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Identifying Peripheral Arterial Disease Cases Using Natural Language Processing of Clinical Notes

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Abstract

Peripheral arterial disease (PAD) is a chronic disease that affects millions of people worldwide. Ascertaining PAD status from clinical notes by manual chart review is labor intensive and time consuming. In this paper, we describe a natural language processing (NLP) algorithm for automated ascertainment of PAD status from clinical notes using predetermined criteria. We developed and evaluated our system against a gold standard that was created by medical experts based on manual chart review. Our system ascertained PAD status from clinical notes with high sensitivity (0.96), positive predictive value (0.92), negative predictive value (0.99) and specificity (0.98). NLP approaches can be used for rapid, efficient and automated ascertainment of PAD cases with implications for patient care and epidemiologic research.

I. INTRODUCTION

Healthcare systems across the US are implementing electronic health records (EHRs) in response to the Health Information Technology for Economic and Clinical Health Act [1–4] which emphasizes need for “meaningful use”, defined as use of EHRs to achieve improvements in patient care. EHRs are a repository of patient information including demographics, symptoms, physical signs, laboratory values, images, medications, diagnoses and outcomes [5, 6]. A potential secondary use of EHRs is to conduct epidemiologic research. In EHRs, some data such as laboratory results, medications and diagnoses have a structured format while clinicians also provide observations in unstructured format (free text) such as consultations, progress notes, discharge summaries and other narratives. The ability to efficiently extract and consolidate information from EHRs will facilitate automated identification of patients with cardiovascular diseases including peripheral arterial disease (PAD) [7, 8].

PAD affects millions of adults worldwide and is associated with increased risk for death, myocardial infarction and stroke [9]. Despite the morbidity associated with PAD and established guidelines for management, [9] PAD patients are often undertreated [10]. Lack

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of physician and public awareness of PAD-associated risks for adverse cardiovascular outcomes likely contribute to this public health problem [10].

The lack of automated processes for identification of PAD patients from EHR is an obstacle to conducting large-scale epidemiologic studies. Previous studies have demonstrated the usefulness of a natural language processing (NLP) for phenotype extraction [11–14]. The unstructured data processed using NLP methods provide important detailed information that is unavailable in structured data. We developed and validated our NLP algorithm for ascertainment of PAD patients from clinical notes and thus automating the chart review process.

II. BACKGROUND

PAD diagnosis is based on the ankle-brachial index (ABI) obtained during lower extremity arterial evaluation in the non-invasive vascular laboratory [9]. Patients at Mayo Clinic with PAD or suspected of having PAD are usually referred for non-invasive evaluation in the vascular laboratory. This evaluation contains measurement of the ABI at rest and one minute post-exercise. The ABI is the ratio of blood pressure (BP) at the ankle to the BP in the arm. PAD is defined as an ABI ≤ 0.9 at rest or 1 min after exercise; or ABI ≥ 1.40 [15, 16]. However results of ABI testing may not be available and medical experts may need to manually review the entire medical record for identification of PAD patients. Such manual review process is labor intensive, time consuming and often impractical for large-scale epidemiological studies. NLP may overcome these shortcomings by processing clinical notes to extract PAD-related information. NLP has been successfully applied in diverse clinical applications such as information extraction from clinical text [17], medical status extraction [18, 19], sentiment analysis [20], text summarization [21], genome-wide association studies [22, 23] diagnosis code assignment [24, 25] and cohort identification [26]. We previously applied NLP to ascertain PAD status from radiology reports [27]. Radiology reports lack information provided by the clinician including history, physical examination, summaries of test results and plan of care. In the present study we address aforementioned shortcomings by developing an NLP system to ascertain PAD status from clinical notes.

III. METHODS

A. Study Setting and Population

This study took place at Mayo Clinic, Rochester Minnesota. All study subjects were part of the PAD case-control cohort from Olmsted County. However, we only included patients seen at Mayo Clinic, because we applied this algorithm to the Mayo EHR. This study was approved by the institutional review board for human subject research at Mayo Clinic. The dataset contains 27 definite cases (PAD) and 90 control cases (not PAD).

