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HEART FAILURE (AM CHANG, SECTION EDITOR)

Using Data Science to Predict Readmissions in Heart Failure

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Abstract

Purpose of Review This review describes the current literature on the use of data science to predict readmissions of patients with heart failure. We examine the chronology of heart failure management from the emergency department, inpatient unit, transition of care, and home care. We examine the software and hardware which may improve readmission rates of this common and complex disease process.

Recent Findings There are multiple novel applications of data science which have been used to predict readmissions of heart failure patients. In the emergency department, efforts are focused on identifying patients who can be safely discharged after a brief period of stabilization; while inpatient endeavors have attempted to predict those patients at risk for decline after discharge. Overall, prediction rules have had mixed results. Outpatient telemonitoring with invasive devices seems to hold promise. New technologies may be the key to future improvements in readmission rates.

Summary Heart failure holds a high morbidity and mortality, and hospitalizations are common. A number of technological interventions have been developed to prevent readmissions in this complex population. Improvements in technology may lead to reductions in heart failure admissions, reduced mortality, and improved quality of care.

Keywords Heart failure · Data science · Informatics · Readmissions · Telemonitoring · Decision support

Introduction

Heart Failure (HF) is associated with high morbidity, mortality, and significant decreases in quality of life. Nearly half the people given a diagnosis of HF die within 5 years of that diagnosis. With a prevalence of 5.7 million people, and an annual incidence of 670,000 in the USA alone, HF is one of the top burdens facing the American healthcare system. The weight of this burden manifests itself in 1 million annual hospital visits and 30.7 billion dollars in annual spending [1, 2].

Hospitalization continues to be the mainstay of HF management in the USA. Once discharged, however, patients are likely to require hospitalization again in the future [3]. The rate of re-hospitalization has risen as a fundamental marker of quality that directly influences hospital re-imbursement [3]. Strategies to reduce HF readmission have thus been the basis for a great deal of HF literature, specifically in the applied data sciences (i.e., transforming data into information then information to usable knowledge to address a problem). This paper will attempt to catalog the many promising ways in which data sciences are being deployed to address the problem of HF readmissions at the pre-hospital, inpatient, and outpatient stages of management. More specifically, we look at prediction and risk modeling, machine learning, telemonitoring, analytics, remote devices, and consumer wearables, to see what their recent effect has been on HF readmissions and what the future holds.

Background

The data sciences have been particularly useful in developing a host of metrics that are, justly or unjustly, used as proxies for

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quality of care. Two decades ago, the Centers for Medicare and Medicaid created the National Heart Failure Project, which tracked four metrics: evaluation of left ventricular (LV) ejection fraction, ACE inhibitor use in patients with left-sided HF, HF discharge instructions, and whether or not smoking cessation counseling had been given [4]. Since that time, these data collected have expanded to include a wider range of structural process, outcome, and patient experience metrics in an attempt to better characterize and benchmark the care of HF patients. Of the metrics that look directly at patient outcome; inpatient mortality, hospital length of stay, and 30-day readmission rates are being used to guide reimbursement, which makes them a vital area of study [5].

The metric of 30-day readmission is unique among the outcome markers; several studies indicate it may be a poor indicator of quality [6], and despite quality of care, a large portion of HF patients experience a readmission [3]. And yet, since 2012, CMS has been tracking 30-day hospital readmission rates with associated financial penalties for underperformance [7, 8]. Given that HF readmissions account for a great deal of hospital spending and reimbursement, it is no wonder that the greater medical community is constantly searching for novel approaches to reduce the rates of HF readmissions.

Emergency Department Management

The most effective method of preventing readmissions may be to stop the initial admission. The Emergency Department (ED) is uniquely positioned to see the majority of HF patients in the acute phase of decompensation. Therefore, ED management of HF represents a critical area of study in the quest to lower readmission rates. Current practices heavily favor admission as the ultimate disposition of patients with heart failure. In the USA, patients with HF are admitted at rates of up to 80% [9]. However, some studies estimate that as many of 50% of patients with HF could be safely discharged from the ED (after stabilization and a brief period of observation) [10].

If the disposition rates could be adjusted by just 5% from admission to observation or discharge in low-risk patients, it would save $80 million and 80 million hospital days [11]. However, objectively defining low-risk patients suitable for discharge is complicated. Even if a patient lacks high-risk markers (i.e., elevated troponin or B-type natriuretic peptide (BNP)), the inability to provide vital bedside education, ensure proper medical regimen, and guarantee proximate follow-up make ED discharge a risky proposition [12]. Therefore supplying instruments with which to risk stratify ED patients presenting in HF has been and remains a main focus of the data sciences.

