Published in final edited form as:
J Card Fail. 2014 July ; 20(7): 459–464. doi:10.1016/j.cardfail.2014.03.008.

Prevalence of Heart Failure Signs and Symptoms in a Large Primary Care Population Identified Through the Use of Text and Data Mining of the Electronic Health Record

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Abstract

Background—The electronic health record contains a tremendous amount of data that if appropriately detected can lead to earlier identification of disease states such as heart failure (HF). Using a novel text and data analytic tool we explored the longitudinal EHR of over 50,000 primary care patients to identify the documentation of the signs and symptoms of HF in the years preceding its diagnosis.

Methods and Results—Retrospective analysis consisting of 4,644 incident HF cases and 45,981 group-matched controls. Documentation of Framingham HF signs and symptoms within

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DISCLOSURES
Rajakrishnan Vijayakrishnan – none
Steven R. Steinhubl – none
Zahra Daar – none
Brent Williams - none
Jimeng Sun, Roy J. Byrd, Kenney Ng and Shahram Ebadollahi are (or were) employed by IBM and developed the natural language processing technology.
Jimeng Sun is now employed by Georgia Institute of Technology, Atlanta, Georgia
Christopher deFilippi - Receives research support and honorarium from Roche Diagnostics, BG
Medicine and Critical Diagnostics for the evaluation of cardiac biomarkers for early detection of heart failure
Walter F. Stewart - none

encounter notes were carried out using a previously validated natural language processing procedure. A total of 892,805 affirmed criteria were documented over an average observation period of 3.4 years. Among eventual HF cases, 85% had at least one criterion within a year prior to their HF diagnosis (as did 55% of controls). Substantial variability in the prevalence of individual signs and symptoms were found in both cases and controls.

Conclusions—HF signs and symptoms are frequently documented in a primary care population as identified through automated text and data mining of EHRs. Their frequent identification demonstrates the rich data available within EHRs that will allow for future work on automated criterion identification to help develop predictive models for HF.

Keywords

Heart Failure; Electronic Health Records; Natural Language Processing

INTRODUCTION

The management of heart failure (HF) is one of the most critical challenges facing the healthcare system today. Over 5.8 million American adults have a diagnosis of HF and nearly 700,000 new cases are diagnosed each year[1]. While the prevalence of HF is forecasted to increase by ~25% over the next 20 years it is already the leading cause of hospitalization for adults >65 years old and is responsible for nearly $25 billion of direct medical costs annually. Those costs are expected to increase a staggering 215% by 2030[2].

Early identification of those at risk of progressing to a HF diagnosis may provide an opportunity to improve both quality of life and reduce costs. However, the complexity and heterogeneity of the early clinical presentation of HF poses substantial challenges to its identification and diagnosis, especially in the primary care setting[3].

The increasing presence of the electronic health record (EHR) in the primary care setting offers several advantages in our ability to explore early markers for the onset of conditions of interest, such as HF, in the years preceding clinical diagnosis. They allow for access to longitudinal individual patient data in tens of thousands of patients, although the amount of data available makes manual review for pertinent findings near impossible. Natural language processing (NLP) overcomes this limitation and allows for the automated extraction of pertinent data from free text information, such as found in medical encounter notes, which could potentially be utilized to provide clinical decision support[4]. We have previously shown that a NLP tool developed by our group to extract signs and symptoms potentially consistent with HF based on the Framingham criteria has good accuracy compared to expert human adjudication[5,6].

In recent guidelines, the accuracy of signs and symptoms for the diagnosis of HF have been questioned[7,8]. The Framingham signs and symptoms criteria for HF diagnosis (Table 1), developed 40 years ago, are those classically associated with HF and still remain used to diagnosis HF in research studies[9,10], although their application to stratify risk for HF in a broad contemporary community based population hasn’t been rigorously evaluated.

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The primary aim of our study is to use natural language processing of the EHR in a large primary care cohort to determine the prevalence of the Framingham criteria findings in both HF cases and controls in order to lay the foundation for work to determine whether automated analytics of encounter notes in the EHR might enable the differentiation of subjects who would ultimately be diagnosed with HF.

