AFGuide System to Support Personalized Management of Atrial Fibrillation

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Abstract

Atrial fibrillation (AF), the most common arrhythmia with clinical significance, is a serious public health problem. Yet a number of studies show that current AF management is suboptimal due to a knowledge gap between primary care physicians and evidence-based treatment recommendations. This gap is caused by a number of barriers such as a lack of knowledge about new therapies, challenges associated with multimorbidity, or a lack of patient engagement in therapy planning. The decision support tools proposed to address these barriers handle individual barriers but none of them tackle them comprehensively. Responding to this challenge, we propose AFGuide – a clinical decision support system to educate and support primary care physicians in developing evidence-based and optimal AF therapies that take into account multi-morbid conditions and patient preferences. AFGuide relies on artificial intelligence techniques (logical reasoning) and preference modeling techniques, and combines them with mobile computing technologies. In this paper we present the design of the system and discuss its proposed implementation and evaluation.

Introduction

Atrial fibrillation (AF) constitutes a serious public health problem and its prevalence is increasing due to an aging population (Chugh et al. 2014). A common oral anticoagulant (OAC) therapy for an AF patient involves vitamin K antagonists (VKAs), however their administration comes with a number of problems (e.g., a need to maintain VKA in a specific target range (Cotte et al. 2014)). Newly developed direct OACs (DOACs) often offer faster, more predictable and sustainable anticoagulation, and in clinical trials they were found to have similar effectiveness as VKAs in stroke prevention and were associated with lower bleeding and risk of death from cardiovascular causes (Giugliano et al. 2013).

A number of studies assessing OAC use for the prevention of stroke in patients with AF have reported that OAC management is suboptimal. A study by Gladstone et al. (2009) found that only 10% of patients with known AF experiencing their first acute stroke were therapeutically anticoagulated at the time of admission. Moreover, a significant portion of primary care patients are not treated following the AF clinical practice guidelines (CPGs) (Valentinis et al. 2014). This deviation from evidence-based care indicates there is a knowledge gap present for primary care physicians (PCPs). Narrowing this gap is an important and timely challenge as delivering optimal OAC therapy can prevent approximately 80% of AF-related strokes.

This knowledge gap calls for novel knowledge translation activities regarding the management of patients with AF and stroke prevention that take into account specific barriers to knowledge uptake (Macle and Andrade 2016). A recent survey (Murray et al. 2011) identified three key barriers: (1) the lack of up-to-date knowledge about new therapies, (2) the challenges in factoring multi-morbidity, and (3) the lack of patients’ engagement in the development of their therapeutic plans. Although a number of tools to improve the use of DOACs have been proposed (e.g. (Yu et al. 2016)) none of them address all these barriers in a comprehensive way. Responding to this challenge, we are developing AFGuide – a clinical decision support system (CDSS) to educate and support PCPs in developing optimal OAC therapy. AFGuide helps PCPs decide whether DOACs or VKAs are most beneficial for their patients with AF while taking into account multi-morbid conditions and personal preferences. In particular, it addresses the knowledge uptake barriers by integrating: (1) the automatic execution of the AF guideline; (2) application of patient adherence-to-therapy and preference models to assess possible therapies; (3) mitigation of potential adverse interactions between therapies for discordant multi-morbidity; (4) provision of supporting evidence for therapeutic choices; and (5) learning from PCP-patient interactions.

AFGuide relies on the Canadian Cardiovascular Society’s (CCS) AF CPG (Verma et al. 2014) and uses various artificial intelligence methodologies and preference modeling techniques. It integrates them within a mobile computing environment to support the process of therapy development by the PCP and to customize therapy for a given patient. Given the patient’s adherence to therapy and preferences, combined with his/her underlying risk of stroke and major bleeding and the presence of multi-morbidity, AFGuide applies logical reasoning to suggest an optimal OAC therapy and provides justification and explanation for its choice.

