Towards an ontology-based decision support system for syndrome-differentiation and treatment of Psoriasis Vulgaris in Traditional Chinese Medicine

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Technical advance

Keywords: clinical guideline, knowledge base, GFO, ontology, TCM, CBR, fuzzy logic, psoriasis vulgaris

DOI: https://doi.org/10.21203/rs.3.rs-38383/v2

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Abstract

**Background:** Psoriasis is a chronic, non-communicable, painful, disfiguring and disabling disease, which is not curable and strongly declines the patients’ quality of life (QoL). However, diagnose and treatment in traditional Chinese medicine (TCM) based on syndrome differentiation has been used in practice for a long time and has also achieved some effect. Though, up to now, only few studies are available reporting on the use of semantic technologies and pertain to knowledge systems that use TCM-syndrome differentiation for information retrieval and automated reasoning. Nowadays, the diagnosis in TCM relies mainly on the personal expertise and clinical experience of the doctors. For various reasons, misdiagnoses or missed diagnoses cannot be completely excluded, leading to unexpected results.

**Methods** In the present paper, we developed a domain ontology for syndrome differentiation of psoriasis vulgaris (PV). For this purpose, we used the ontology editor Protégé and applied a top-down approach which adopts the framework of general formal ontology (GFO) and its middle-level core ontology GFO-TCM. Furthermore, we implemented a prototype which is based on this ontology. Additionally, we also used a case-database for CBR (Case Based Reasoning) combined with fuzzy pattern recognition.

**Results:** A prototype for diagnosis and treatment of psoriasis vulgaris, named ONTOPV-system, is proposed which is based on the principle of syndrome differentiation and treatment in TCM; this system realizes an expert-assisted decision support method which relies on a domain ontology, uses fuzzy logic reasoning, and case retrieval and is intended to support clinical diagnostic decisions for TCM practitioners.

**Conclusions:** We designed and implemented a prototype for psoriasis diagnosis in terms of syndrome differentiation. The system realizes the basic functionalities of data collection, querying, browsing and navigation, and supports rule-based knowledge reasoning and integrates approximative reasoning, based on CBR and fuzzy logic. The system provides users with clinical decision support for TCM syndrome differentiation in diagnosis of psoriasis. In addition, it comprises a domain knowledge base of psoriasis, which is developed in the GFO framework with good extensibility.

**Background**

Ontologies play an increasing role in the field of knowledge representation; actually, they present the most advanced techniques to analyse, conceptualize and axiomatize the knowledge of a domain of interest. Knowledge exhibits various levels of abstraction; we may distinguish general knowledge, presented often by rules and formal axioms, from knowledge about individual cases. Furthermore, ontologies are more and more combined with other methods of artificial intelligence, notably with techniques of machine learning. A particular interesting method is case-based reasoning (CBR) which originates from cognitive psychology and is today a hot subtopic of artificial intelligence. Case based reasoning is a form of analogical reasoning: when encountering a novel problem, one searches for an already solved case which is closest to the problem. Then, the solution of the known case is adapted to a solution of the new
problem. After the new problem is solved, the revised case will be recorded and added as an experience [1]. Compared with western medicine, the diagnosis and treatment in traditional Chinese medicine (TCM) pursues a personalized approach. According to the patient’s behavior of yin and yang, of cold and heat, as well as of the course of the disease, a corresponding interventional plan will be proposed, using a large number of typical and distinct cases. The CBR’s process is similar to that of TCM’s diagnosis process which uses previous experience [2] and relies on the thinking way in terms of imagery and gets help from analogical reasoning [3-4]. Therefore, the unique characteristics of TCM about personalized diagnosis and treatment makes itself more suitable for application of CBR. Until now, CBR has been gradually applied into the field of TCM, particularly focusing on the design of expert systems and clinical decision support systems (CDSS). For example, Yang Li et al. established a TCM expert system based on CBR [5]; Peng et al. developed a syndrome differentiation and treatment system in TCM [6]. Wang et al. proposed a CBR-based TCM expert system combined with fuzzy rule-based reasoning [7]. These works show that the reasoning mechanisms for CDSS of TCM, based on CBR, are becoming more and more mature. However, due to the insufficient amount of cases, poor data quality, and limited clinical applications, most of these systems do not provide sufficient support for an accurate clinical decision-making in TCM. And the lack of consideration of functionality and expansibility of the knowledge base has also weakened the accuracy and reliability of the embedded information, needed for clinical decision support.