METHODS

Study Subjects

This is a case-control design study utilizing a retrospectively identified cohort of primary care patients who eventually developed HF and controls who didn't. Patient EHRs dating from 2001 to 2010 within the Geisinger Health System were utilized to identify cases and controls. The Geisinger Health System is an integrated health care system that provides health services in 31 counties of central and northeastern Pennsylvania and includes 41 community practice clinics which have been utilizing the EPIC EHR since 2001. Data for this study were derived from the approximately 400,000 primary care patients served by these clinics.

From these EHRs, we identified 4644 incident HF cases with a clinical diagnosis based on meeting at least one of the following criteria: 1) HF diagnosis appearing on the problem list at least once; 2) HF diagnosis appeared in the EHR for two outpatient encounters; 3) at least two medications prescribed with the ordering provider associating that medication order with an ICD-9 diagnosis of HF; or 4) HF diagnosis appearing on one or more outpatient encounters and at least one medication prescribed with an associated ICD-9 diagnosis for HF. This operational diagnostic method for heart failure diagnosis has been previously validated[11]. The diagnosis date was defined as the first appearance of a HF diagnosis in the EHR. This means that the diagnosis of HF is based on EPIC EHR records which comprises of inpatient diagnoses as well as outpatient diagnoses (former more than latter as mentioned in the criteria no:1). Regarding criterion 2 (HF diagnosis appeared in the EHR for two outpatient encounters), once the HF diagnosis is confirmed based on this criterion, we considered the first of these visits as the HF diagnosis date.

Approximately 10 eligible clinic-, sex-, and age-matched (in five-year age intervals) controls were selected for each incident HF case (45981 group-matched controls). Primary care patients were eligible as controls if they had no history of HF diagnosis before December 31, 2010. Control patients were required to have had their first Geisinger Clinic office encounter within one year of the incident HF case's first office visit and had at least one office encounter 30 days before or any time after the case's HF diagnosis date in order to ensure similar durations of observations among cases and controls. In situations where 10 matches were not available, all available matches were selected. Therefore, for the purposes of this study we extracted the clinical notes portion of the EHRs for 51,625 patients. All patient encounters preceding the diagnosis of HF in cases, and the matched date in controls were analyzed. In total, there are over 3.3 million clinical notes, comprising over four gigabytes of text. The average number of clinical notes reviewed for cases were 25 (SD 19) and for controls 19 (SD 15).

HF signs and symptoms EMR data extraction

A natural language processing application was developed and validated for identifying affirmations and denials of 14 of the 17 Framingham criteria for HF. (Table 1) The remaining 3, circulation time of 25 seconds, increased central venous pressure, and a decrease in vital capacity by 1/3 of maximum on serial testing, were not identified as they are not routinely carried out in clinical practice. Details of the methods behind developing the automated text mining tool have previously been published[5]. The program had a precision (or positive predictive value) of 0.925 and recall (or sensitivity) of 0.896 relative to manual chart review[6].

Natural Language Processing

NLP systems recognize words or phrases as medical terms (in this case, Framingham Criteria) that represent the domain concepts (named entity recognition) and understanding the relations between the identified concepts. We use Unstructured Information Management Architecture (UIMA) to identify clinically relevant entities in clinical notes mentioned as a part of EHR. The entities are subsequently used for information retrieval and data mining of vast information available in the health records of patients[4,5,6]. Using this method can potentially identify any information available in the medical records of patients quickly and with very good precision without manual chart reviews and thus the gap between the vast amount of important data available within clinical notes in the EHR and the clinical research investigator is minimized.

Statistical Methods

All study variables are reported by case-control status and reported as means (standard deviation) or median (interquartile range [IQR]) for continuous variables and number (percent) for categorical variables. Comparisons across case-control groups were made by either chisquare tests (for categorical variables) or t-tests (for continuous variables). Analyses were performed with R software (version 2.12). A P-value < 0.05 was considered significant.

RESULTS

Patient characteristics of case and controls documented in the 6 to 12 months prior to the diagnosis date or matched control date are detailed in Table 2. As expected cases were taking more cardiac medications and had more co-morbidity such as coronary disease, hypertension and diabetes.