In this paper we describe the high-level design of AFGuide and discuss its essential components. Moreover,
Table 1: Comparison of tools for the management of patients with AF (* patient preferences only)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOACs considered</td>
<td>AnticoagEvaluator</td>
</tr>
<tr>
<td></td>
<td>Anticoagulant Dosing In Arterial Fibrillation</td>
</tr>
<tr>
<td></td>
<td>Keele University tool</td>
</tr>
<tr>
<td></td>
<td>Impact-AF</td>
</tr>
<tr>
<td></td>
<td>MobiGuide</td>
</tr>
<tr>
<td></td>
<td>AFGuide</td>
</tr>
<tr>
<td>Multi-morbidity</td>
<td>✓</td>
</tr>
<tr>
<td>Patient preferences and adherence</td>
<td>✓</td>
</tr>
<tr>
<td>Automatically or semi-automatically executable</td>
<td>✓</td>
</tr>
<tr>
<td>Mobile</td>
<td>✓</td>
</tr>
<tr>
<td>Comparison of therapies</td>
<td>✓</td>
</tr>
<tr>
<td>Supporting evidence for therapeutic choices</td>
<td>✓</td>
</tr>
<tr>
<td>Reasoning and learning</td>
<td>✓</td>
</tr>
</tbody>
</table>

we summarize our implementation plans and the system’s evaluation in a clinical setting.

Related Work

The education of and support for PCPs with respect to OACs in general, and DOACs in particular, takes a number of different forms. They range from textual “primers” (Giugliano et al. 2013) to web-based or mobile CDSSs for helping patients and providers better manage AF. Below we review tools from the latter group as they are most closely related to AFGuide.

CDSSs for the management of AF typically use rules or scoring algorithms derived from CPGs to recommend therapies for patients. For example, AnticoagEvaluator developed by the American College of Cardiology (ACC) and based on the ACC 2014 CPG for the management of patients with AF, can be used as a web-based or mobile app to calculate a patient’s stroke risk (CHA2DS2-VASc), bleeding risk (HAS-BLED), and renal function. It determines the appropriate therapy for a patient by calculating individualized annual risk of major bleeding using relative risk reduction from clinical trials in combination with individual risk factors using data provided by the SPARCTool. It does not provide explanations for its recommendations nor does it incorporate patient preferences. A similar tool is the Anticoagulant Dosing In Atrial Fibrillation developed by Thrombosis Canada that uses patient data (age, sex, weight) and history (heart failure, hypertension, diabetes, stroke) to compute a CHA2DS2 score and recommend a therapy where DOACs are weighted in relation to warfarin on the basis of the supporting evidence. The system uses a simple CPG-based algorithm and does not consider patient preferences.

A slightly more sophisticated tool is the web-based OAC Therapy for the Prevention of Stroke and Systemic Embolism in Atrial Fibrillation decision support system developed at Keele University. The tool is a direct implementation of the prescribing recommendations of the NICE AF CPG. It collects patient information, stroke risk (CHA2DS2-VASc), bleeding risk (HAS-BLED), current medications, contraindications and interactions, and uses this data to execute the NICE AF guideline to derive a therapy recommendation for the patient. Unlike our proposed AFGuide, it does not explain why alternative therapies were not suggested nor does it use any advanced reasoning methods. It does incorporate an informational patient decision aid to help patients weigh their possible benefits, harms, and advantages and disadvantages of different therapeutic options; however patient preferences are simply expressed and not directly incorporated into the therapy generation process.

Impact-AF is a web-based decision support system that computerizes the CPG proposed by CCS and focuses on community-based AF management with the goal of bringing specialized cardiology care to the primary care level. It uses semantic web principles for knowledge representation and workflow modeling. The system includes a mobile patient diary for recording information about AF management from the patient’s perspective. AFGuide differs as it learns from PCP-patient interactions and has built-in patient preference and adherence-to-therapy models. Moreover, our proposed system revises a therapy dynamically when taking into account the patient’s multi-morbidity.