Hsieh et al. retrospectively derived a model from a database of 8384 adult patients admitted with HF using medical history, vitals, leukocytes, glucose, electrocardiogram (ECG) changes, renal function, and imaging findings. The model found that 19.2% of patients admitted for HF were at low risk for serious adverse events (SAE) within 30 days, with an inpatient mortality of 0.7% and 30-day mortality of 0.7% [13]. Collins et al. attempted to prospectively validate a HF ED decision tool. The STRATIFY study enrolled 1033 adult ED patients admitted with HF at four US hospitals. By using data commonly obtained during routine evaluation of HF (history, medications, vital signs, lab results, and ECG findings), they were able to identify 105 patients (10%) that could have potentially been discharged from the ED [14].

In an effort to validate the Ottawa Heart Failure Risk Score (OHFRS), Stiell et al. examined discharged and admitted patients, enrolled at 6 different Canadian teaching hospitals. Regardless of disposition, 1100 patients were monitored to a primary outcome of adverse event at 30 days. The analysis showed SAE rates of 19.4% for admitted patients and 10.2% in discharged patients. When compared with actual practice, an OHFRS threshold of 2 or greater was more sensitive for the detection of SAEs and had a similar admission rate [15]. Nonconsecutive sampling and small sample size is a valid criticism of the OHFRS. In response, the Multiple Estimation of Risk based on the Emergency Department Spanish Score in patients with HF (MEESSI-AHF) was derived using a cohort of 4867 consecutive patients, enrolled from 34 Spanish EDs [16]. Although the score only predicts mortality and not SAEs, it was found to be discriminating in categorizing the 10% of patients at very high risk for 30-day mortality (45%), as well as the 40% of patients at low risk for 30-day mortality (< 2%) with *C*-statistics of 0.836 in the validation cohort. By virtue of having such a large and coordinated data set, the study was prone to missing data, and as the study was only conducted in non-randomly selected Spanish EDs, it may not be generalizable to populations in the USA [16].

The most recent and promising attempt at developing an ED decision rule for HF has been the Emergency Heart Failure Risk Grade (EHMRG). The EHMRG is a 7-day mortality estimator for HF patients presenting an ED. With the addition of a single variable (ST depression on a 12 lead ECG), the EHMRG30-ST can be used to predict 30-day mortality. Lee et al. prospectively validated the rule, in a cohort of 1983 patients at 9 Canadian EDs, compared it with physician-estimated risk and performed comprehensive follow-up. Patients were stratified into 5 groups from very low to very high risk. Patients stratified into the very low category by EHMRG30-ST had a 0% mortality rate at 30 days. At 7 days, patients stratified into the "very low–risk" or "low-risk" categories by the EHMRG7 had a 0% mortality rate. When physicians were asked to estimate the risk of the same cohort, they tended to overestimate. When physicians were allowed to reclassify their estimates, based on EHMRG calculation, the study showed a significant trend towards the improved reclassification as compared with physician estimate alone [17, 18••, 19].

Despite the significant steps in deriving and validating predictive instruments to aid in determination of ED disposition in patients with HF, there has yet to be a randomized control trial (RCT) that looks directly at the implementation of such an instrument. The future goal of the data sciences with regard to the ED management of HF is thus a very clear one: continue to design and improve decision tools that can then be applied and validated, both prospectively and clinically, to assist in the selection of candidates for safe discharge. By diverting patients from typical admission pathways, it is possible that HF readmission rates can also be lowered, subsequently decreasing the overall financial burden of HF.

Inpatient

If the ED is the point of primary stabilization for patients with HF, then inpatient floors are the definitive point of stabilization. Once admitted to the hospital, patient's diet, medication regimen, vitals, laboratory analyses, and imaging are all scheduled and optimized by using computerized provider order entry (CPOE) systems in an electronic health record (EHR). By building in clinical decision support systems (CDSS) into EMRs, providers get prudent evidence-based recommendations at the appropriate time. The data sciences have therefore had a crucial role on inpatient care for decades. While both CPOE and CDSS have been shown to change provider behaviors, decrease mortality, as well as length of stay metrics, they have not been shown to directly reduce readmission for HF patients [20]. Standardized order sets and efforts to systematize best practices have shown similar limitations [21].