Lower extremity arterial evaluation is performed using standardized protocols in the noninvasive Vascular Laboratory. Systolic BP is measured in each arm and dorsalis pedis and posterior tibial arteries bilaterally using a hand-held 8.3-MHz Doppler probe. The higher of the 2 arm pressures and lower of the 2 ankle pressures is used to calculate the ankle-brachial index (ABI) for each leg [9]. Data is interpreted and reported by a vascular medicine specialist. We define normal ABI as 1.0–1.3. We define PAD as an ABI ≤0.9 at rest or 1 min after exercise; or ABI ≥1.40.

Two independent abstractors who were unaware of PAD status of the patients' ascertained PAD status from the EHR and abstracted terms related to lower extremities, which are mentioned in Table 1. Both abstractors completed an orientation session that was led by an expert cardiovascular specialist (AAO). Abstractors followed a manual that guided the abstraction process. The two independent abstractors were blinded to clinical diagnosis classified each patient as case (PAD) or control (not PAD) using criteria summarized in Table 1. The inter-annotator agreement between two abstractors was high (95%) and it was calculated using kappa score. In addition to PAD status, an index date of PAD ascertainment was determined for all subjects during manual review of EHRs. This index date was defined as the earliest indication of PAD symptoms found in EHR that met the predetermined criteria for PAD ascertainment.

B. Study Design

Automated NLP systems were validated by comprehensive manual medical record review.

Figure 1 shows the overall design of the study. All retrieved clinical notes for each subject were used to ascertain patients' PAD status as an output.

C. PAD Status by NLP Algorithms

The authors retrieved clinical notes from the EHR of each patient that were created until the date of completion of manual chart abstraction. The NLP algorithm included a text-processing component, which found concepts in text that match specified criteria, and a patient classification component, which defined the PAD status, based on the available evidence from clinical notes For text processing, we used our in-house program MedTagger [29], a NLP pipeline with a fast dictionary lookup, to process clinical text and annotate clinical concepts. MedTagger is built using the Apache Unstructured Information Management Architecture (UIMA) framework.

The main annotations used by MedTagger included sentence detection that parsed sentences, tokenization found word token boundaries, normalization generated one form for the various morphological variants of the word through the NLM's Lexical Variant Generation tool (http://SPECIALIST.nlm.nih.gov), which made it possible to use normalized terms for dictionary lookup. Concept identification used PAD named entity detection according to PAD specific dictionary compiled by medical experts and expanded by synonyms through MedLex [30] to discover PAD related concepts based on dictionary lookup while assertion checked concept certainty (i.e. positive, negative and possible) and experiencer (i.e., associated with someone else or patient).

The whole assertion process can be explained from the following example:

> His leg should continue to be monitored for signs of improvement to demarcate the level of ischemia at which point an amputation may be considered.

Here both *leg* and *ischemia* are PAD related concepts and the certainty levels of both concepts are positive and experiencer is the patient.

Patient classification component used a set of rules to classify patient status. The NLP system used of information described in Table 2 and the following rule for PAD cases (definite):

One disease location keyword + one diagnostic keyword within two sentences anchored by a diagnosis

For non-PAD control the system used the following rules:

1. If not satisfied the PAD criteria listed above OR
2. If the PAD cases are associated with exclusion keywords

In case of PAD cases, the system also provided the index date (i.e., the earliest date that satisfies PAD conditions) along with the evidence in the form of +/− 2 sentences anchored by diagnosis keyword that lead the system to classify the patient status.

IV. RESULTS

Figure 2 shows the concept types and values of a de-identified sample clinical note in UIMA CAS Visual Debugger. The right window shows a clinical note snippet that is processed to populate annotations as they appear in the upper left window.

The lower left window shows concept types and their respective values. The highlighted concept on the right side window is the concept identified by NLP system while lower left window contains information about that concept which includes its category (either it is from disease location, diagnosis or excluding keywords), certainty (positive, negative and possible), status and experiencer.