Finally, MobiGuide is a shared patient-provider decision support system for the prevention and management of the risk of thromboembolism in patients with AF. The system includes wearable monitoring devices that measure the patient’s biosignals such as heart rate and electrical activity of the heart. Analysis of data from these monitoring devices is used by the system to identify patterns that require a physician’s attention. The system can issue context-sensitive

1www.acc.org/anticoagevaluator  
2www.sparctool.com  
3thrombosiscanada.ca/?page_id=502  
4www.anticoagulation-dst.co.uk  
5impact-af.ca  
6www.mobiguide-project.eu
alerts to patients and guideline-based recommendations to their care providers. The CPG used by MobiGuide is customized and expanded to include all the different circumstances that could affect management of a patient with AF (e.g. lifestyle). MobiGuide computes outcomes associated with no therapy, aspirin, and warfarin, excluding DOACs. The proposed AFGuide applies the CCS AF CPG without modification from the source document and enhances it with two layers; one that models direct multi-morbid interactions with AF management, and the other that models adherence to therapy and patient preference for AF management. It also considers all possible therapies, including DOACs.

Table 1 summarizes the reviewed tools for the management of patients with AF and compares them to the proposed AFGuide. It demonstrates that none of these tools, except our proposed AFGuide, combines all desired features needed to educate and support PCPs in the development of evidence-based OAC therapy and to increase patient engagement.

Methods

AFGuide Design

A high-level design of AFGuide is given in Figure 1. In order to develop the proposed system, we apply a number of methods, techniques, and tools from artificial intelligence, knowledge translation, multi-criteria decision analysis (MDA), and software design. These are outlined below.

Executable CPG. The CCS CPG for AF is summarized and presented in a formal and executable representation called first-order logic (FOL). We previously successfully used this representation for guidelines requiring mitigation of adverse events for co-morbid patients (Michalowski et al. 2014; Wilk et al. 2014). The translation of a textual CPG into FOL happens in three stages. The first stage follows the process described in (Shalom et al. 2008). With the help of medical experts on our research team we create a clinical consensus document (CCD) summarizing the CCS AF guideline. The CCD also lists adverse events (e.g. drug-drug or drug-food interactions) that are most likely to occur when managing a multi-morbid patient with AF (e.g., hypertension) and describes ways to mitigate these events.

In the second stage, we use the CCD to construct an actionable graph (AG) (Wilk et al. 2013a) representing the CCS AF guideline, and risk-related and mitigation-related operators (Michalowski et al. 2014). An AG is a graphical representation of a guideline consistent with the task-network model typically used to represent CPGs for computer-based interpretation (Peleg 2013). Risk-related operators formally capture knowledge about assessing stroke and bleeding risk and establishing a wider context for its representation (explained below), and mitigation-related operators formally model adverse events and revisions to guideline actions that are needed to mitigate these events (Wilk et al. 2013a).

In the third stage we create a FOL theory from the AG (which encodes the primary medical knowledge) and risk-related and mitigation-related operators (encoding secondary medical knowledge). The former are used to identify and enumerate all possible OAC therapies for a given patient, and the
latter are applied to check for potential adverse events that may be encountered when managing a multi-morbid patient with AF.

**Patient Adherence-to-Therapy and Preference Models.** These models are used in AFGuide for the advanced evaluation of derived OAC therapies given a patient’s past adherence to therapy and preferences, respectively. When creating these models we rely on our earlier research on capturing and operationalizing patient preferences (Michalowski et al. 2015). We develop these models by defining preferential factors (criteria) characterizing patients and possible therapies. These are identified from published review papers (e.g., (Jin et al. 2008)) and patient specific websites (e.g., patientslikeme.com). Then, we create baseline adherence-to-therapy models corresponding to good, moderate, and poor adherence profiles. Specifically, for each model we use the MDA method GRIP (O’Sullivan et al. 2014b) to capture high-level preferential information regarding therapies (e.g., a model corresponding to poor adherence to therapy may strongly suggest therapies with lower complexity over more complex ones and thus more cumbersome for a patient to follow). GRIP allows us to build a scoring (value) function associated with each individual adherence-to-therapy model. These functions are later used to derive assessments of OAC therapies incorporating a patient’s adherence.