There are very few inpatient interventions that have been shown to have a mortality benefit and reduce HF readmissions. The list can be reduced to medication reconciliation with neurohormonal blockade (ACE-I, ARBs, beta blockers, and aldosterone), cardiac resynchronization therapy (CRT), aerobic exercise, and early palliative care consultation [22]. When examining readmission risk only, pre-discharge planning, patient education, and ensuring timely follow-up have shown benefit [23]. Combined with close monitoring and increased physician regulation of the patient's daily regimen, these interventions can aid most patients admitted for HF. Naturally, some patients will maintain this modified baseline longer than others. Developing tools to identify HF patients, who are at risk of declining more precipitously post-discharge is paramount to ensuring high-quality low-cost care.

Several models have been proposed to achieve this goal. The models vary widely based on data types, timing, sources, and number of variables studied. A systematic review done by Ross et al. attempted to identify models to compare hospital readmission rates or predict readmissions. They identified five prediction models which utilized administrative or clinical data only, but methodologies and results were inconsistent [24]. Other models showed comparably poor predictive ability ranging from *C*-statistics of 0.59 to 0.60 [25–27].

Machine learning (ML) is expected to aid in development of predicting HF readmissions. Recently, Frizzell et al. used three different ML approaches to analyze the Get With The Guidelines Heart Failure registry with Medicare (GWTG-HF) data [28]. ML was set to the task of predicting 30-day readmission and then compared with standard admin and clinical models. While the ML approaches did yield better predictive ability (*C*-statistic 0.607–0.624) compared with a non-ML approach (*C*-statistic 0.589), both ML and standard models failed to predict 30-day readmission in HF patients with enough discrimination to be widely applied [28].

Some have posited that non-clinical factors (such as socioeconomic status or functional ability), when combined with clinical data, may have better discrimination. In 2011, Amarasingham et al. collected markers of social instability and lower socioeconomic status as well as clinical data. They found that it led to a significant increase in the predictive ability of their model (*C*-statistic 0.72) when compared with models that relied on clinical or administrative data alone [29]. In 2018, Huynh et al. built upon previous studies by deriving and then validating a model that incorporated mental health (PHQ9 and GAD-7 scores), cognitive ability (MOCA), and pre-discharge echocardiogram in addition to demographics, socioeconomic status, admin, and clinical data [30•]. The model generated a *C*-statistic of 0.77 for prediction of 30-day readmission or death in patients with HF, and to date appears to be the most discriminatory instrument for short-term adverse events in this population. This instrument, however, was derived using a nationwide Australian (mostly Caucasian) cohort. Validating the model in other populations will be an important future step [30•].

Over the last decade, several 30-day readmission risk prediction tools for patients with HF have been developed. Despite numerous novel techniques, using clinical and administrative data alone only produces modest to poor discrimination. The addition of non-clinical factors has shown the ability to increase discrimination, yet further research is required. ML, a nascent field, has already shown some promise. In the future, the data sciences will continue to identify important non-clinical factors, create improved ML algorithms, and conceive new statistical tools, to better understand HF patients and derive better prediction instruments. Without these advancements, it is likely that readmission rates for HF patients will remain extremely high.

Transitions of Care and Outpatient Management

Per the American college of cardiology's (ACC) 2013 guidelines on the management of heart failure: "The transition from

inpatient to outpatient care can be an especially vulnerable period" [31, 32]. A transition of care is the movement of a population from one care setting to another, and interventions established to prevent returns are considered "transitional care interventions" [33]. Advances in new technologies may hold the key to improving transition of care and chronic outpatient management of patients with HF. The 2016 European Society of Cardiology guidelines for the diagnosis and treatment of acute and chronic HF specifically make a class IIb recommendation for some forms of remote monitoring [34]. Physiologic telemonitoring through either structured outpatient management programs or consumer grade devices, with or without the benefit of ML and predictive analytics may aid in the predictions of failure of management in the outpatient setting.

Telemonitoring

Telemonitoring has been extensively studied in the management of HF. Andrès et al. summarize the literature and divided the history of telemedicine research in the setting of the management of HF into two generations [35].

First-generation studies were very heterogeneous in their methodology and inconclusive in their results. These studies generally used nurses for phone or inperson follow-up and lacked the advanced home monitoring technologies we consider part of modern telemedicine, such as remote sensors [35]. Some meta-analyses did demonstrate positive results, with reductions in all-cause mortality [36, 37] as well as all hospitalizations and heart failure–related hospitalizations [37].

Despite some evidence of value in telemedicine through meta-analsysis, prospective randomized trials have had mixed results [35]. Some randomized trials showed that telemonitoring reduced mortality and hospital length of stay [38], while others demonstrated no difference in readmissions or mortality [39–41], though some suggest this may be attributable to patient non-compliance [40]. Specifically, one study had 14% of its participants never used the telemonitoring system and experienced a large drop in particpation during the study period [39]. Despite these shortcomings, many studies did demonstrate cost reduction [35].