The dataset processed by the NLP system consisted of 117 patients and 26,656 clinical notes. Our NLP system classified PAD cases from that data with high PPV (positive predictive value), sensitivity, NPV (negative predictive value) and specificity (Table 3).

Moreover, whenever the NLP system classifies PAD status it also provides the part of clinical note with the evidence is used by the system to classify the patient. This is illustrated in the following example where our NLP system identified a patient as a PAD case and provided the following information: index date when system found the first evidence of PAD along with clinical notes information with the evidence used to decide PAD status.

```
2008****
mcn_cn.txt
```

revascularization::femoral artery

Given his multiple medical comorbidities, his currently questionable cardiac function, and his functional debility overall our options are very limited. Furthermore, an ultrasound was obtained in the ER which demonstrated occlusion of the superficial *femoral artery*. Further intervention and *revascularization* of this limb would carry the risk of compartment syndrome and myoneuropathic consequences which may be detrimental in his case. Furthermore, his DNR/DNI status limits our attempts at operative intervention. At this point, we would recommend admission to a Medicine Service for stabilization and hydration with IV fluids and further work up of his cardiac status.

ischemia::leg

His *leg* should continue to be monitored for signs of improvement to demarcate the level of *ischemia* at which point an amputation may be considered.

In this study, we also compared the temporal association between our NLP systems with manual chart review regarding diagnosis of PAD. During the preparation of gold standard data manual abstractors documented the index date when they first found evidence of PAD in clinical notes. The NLP system also generated an index date for each subject when it found the first evidence of PAD in clinical notes. We found that in 13 cases (54%) NLP system identified PAD cases before the manual index date while in 4 cases (17%) the manual index date and NLP index date were similar. In 7 cases (29%) NLP system index date was after the manual index date and in majority cases the difference was a few days as shown in Figure 3.

A cardiovascular expert (AAO) further abstracted the EHR of the 7 cases where NLP index dates were after the manual review index date. We then identified two main reasons for these discrepancies. First, our NLP system only used clinical notes while manual abstractors made use of all available information in the EHR including angiograms and radiology reports. Thus NLP was unable to find the information on same date as manual abstractors' index date when the diagnostic information was not documented in the clinical notes, but documented as another type of document. Second, when abstractors found earliest possible indication of PAD, patient was classified as probable PAD and abstractors documented that date as index date. On later date after tests were performed (e.g. angiograms or radiology), the results of these tests were then incorporated in the subsequent clinical notes which confirmed presence of PAD. The NLP system classified as PAD only when there was evidence of definitive PAD.

V. DISCUSSION

The results in this paper demonstrate that our NLP system can accurately ascertain the PAD status of patients in a timely manner with high PPV and sensitivity by using information present in clinical notes from 27 cases and 90 controls. There was one false negative and two false positives. A false negative case was due to the following sentence in clinical notes:

> Patient has what appear to be an acute arterial occlusion as well as a DVT in the right lower extremity.

The system identifies two PAD related concepts (*arterial occlusion and lower extremity*) but due to the word 'appear' it classify these concepts certainty as 'Possible' for PAD-related concepts while in order to be consider as a PAD case concepts certainty should be 'Positive' for both PAD-related concepts.

False positive cases were due to the following two sentences:

> An old woman with degenerative central lumbar spinal canal stenosis that may account for her current back and leg pain symptoms.
>
> Left lower extremity pain likely secondary to l4 foraminal stenosis.

Here in both cases due to concept '*stenosis*' NLP system identifies them as PAD cases, but feedback from medical experts stated that patients with *spinal stenosis*, *spinal canal stenosis* and *foraminal stenosis* should not be considered as PAD cases. Accordingly, we updated our NLP system and added the aforementioned words with in the list of exclusion keywords.

Strengths of this study include the use of predetermined criteria for automatic ascertainment of PAD status based on clinical notes compared to lengthy manual chart review. Consequently, this study objectively compared how these predetermined criteria were implemented by medical experts vs. automated system. Another strength is the evaluation of the temporal aspects of PAD diagnosis, which may be relevant to research related to PAD and other chronic diseases. Study limitations include that we only considered clinical notes and NLP system would not identify PAD-related information reported outside clinical visits such as angiogram or radiology reports. However, previously we have demonstrated that another NLP algorithm identified PAD-related information from radiology reports [27] with high PPV and sensitivity.