Identification of Framingham HF Signs and Symptoms

The average duration of patient observation preceding the diagnosis or matched control date was 3.4 years. During this period a total of 4,484,666 Framingham sign and symptom mentions were identified; 892,805 of these were affirmed as being present and the remaining 3,591,861 were documented as not being present (negated). For this study only the affirmed criteria were analyzed. As noted in Table 3, Framingham signs and symptoms were recognized at least once in a substantial percentage of both cases and controls, although significantly more frequently in cases. Ankle edema and dyspnea on exertion (DOE) were documented in the majority of both cases and controls.

The median number of different Framingham HF signs and symptoms affirmed at least once per patient was 3 (IQR=2) for cases and 2 (IQR=2) for controls, whereas the median number of all affirmed mentions (including multiple mentions of the same sign or symptom) was 13 (IQR=19) for cases and 8 (IQR=17) for matched controls.

Among HF cases, for patients who had a specific criterion identified, the median duration between documentation of the criterion and the clinical diagnosis of HF was more than 6 months for almost all of the signs and symptoms, with some, such as paroxysmal nocturnal dyspnea (PND), hepatojugular reflux, ankle edema, DOE, hepatomegaly and tachycardia being first documented as much as one to two years prior to a clinical diagnosis of HF. (Table 3)

For the subset of individuals with ejection fraction documented in their encounter notes (62% of HF cases and 24% of controls) prevalence of signs and symptoms were determined based on documentation of preserved or reduced ejection fraction. In general no statistically significant difference (in patients with HF[cases]) was noted except that ankle edema, DOE and night cough were more prevalent in those with preserved ejection fractions. (Table 4)

DISCUSSION

In the present study we explored the application of a validated sophisticated text and data mining tool to identify the presence of Framingham HF signs/symptoms criteria in the EHRs of a large primary care population. We found that the Framingham signs and symptoms were frequently documented in both the case and control populations, albeit much more frequently among the eventual HF cases. These findings are novel and to our knowledge the first automated evaluation of HF signs and symptoms utilizing EHR data in a large contemporary population of primary care patients. The fact that many signs and symptoms associated with HF were identified in eventual cases years before diagnosis would suggest a potential future role for automated detection and clinical decision support to aid in the early detection of HF, whereas the surprisingly high frequency of these signs and symptoms in a control population supports the need for additional data, such as biomarker, ECG or imaging data to improve the accuracy of the identification of the high-risk individuals.

The American Heart Association/ American College of Cardiology over the past decade have redefined heart failure classification from symptoms (i.e. New York Heart Association class) to stages A through D with stage A and B representing those with risk factors or structural heart disease who are asymptomatic, but at risk for symptomatic disease[12]. A persistent challenge in addressing HF management is in the inability to detect it early enough to implement proven lifestyle and pharmacologic interventions that can delay and possibly even prevent disease progression. The rapid growth in adoption of EHRs affords a unique opportunity to develop novel, cost-effective strategies to detect HF in its earliest stage as a means to monitor patient status, motivate engagement, initiate proven disease-modifying interventions, and test preventive treatments. We tested whether early sentinel

Framingham signs and symptoms, appropriately abstracted from an EHR could be potentially be used alone to identify those at higher risk of HF. Unfortunately, our data suggests this is unlikely to be the case due to the substantial overlap between cases (52.22%) and controls (24.23%).

The vast amount of EHR data available is structured for primarily clinical purposes and is not necessarily research-friendly due to the high degree of variability in data entry, especially with subjective provider documentation. Real world population studies are possible only if we can exploit these provider data in a precise and accurate manner[13,14]. This is made possible by the use of NPL tool which utilizes techniques like UIMA text analysis pipeline to accurately analyze the provider documentation for clinical research purposes[5,6,11]. The gap between the vast amount of important data available within clinical notes in the EHR and the clinical research investigator is minimized by the use of NLP tools.