A more recent investigation by Burdese et al. examined 48 elderly Italian HF patients discharged from the hospital over 20 months. A visiting nurse performed a tele-examination with ECG, scale, oxymeter, and sphygmomometer. Alarm criteria prompted a cardiologist to initiate an intervention such as alert the ED or contact the patient's primary care provider. The results demonstrate a high adherence to the protocol with significant reduction in annual re-hospitalizations, ED visits, and overall costs [42].

Second-generation telehealth studies incorporate many more of the technologies commonly associated with telemedicine today such as web 2.0 tools, cloud-based technologies, ML, and wirelessly connected devices [35]. Monitoring of HF in France with bluetooth-connected devices and automated alerts demonstrated high positive and negative predictive values for cardiovascular decompensation [43]. Another system developed in California showed a reduction in the number of biometric readings above a predetermined threshold for weight and blood pressure, and a statistically significant reduction in weight for those who participated longer than 2 months [44–46].

In 2018, Koehler et al. published the first second-generation RCT demonstrating a reduction in unplanned cardiovascular admissions and all-cause mortality [47••]. The TIM-HF2 study examined a multicenter population in Germany of 1571 New York Heart Association class II and III patients. They compared remote patient monitoring and usual care with usual care alone. The authors demonstrated a reduction in days lost due to unplanned cardiovascular hospital admissions and all-cause mortality for the intervention arm of 4.88% compared with 6.64% in the control arm. There was a lower all-cause death rate per 100 patient years in the control arm with a hazards ratio of 0.7, though there was no statistical difference for cardiovascular mortality [47••]. While the results of this study are promising, questions have risen as to whether the intervention versus the resources provided to the intervention group played a larger role in the results observed [35].

Some of the most convincing evidence to support telemonitoring comes from research on invasive devices [48]. The EVOLVO study demonstrated that monitoring through implantable cardioverter-defibrillators (ICD) or cardiac resynchronization therapy defibrillators (CRT-Ds) resulted in fewer ED and urgent office visits [49]. Following this, the IN-TIME trial demonstrated improved clinical outcomes from multiparameter telemonitoring of ICD and CRT-Ds when comparing telemonitoring and standard of care with standard of care alone; the telemonitoring group had better composite clinical HF scores and lower all-cause mortality rates [50]. Similarly, the EFFECT trial demonstrated that remote monitoring of ICDs led to reduced cardiovascular hospitalizations and all-cause mortality [51], while the COMMIT-HF trial demonstrated a reduction in mortality at 3-year follow-up [52]. Contrary to the previously described studies, the OptiLink HF RCT found no difference in all-cause death or cardiac hospitalizations with ICD telemonitoring of intrathoracic fluid status [53].

A meta-analysis of 9 RCTs studying ICD remote monitoring demonstrated no difference between all-cause mortality and cardiovascular mortality when compared with conventional office follow- up, but did demonstrate a reduction in all-cause mortality for those trails that used daily verifications of transmission [54]. A later meta-analysis of 11 RCTs showed that remote monitoring reduced overall visits but increased unplanned hospital and ED visits. Survival was similar but remote monitoring appeared to reduce costs by 15–50% [55].

Invasive monitoring is not limited to ICDs. Rizema et al. demonstrated in a small 40-person cohort that remote monitoring

of left atrial filling pressure was safe and effective in physician-directed patient self-management of HF [56]. In 2011, Abraham et al. published the CHAMPION trial that used a wireless, battery-less radiofrequency sensor that measured pulmonary artery pressures. The authors demonstrated a reduction in cardiac hospitalizations of 37% over the study period [57]. A 2016 update to the trial showed that these effects were long term and access to device data in the previous control group improved HF hospitalization rates by 48% [58]. A post hoc analysis of the initial study demonstrated a 50% reduction in hospitalizations for those with preserved ejection fraction [59].

The COMPASS-HF trail examined an implantable device that monitors right ventricular pressures and estimated pulmonary artery diastolic pressure, as well as other hemodynamic measurements. The intervention group had a 21% reduction in rate of HF events but this was not statistically significant [60].

These studies may support continuous monitoring of cardiopulmonary pressures, especially in patients with preserved ejection fraction for which there are limited interventions [61]. Criticism of these studies includes the lack of standardization of medication interventions, which were at the discretion of the physician responding to the telemonitoring system [48].