We also construct baseline patient preference models. These include criteria such as the convenience of therapy and perspectives such as the trade-offs between the risk of stroke and the risk of bleeding and a patient’s perception of their convenience and willingness to pay additional costs associated with DOACs therapy. Similarly to adherence-to-therapy models, we use GRIP to build a scoring function for each individual patient preference model. Developing baseline models in advance limits the burden associated with eliciting preferences during every PCP-patient encounter and these models are revised only when there is a significant change in the health status describing a patient.

**Stroke and Bleeding Risk Assessor.** The risk assessor uses reasoning techniques and risk-related operators represented as a FOL theory to compute stroke and bleeding risk scores based on comprehensive patient data that defines a patient context. It synthesizes these scores with the results of relevant clinical trials into a final risk assessment. This risk assessment takes into account the broader patient context and is later used in therapy development.

**Therapy Generator.** The therapy generator uses the CCS AF CPG and mitigation-related operators (both represented as a FOL theory) to derive feasible OAC therapies. Its automated reasoning capabilities come from applying theorem proving and model finding techniques with the purpose to mitigate any adverse interactions (if a discordant multimorbidity is present) and to generate therapies specific to the patient context. The therapy generator ranks recommended OAC therapies from most to least suitable according to their confidence levels, taking into account the stroke and bleeding risk assessment produced by the stroke and bleeding risk assessor component, and the weights produced by the scoring functions associated with the adherence-to-therapy and preference models. This ranked list is provided to the PCP for consideration. The PCP can select any therapy from the list and revise the patient context to include assumptions about the patient’s future state. AFGuide learns from these actions and assesses the impact of these changes on the OAC therapies.

**Therapy Explainer.** The therapy explainer provides justification and explanation for specific therapeutic recommendations with a summary of clinical evidence. It acts in a passive mode, providing on-request justification for each therapy in the ranked list produced by the therapy generator. The retrieved evidence is displayed at varying levels of detail as defined by the PCP. Specifically, we focus on reviews from the Cochrane Database of Systematic Reviews and use our framework for the indexing and retrieval of medical publications for point-of-care use described in (O’Sullivan et al. 2010). The framework summarizes a PCP-patient encounter using three pertinent elements of a patient’s context, namely diagnosis, therapy, and history/clinical data. These elements guide the indexing and retrieval of systematic reviews and associated underlying studies. Retrieved studies are subsequently used to provide justification for a selected therapy for the specific patient with AF. Patient context specific to his/her condition is identified with the help of medical experts on our research team.

**Model Manager and Learner.** The model manager and learner performs two functions. First, for a new patient it automatically selects the most appropriate adherence-to-therapy and preference models from the available ones. These models are selected using presentation-specific similarity measures that take into account how well the context of a new patient matches the model’s parameters. The selected models are associated with the patient and used to derive an initial list of feasible OAC therapies.

Second, during a PCP-patient encounter the model manager and learner component monitor interactions between the PCP and the patient leading to the selection of the optimal OAC therapy, and apply preference learning techniques (Fünnkranz and Hüllermeier 2010) to customize the baseline adherence-to-therapy and preference models for a given patient. This customization includes replicating the initially selected models and modifying their scoring functions according to observed interactions and therapy choices. In this way, the model manager and learner component are able to transform population-based baseline models into customized patient-specific ones. These customized models are stored in a model repository, so they can be later used for similar patients. Thus over time, AFGuide improves its ability to handle a diversified population of patients with AF.