Manual data abstraction for large epidemiological studies is laborious, expensive and time consuming. In this paper, we described a NLP-based system to automatically ascertain PAD status from clinical notes in a timely and accurate manner. Such a tool will enhance capabilities for PAD research including epidemiologic studies with potential impact on public health. In future studies, we will apply and validate our NLP system to a larger PAD cohort from multiple institutions and EHRs settings.

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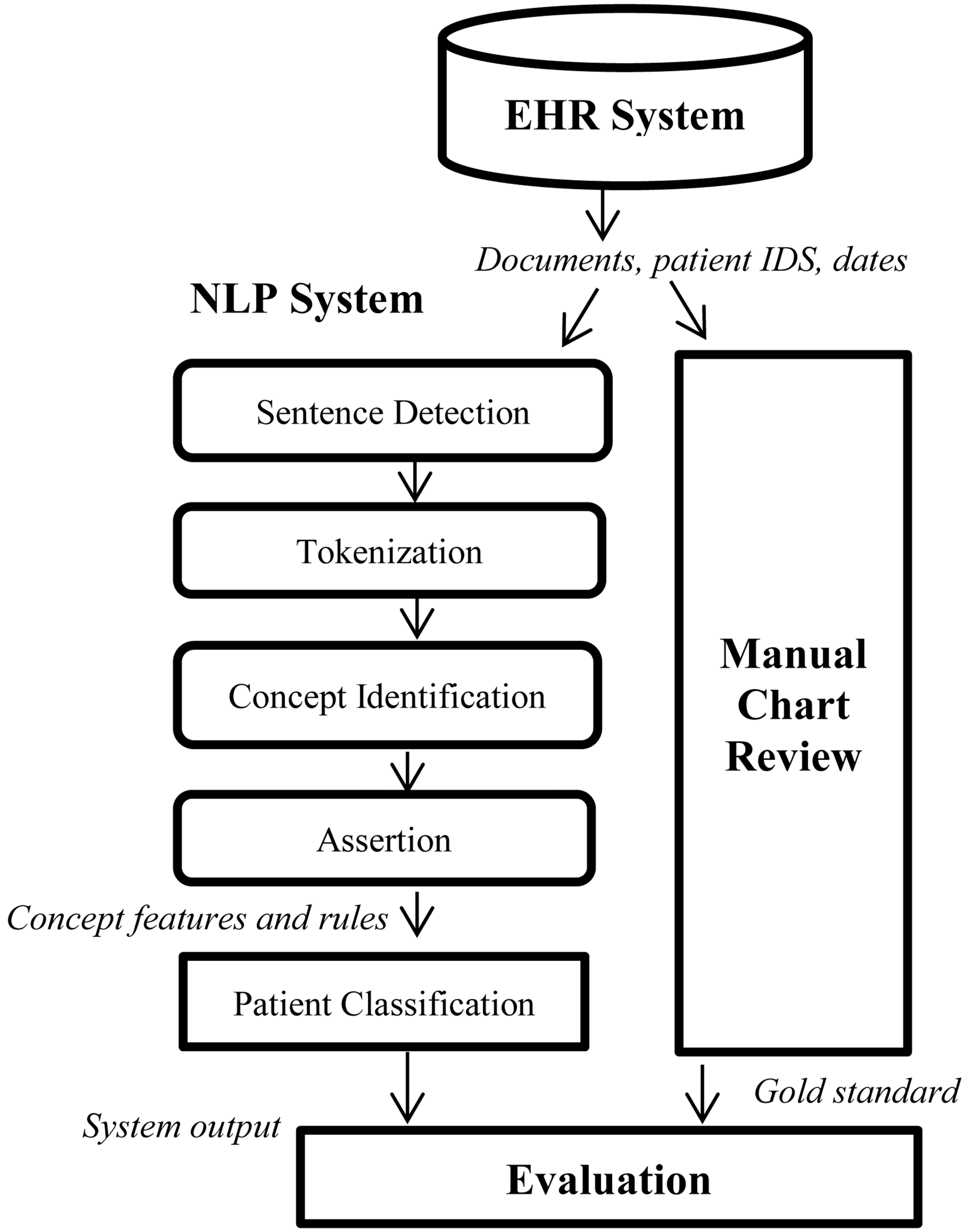

