 predictors have up to 20% relative importance to the most important predictor and include features like hypertension and diabetes that when evaluated alone contain minimal predictive power.

Despite the lack of echocardiographic measurements of cardiomyopathy in the STS dataset, there were some novel findings. In this paper, of the five most important predictors of recurrent MR, three of them (bypass to the ramus, obtuse marginal II and diagonal II) represent revascularization targets. Perhaps these represent the geometric changes that take place due to ischemia and ventricular remodelling, that result in leaflet tethering and mitral annular dilation and circularization [1]. These measures are consistent with previously identified markers of recurrent MR such as basal inferior aneurysms or dyskinesia. This suggests that certain patterns of myocardial ischemia may be more likely to suffer from recurrent MR post repair. Additionally, these insights can be used to deliver surgical strategies that reduce risk of recurrent MR. For example, as a bypass to the ramus is an important predictor of recurrent MR, surgeons would be more vigilant about revascularization of the anterior wall. The use of beta blockers also was one of the five most important predictors and is likely collinear with NYHA III/IV symptoms and represents symptomatic reduced ejection fraction heart failure. In this setting, it is likely that patients that were not in beta blockers were at higher risk for recurrent MR. This shines light on the role of ventricular reverse remodelling and the role of ongoing optimal guideline directed medical therapy in order for valve repair to be durable.

In summary, the great benefit of the STS database is that these predictors are easy to obtain and do not rely on patient reported outcomes or subjective and expensive echocardiographic assessment of the heart. In this way, Kachroo *et. al* . have succeeded in using universally accessible, objective measures that are routinely collected at a national level to identify patients that receive durable mitral valve repairs. This tool can be used by all surgeons for all patients using only clinical demographics and a revascularization plan. As the amount of data collected in medicine continues to grow and become more digitized and multidimensional, ML will be the tool that can amalgamate, analyze and interpret this high dimensionality data. ML and its counterpart, Artificial Intelligence, will allow for the integration of datasets, like the STS, with raw imaging data, such as echocardiograms and cardiac MRI, with waveform data, such as electrocardiograms, with genomic data for highly personalized care (Figure). This study by Kachroo *et. al.* is the first building block in this pursuit, showing that high prediction accuracy can be achieved from routinely collected STS variables, and can only be improved as datasets continue to grow in dimensionality. We can look forward to a rich future in data and data analytics and using ML with the STS database can prove to be beneficial for clinicians, scientists and patients.

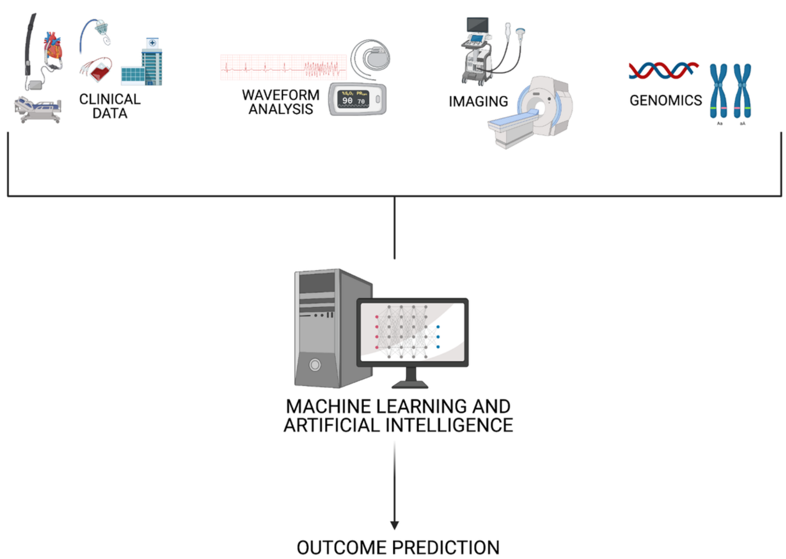

Figure. Future of AI in medicine involves high dimensionality data from multimodal data integration

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