ML has also been applied to telemonitoring data. Motrazavi et al. demonstrated that when using data from a previously published telemonitoring study, ML performed better than some standard statistical techniques. ML predicted 30-day all-cause mortality with a 17.8% improvement over logistic regression and improved prediction of admissions for HF by 24.9% [62]. Further work is expected to yield improved methods for prediction of adverse outcomes using these advanced software technologies.

Expanding Data Sources

Technological advancements in the twenty-first century have led to a growth of Mobile Health (mHealth) devices, portable technologies that allow powerful health monitoring in small footprints [61, 63]. mHealth devices are anticipated to have a major impact on the global delivery of healthcare [64], and integrated data generated by the mHealth revolution could play significant roles in the future of reducing HF readmissions.

The vast majority of Americans own smart phones [65], and with these have come a wealth of cardiovascular health mobile phone applications that can integrate smartphone sensors to monitor activity and aid in medication adherence [66]. Mobile phone developers are integrating health records from multiple health systems into their applications so patients have concise medical records on their mobile device [67], and mobile frameworks allow smartphone and wearable sensory data integration into research and health-related software [66, 68].

In addition to software, a number of mHealth devices exist on the market that focus specifically on cardiovascular health. Smartphones can be used for arrhythmia detection where connected devices can generate complete sets of vital signs and hand-held ultrasound can be utilized for echocardiography [69]. These devices have even been used to identify onset of atrial fibrillation and provide support for ED cardioversion [70]. Single-lead ECG monitors are available as phone adaptors, patches, and on watches which connect to mobile devices via bluetooth [69, 71, 72].

Physical activity as measured by actinography has been shown to have independent predictive value for morbidity and mortality in patients with HF and in general was associated with higher health-related quality of life [73]. Both patients and providers are including the application of wearable devices with activity monitoring in their management [66], and some of these devices record similar measurements that could be useful in HF care [74, 75].

It is also known that medication nonadherence is associated with readmissions and mortality in HF [76], and many HF patients forget to take their medications [77]. There have been many attempts at electronic solutions to medication adherence with mixed results [78]. Murray et al. were able to demonstrate improved adherence to medications via a pharmacist-led intervention that was measured by electronic monitors in prescription container lids. However, the digital health tool was not the intervention, and the positive effects of pharmacy-led methods reduced after the intervention ended [79]. Volpp et al. studied the effects of electronic pill bottles on medication noncompliance in survivors of acute myocardial infarction and found no difference in medication adherence or readmissions [80].

While many mHealth devices may hold future potential for application in the management of HF, some have been designed specifically for this purpose. The MUSE clinical system is a noninvasive monitoring devise that measures heart rate, respiratory rate, body impedance, posture, and overall activity [81]. The MUSIC trial demonstrated 65% sensitivity and 90% specificity for identification of a HF event with rehospitalization, with a false positive rate of 0.7 per year. However, the device had a high failure rate [82]. The CoVA necklace is a connected device under development which may be able to monitor thoracic fluid index, heart rate variability, and respiratory rate which may improve management of HF [69]. The Cova Monitoring System 2 was recently cleared by the FDA to cover stroke volume, cardiac output, and single-wave ECG [83, 84].

The VitalConnect [85] biosensor was used in conjunction with analytics software to study one hundred subjects from 4 US veterans' affairs hospitals with HF for 3 months. The system had a sensitivity of 84.2% and a specificity of 85.9% for the prediction of readmission [86, 87].

Finally, The ReDS™ system [88] is a noninvasive vest that measures a patient's fluids status through remote dielectric sensing [89]. A longitudinal study of 50 patients in Israel demonstrated a reduction in hospital admissions with use of the device and an increase in readmissions once the study period ended [90].

While the popularity of mHealth devices continues to grow, questions remain about the evidence to support their use clinically, what factors maximize their efficacy, and when and how their use should be initiated [61]. However, the future of telemonitoring will require rapid access to data with information returning to the patient allowing for self-empowered interventions [91]. As technologies improve future devices may require less physician intervention and allow increased patient-drive management [91]. We anticipate that devices like these will become more integrated into the technology-driven healthcare environment and will have a larger role to play in the management of HF.

Conclusion

The application of health information technology and data science in the management of heart failure is developing at a rapid pace. Novel decision instruments, ML, and advanced statistical techniques combined with ubiquitous mobile networks and ever smaller complex wearable devices are expanding the possibilities of ED, inpatient, and outpatient management.

Further research should focus on developing improved predictive models and decision instruments to aid in characterizing HF patients. Improvements in interoperability and future devices could add additional data sources to predictive models, possibly linking the various stages of HF care, thus improving transitions and reducing need for repeat admission. This could ultimately lead to improved quality of care and reduced overall costs.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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