Figure 1.
Study Design

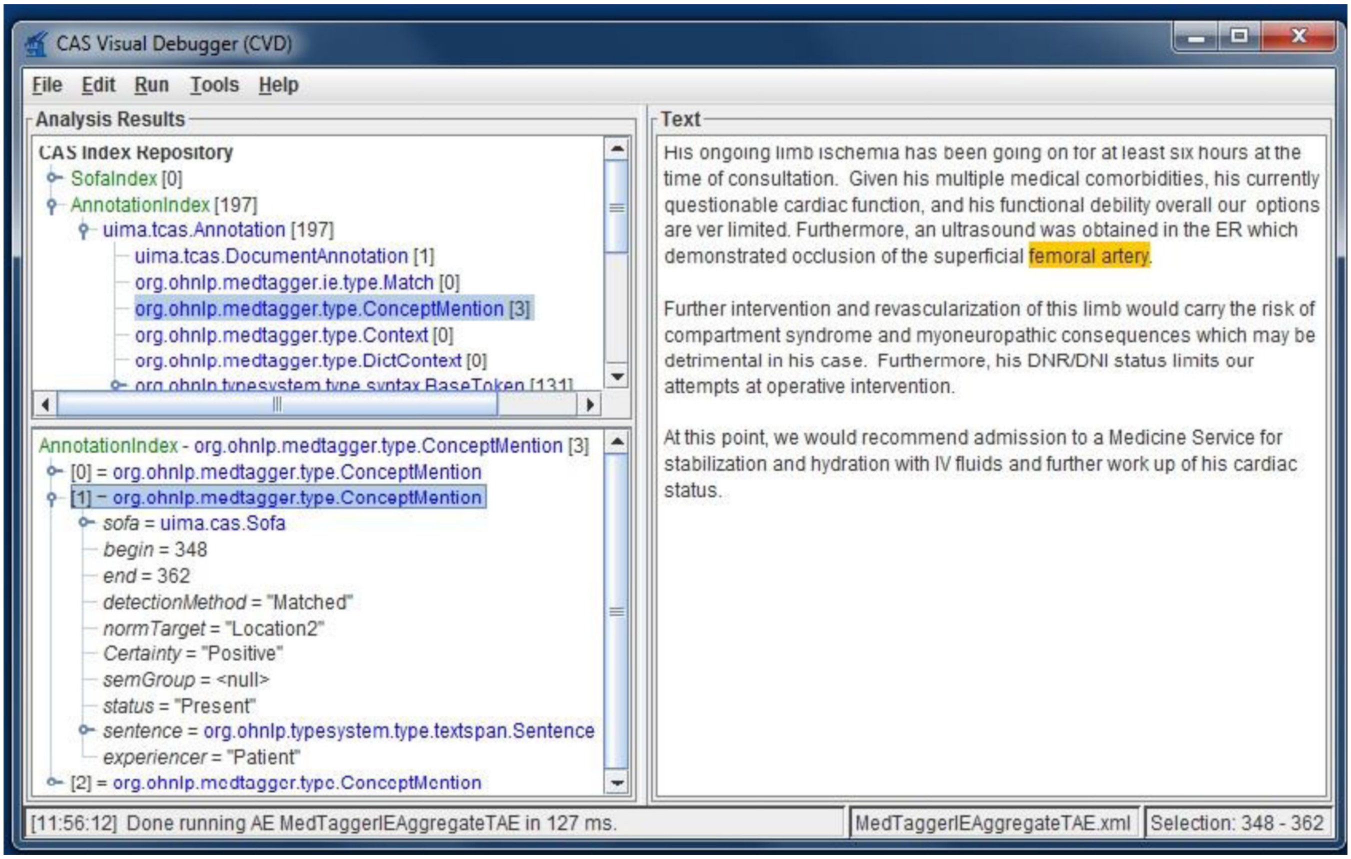

Figure 2.