Retrospective longitudinal assessment of clinically documented (i.e., positive and negative affirmation) signs and symptoms holds the potential to improve our ability to evaluate a patient's underlying health status. However, visual inspection of progress notes from serial encounters is impractical and probably not feasible, as the provider would have to have the time and ability to accurately interpret and detect sometimes subtle patterns in dozens of notes. In contrast, text analytics and quantitative modeling could be readily applied to reveal and display patterns for clinical confirmation. There remains tremendous potential for further refinement of this work with the identification of more sensitive and specific contemporary clinical findings, as well as the addition of biomarker, imaging, and genetic information. The addition of this type of information to the greater than 40 year old Framingham criteria will very likely allow for earlier and likely more specific prediction of HF. The inclusion of biomarker data has already been shown to improve the earlier identification of a HF patient well prior to clinical manifestations[15–17], and genetic information also appears to hold great promise[18,19].

There are important limitations to our study that need to be highlighted. First, unlike the Framingham investigators, we were unable to accurately account for other, non-cardiac causes for a patient to have experienced minor signs and symptoms. Since the Framingham definition of definite heart failure excludes minor criteria if they can be attributed to another medical condition our findings likely over-represent HF-induced signs and symptoms, potentially leading to an over diagnosis of HF by Framingham criteria. Another important limitation is the variability in the documentation of HF signs and symptoms by various clinicians. Both of these issues reflect real-world practice and will likely not be overcome by further refinement in EHR data extraction. ***Our study is a retrospective analysis and some control patients could have potentially progressed to a HF diagnosis outside the observational window of this study***. Lastly, even though the automated algorithm utilized in the study has very high precision and sensitivity, when this tool is applied to millions of medical records there will be a good number of false positives and negatives generated.

At this point it might be reasonable to evaluate the automated detection and notification of a primary care physician if the Framingham criteria is met based on the clinical evaluation so that the further work up of heart failure could be initiated in carefully selected patient population (if the physician feels that there are no other explanation of the patient's signs/ symptoms).

In conclusion, we demonstrated that applying automated text and data mining of EHRs for HF signs and symptoms is feasible and that they are frequently documented in cases years prior to a clinical diagnosis, but also frequently identified in controls. While further refinement is necessary, these results support the future potential to improve patient care by informing physicians additional measures through biomarkers, ECG or even imaging may be necessary to optimize early identification of those at highest risk for HF.

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Table 1

Framingham Diagnostic Criteria for Definite Heart Failure

MAJOR SYMPTOMS	MINOR SYMPTOMS
1. Paroxysmal Nocturnal Dyspnea (PND) or Orthopnea	1. Bilateral Ankle Edema
2. Neck Vein Distension (JVD)	2. Nocturnal Cough
3. Rales	3. Dyspnea on ordinary exertion
4. Radiographic Cardiomegaly	4. Hepatomegaly
5. Acute Pulmonary Edema	5. Pleural effusion
6. S3 Gallop	6. A decrease in vital capacity by 1/3 of the maximal value recorded*
7. Increased Central Venous Pressure (> 16 cm H2O at RA)*	7. Tachycardia (>120 BPM)
8. Circulation Time of 25 seconds*	
9. Hepatojugular Reflux (HJR)	
10.Weight loss 4.5kg in 5 days in response to treatment	

*Not utilized in this analysis as not documented in routine clinical practice.

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Table 2

Demographics and key clinical features of cases and controls within 12 months prior to diagnosis date.

	Cases (n=4,644)	**Controls (n=45,981)**	**p-value**
Age (mean ± SD)	70.88±9.91	70.71±10.00	0.27
Female (%)	48.45%	48.37%	0.92
Caucasian (%)	98.65%	99.06%	<0.01
Documented EF <50%	42.6% (1227 of 2880)	29.1% (3164 of 10888)	<0.001
Hypertension	2874 (61.89%)	24939 (54.24%)	<0.001
Diabetes	1478 (31.83%)	11037 (24.00%)	<0.001
Prior Myocardial Infarction	34 (0.73%)	192 (0.42%)	<0.01
Known Coronary Disease	1183 (25.47%)	7240 (15.75%)	<0.001
Peripheral Vascular Disease	190 (4.09%)	1106 (2.41%)	<0.001
Cerebrovascular Disease	460 (8.74%)	3033 (6.60%)	<0.001
Chronic Obstructive Pulmonary Disease	855 (18.41%)	5621 (12.22%)	<0.001
Valvular Heart Disease			
Aortic	111 (2.39%)	541 (1.18%)	<0.001
Mitral	83 (1.79%)	427 (0.93%)	
Chronic Kidney Disease	202 (4.41%)	1243 (2.70%)	<0.001
Stage 3	119 (2.56%)	800 (1.74%)	
Stage 4	37 (0.80%)	163 (0.35%)	
Stage 5	13 (0.28%)	31 (0.067%)	
Baseline Medications			
Beta-blocker	2279 (49.07%)	16925 (36.80%)	<0.001
ACE Inhibitor	1622 (34.93%)	12032 (26.17%)	<0.001
Angiotensin Receptor Blocker	496 (10.68%)	3350 (7.29%)	<0.001
Thiazide Diuretic	721 (15.53%)	6780 (14.75%)	0.15
Calcium Channel Blocker	1068 (23.00%)	7698 (16.74%)	<0.001
Thienopyridine	407 (10.14%)	2973 (6.47%)	<0.001
HMG CoA Reductase Inhibitiors	2063 (44.42%)	18139 (39.45%)	<0.001
Insulin	409 (8.81%)	1985 (4.32%)	<0.001
Oral Hypoglycemics	1096 (23.60%)	7967 (17.33%)	<0.001