**AFGuide Implementation**

AFGuide is implemented as a mobile system, drawing on our earlier research (Wilk et al. 2013b), and its technical architecture is given in Figure 2. The design of AFGuide follows ontology-driven principles where the functionality
of a system is partitioned into independent components described by ontological models (Wilk et al. 2013b). In contrast to a traditional monolithic design, this ensures flexibility and scalability of the system (individual components can be combined in a number of ways thus responding to the changing needs of PCPs, and new components can be easily added to the system). The system uses the client-server architecture, with the client running on mobile devices (and on the Web) and a front-end accessed by the PCP, and the server is tasked with performing intensive computations. To implement the server we use the service-oriented OpenCDS framework\(^7\). This framework supports interoperability with existing healthcare information systems and it supports adherence to HL7 standards for clinical decision support services and clinical data exchange. We are also exploring the use of HL7 FIHR for interoperability.

The OpenCDS framework has been developed in Java and we use this programming language to implement structural components of AFGuide. The FOL theory derived from the AG is expressed using the SMT-LIB language that is a standard for the computer-based representation of FOL. The Z3 solver\(^8\) is used for consistency checking and model finding as it is one of the best solvers of this type and our team has successfully used it in previous research (Wilk et al. 2016). The mobile client is developed using the Apache Cordova and Sencha Touch frameworks. These frameworks use Web-based technologies (HTML, CSS, JavaScript) and allow for creating applications for popular mobile platforms (iOS, Android). Our goal is to integrate AFGuide with our MET3\(^9\) system and eventually with the SMART Health IT platform\(^10\).

**AFGuide Evaluation**

Considering the importance of a reliable system from the patient safety perspective, we will conduct a two-phase evaluation study of AFGuide. In the first phase we will conduct a usability study involving PCPs with the purpose of establishing if AFGuide functionally meets PCPs’ expectations. We will involve PCPs outside our team (i.e., not involved with the development of AFGuide) who will interact with the system when deriving a therapy for hypothetical patients with predefined preferences and multi-morbidities (all represented as clinical vignettes). The usability of the system will be evaluated through direct observations and interviews, and assessed using the System Usability Scale (U.S. Department of Health & Human Services 2016). The design of this phase of the study will build on our earlier research (O’Sullivan et al. 2014a) and the results will allow us to improve the human-computer interactions of AFGuide.

The second phase will clinically validate AFGuide and this phase will allow us to hypothesize if using AFGuide has a positive impact on PCPs’ adherence to the CCS AF guideline. Validation will be conducted in collaboration with selected Canadian hospitals.

**Conclusions**

Our long-term goal is to contribute to the narrowing of the knowledge gap among PCPs with regards to the development of an optimal OAC therapy for patients with AF. Accomplishing this goal requires the development of innovative knowledge transfer strategies that take full advantage of modern communication and information technologies. Our first and important step is to develop the AFGuide system to address the knowledge gap discussed earlier. On one hand, AFGuide plays the role of an advisor to PCPs that helps address the complexities of evidence-based OAC therapy development for patients with AF. On the other hand, it will derive an evidence-based OAC therapy while considering multiple factors that will also educate the PCP about context-specific prescribing of OACs for patients with AF. We believe these capabilities will result in better and more efficient management of AF.

Currently we have designed AFGuide as described in this paper. Some of its components have been developed (executable CPG, FOL models, therapy explainer and generator) while others (model manager and learner, stroke and bleeding risk assessor) have yet to be implemented. Our

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\(^7\)www.opencds.org  
\(^8\)github.com/Z3Prover  
\(^9\)www.mobiledss.uottawa.ca/  
\(^10\)smarthealthit.org/
next steps include the development of the remaining necessary components and the integration of all components as described above. We are working in parallel with clinical partners to design the evaluation studies, so they are ready once AFGuide is deployable in simulation environments.

Acknowledgments

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References