PAD annotations visualized through the UIMA CAS Visual Debugger

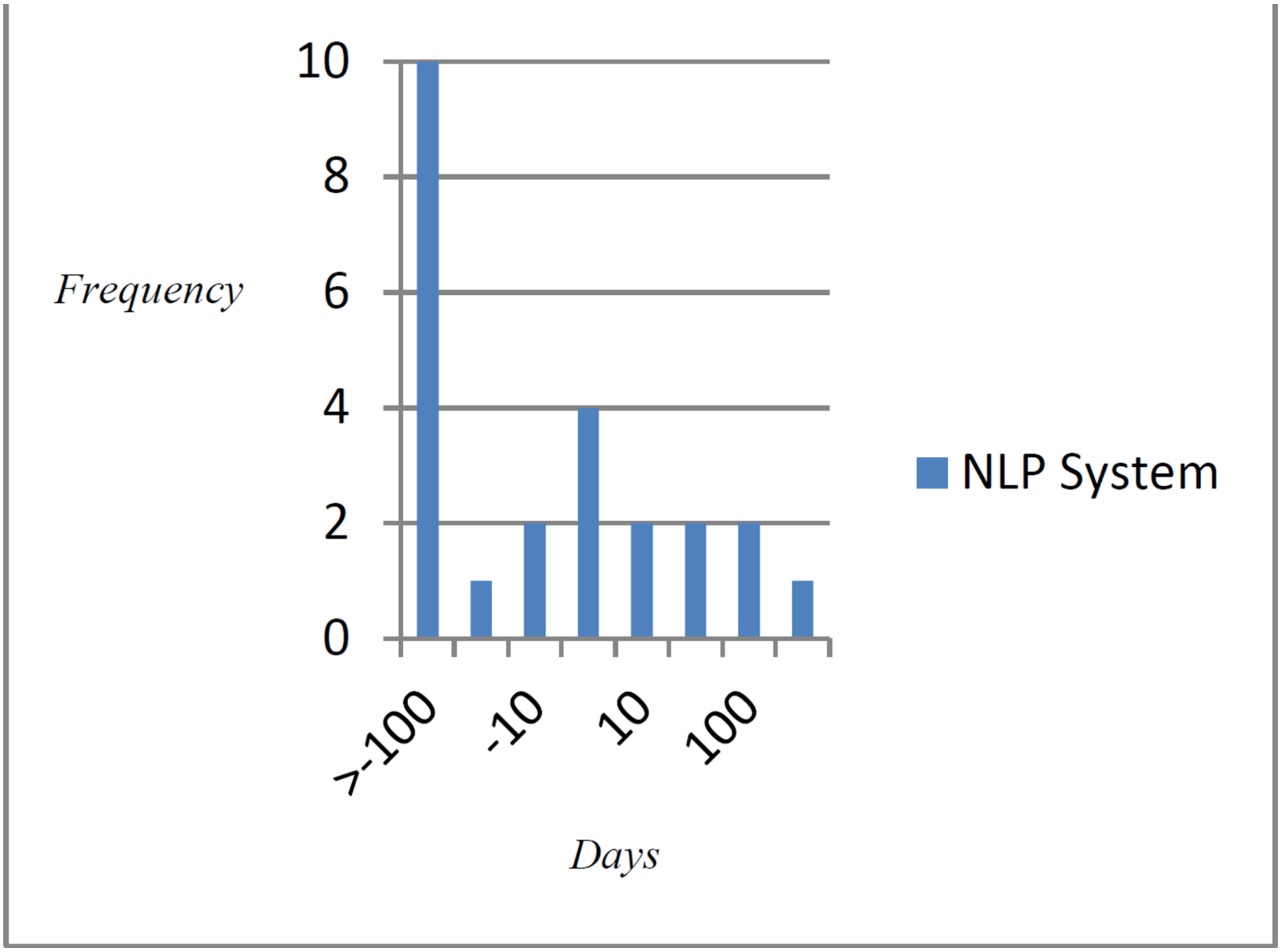

Figure 3.
Temporality of NLP system for PAD ascertainment

Table 1

List of terms and diagnostic criteria for PAD by manual abstraction

List of terms used for manual abstraction	
ABI	0: if performed and negative; 1: if performed and positive; 9: if not performed
Claudication/ weak peripheral pulse/ulcer	0: if not reported in clinical history, 1: if reported
PAD clinic note	Is there a mention in the clinical notes regarding history of peripheral arterial disease defined as "Arteriosclerosis obliterans" (ASO) or other definitions of ascertained PAD? 0: No. 1: Yes.
Imaging	Assess whether there are previous ultrasounds (US), computed tomography angiography (CTA) or magnetic resonance angiography (MRA) studies. 0: present and normal. 1: present and abnormal (<u>indicating stenosis >=50% or > then MILD</u>). Use 9 if they are not available or not performed at all.
Lower extremity revascularization procedure (surgical or catheter-based)	0: if not performed, 1: if performed
Lower extremity amputation	0 = no history of amputation; 1A: ischemic major (below knee or greater); 1B ischemic minor (distal to below knee e.g. toe or metatarsal); 1C non-ischemic major or minor
Criteria for PAD by manual abstraction	
PAD	Abnormal ABI (<= 0.90 or >= 1.40), poorly compressible arteries (PCA)/ non compressible vessels (NCV), positive angiogram result with "severe stenosis" or "occlusion", prior revascularization of the lower extremity, positive US, CTA or MRA studies of the lower extremity indicating stenosis.
Not PAD	Normal ABI values or negatives imaging results or no mention of PAD in clinical notes.

Table 2

Key Words - NLP algorithm for ascertainment of PAD status

Confirmation Key Words - Disease Location