Table 3

Prevalence of Framingham criteria at any time among cases and controls.

Framingham Sign or Symptom	Total HF cases (N = 4,644)		Total Controls (N = 45,981)		p-value (Difference in prevalence between cases and controls)
	Total Cases (% of HF cases who ever had the specific criterion affirmed)	Median and (IQR) number of days between first documented affirmation and diagnosis date in cases	Total Controls (% of controls who ever had the specific criterion affirmed)	Median and (IQR) number of days between first documented affirmation and matched date in controls	
Major Criteria					
Pulmonary Edema	9.0%	145 (632)	2.9%	650 (823)	<0.001
Paroxysmal Nocturnal Dyspnea	41.0%	599 (1064)	28.1%	904 (909)	<0.001
Jugular Venous Distention	15.6%	347 (989)	8.1%	871 (912)	<0.001
Rales	36.4%	408 (956)	18.9%	814 (883)	<0.001
Radiographic Cardiomegaly	28.6%	277 (697)	3.4%	493 (744)	<0.001
S3 Gallop	3.7%	345 (879)	1.9%	834 (927)	<0.001
Hepatojugular Reflux	3.3%	596 (822)	1.3%	824 (851)	<0.001
Weight Loss	3.8%	301 (785)	1.3%	625 (783)	<0.001
Minor Criteria					
Ankle Edema	87.1%	886 (949)	72.3%	1002 (933)	<0.001
DOE	87.4%	780 (1025)	59.9%	985 (920)	<0.001
Hepatomegaly	5.6%	764 (918)	3.8%	869 (926)	<0.001
Night Cough	8.6%	596 (822)	5.5%	747 (866)	<0.001
Pleural Effusion	18.9%	83 (515)	3.0%	574 (758)	<0.001
Tachycardia	9.6%	518 (916)	5.2%	726 (792)	<0.001

Table 4

Prevalence of Framingham Heart Failure signs/symptoms at any time among HF patients reduced LV systolic function (LVEF < 50%) (Total N = 1227) and with preserved LV systolic function (Total N = 1653)

Framingham Sign or Symptom	HF patients with LVEF < 50% N=1227	HF patients with LVEF ≥ 50% N=1653	p-value
Major Criteria			
Pulmonary Edema	9.40%	10.60%	0.74
Paroxysmal Nocturnal Dyspnea	43.50%	47.30%	0.25
Jugular Venous Distention	17.80%	19.10%	0.84
Rales	40.00%	39.40%	0.98
Radiographic Cardiomegaly	35.60%	31.70%	0.18
S3 Gallop	5.90%	4.00%	0.12
Hepatojugular Reflux	4.40%	5.00%	0.90
Weight Loss	3.30%	5.40%	0.05
Minor Criteria			
Ankle Edema	86.50%	90.40%	0.01
DOE	87.70%	91.20%	0.03
Hepatomegaly	5.30%	7.10%	0.26
Night Cough	7.30%	10.60%	0.03
Pleural Effusion	24.60%	21.40%	0.24
Tachycardia	11.30%	11.60%	0.99