lower extremities/extremity; lower limbs/limb; Leg /legs; Iliac/femoral/tibial/popliteal artery/arteries; Distal/ infrarenal /abdominal aorta/aorto (bi)iliac/ aorto (bi)iliac/aorto(bi)-iliac; aorto-(bi)femoral; foot, toe, toes, shin; plantar, heel, ankle, interdigital; below/above knee, Claudication/calf pain; Ischemic ulcer/ulcers; ASO/Arteriosclerosis obliterans/ arterial sclerosis obliterans/atherosclerotic disease; PAD/ Peripheral arterial disease/Peripheral vascular disease /Peripheral arterial occlusive disease.
Confirmation Key Words - Diagnosis
Arterial occlusive disease/occlusion/occluded; Stenosis; non compressible vessels (NCV), non-compressible arteries (NCA), poorly compressible vessels (PCV), stiff vessels/ arteries ischemia; positive ABI/ankle brachial index/ vascular labs/ extremities study /arterial studies; revascularization/ recanalization / bypass / angioplasty/PTA/stenting/stent/graft/endarterectomy/ endarterectomies; thrombectomy/ thrombosis/ thromboembolectomy/ embolectomy/embolectomies.
Exclusion Key Words
Family history of, Upper extremities/Upper extremity; Arm/arms, hand(s); Brachial artery, axillary artery, radial artery, ulnar artery; carotid, innominate artery, subclavian artery; mesenteric artery; celiac artery; AAA, abdominal aortic aneurysm/abd aortic aneurysm; renal arteries/artery; coronaries, coronary arteries/ artery /cerebrovascular-disease /arteries/artery; Amputation; traumatic/trauma; sarcoma/osteoma; pseudoclaudication /pseudoclaudicatory pain. diabetic foot, hammer toe/ toes; vascular calcification; varicose veins

Table 3

Results of NLP algorithm for ascertainment of PAD status

True Positives	24
False Positives	2
False Negatives	1
True Negatives	90
PPV	**0.92**
Sensitivity	**0.96**
NPV	**0.99**
Specificity	**0.98**