Psoriasis, classified by the WHO as a severe disease [8], is a chronic, non-communicable, painful, disfiguring, non-curable and disabling disease, which heavily affects the patients’ quality of life (QoL). However, diagnosis and treatment with TCM based on syndrome differentiation has a long practical history and achieved some effect. [9-11]. According to TCM theory, Psoriasis is caused by many factors, such as blood deficiency, blood heat, dryness and wind, as well as lack of nutrition. It can be divided into different syndrome types, based on characteristics of clinical symptoms. Accordingly, different treatment principles and methods shall be applied. The diagnosis in TCM is based on the comprehension of manifestation of pulse, tongue coating, complexion, physical constitution and other signs and symptoms, some of which are certain, while many of them are fuzzy, ambiguous, nonlinear and uncertain [12]. In the process of diagnosis, TCM doctors often rely more on their own knowledge and experience to find solutions, rather than using logical reasoning. Therefore, it is difficult to establish a TCM expert system, due to uncertainty of knowledge representation, data acquisition and the lack of logic reasoning. The complexity and fuzziness of TCM-knowledge leads to new challenges because there is the need to develop new forms of on knowledge representation and reasoning mechanism.

In clinical practice, TCM doctors make the diagnosis of psoriasis mainly on their professional knowledge and clinical experience. Young and inexperienced doctors are prone to make misdiagnosis or to overlook diagnoses, resulting in the lower-than-expected curative effect. In this paper we propose a prototypical TCM-decision support system for diagnosing and treating of psoriasis, called ONTOPV, which is based on a domain ontology and which uses CBR (Case-Based Reasoning) combined with fuzzy pattern recognition. This system exploits the valuable and extensive heritage of TCM knowledge.
Methods

Architecture of the ONTOPV system

Up to now, many ontology-based clinical decision support systems for different types of diseases have been developed and achieved convincing results in the clinical practice\(^{13-16}[31-34]\). This valuable work provides us with many inspirations. In this paper we present a prototype towards an expert-system, named ONTOPV, which is based on an ontology of TCM-diagnostic knowledge of psoriasis vulgaris, and which uses a case-database for CBR (Case Based Reasoning). This system is intended to help doctors or other users to diagnose psoriasis related diseases, and to provide clinical decision support if necessary. The prototype of the ONTOPV-system is elaborated to realize at least the following three procedures:

1. *Diagnosis of PV*: The doctor gathers the required information by querying and observing the patient, including age, gender, lifestyle, family history, signs and symptoms. Then, the patient’s main complaint and the acquired information is put into a template, the content of which is transformed as input to the rule basis and diagnosis ontology. The inference engine derives possible diagnoses which is provided to the doctor who receives advice for diagnosis and treatment.

2. *Development of intervention plans*: according to the recommended diagnostic results, an intervention plan is (semi-) automatically generated for the patient diagnosed. This intervention plan includes some TCM treatments and/or common therapies of Western medicine, like topic- and photo therapy, etc. Further, a personalized care plan on demand will be, and a solution is recommended for the patients.

3. *Information Retrieval*: with a semantic querying mechanism, users may access the system to ask questions about the Information or required Data that are stored in the Ontology and in the CBR based KB of PV. Then, the answers together with relevant graphic displays will be returned to the user.

Figure 1. gives an overview of the system-ONTOPV. It shows that the diagnostic information collected by the doctor from the patient, such as symptoms, signs, skin lesion area, pulse- and tongue manifestation, chief complaint, etc. and other diagnostic information, is put into the knowledge based system as input parameters, compared with the basic syndrome types defined in guideline 2013 \[21\], stored in the ontology, and matched against the customized reasoning rules in the SWRL rule base. If the given prerequisites are met, one or more inference rules are triggered to obtain the corresponding diagnosis result and the related treatment plan. The input is also compared with the past cases in the case database. If there are matching case records, the cases with higher similarity are extracted as reference case and provided to the user for comparative analysis and diagnostic decision making.
Construction of domain ontology for syndrome differentiation of psoriasis vulgaris

In our work we developed a domain ontology for syndrome differentiation of psoriasis vulgaris. For this purpose, we used the ontology-editor Protégé and applied a top-down approach which adopts the framework of general formal ontology (GFO) and its middle-level core ontology GFO-TCM described in [17-20].

1) Basic conceptual hierarchy

For the construction of the basic conceptual hierarchy we used various documents, such as Evidence-Based Clinical Practice Guideline of TCM for psoriasis vulgaris (2013) [21] (hereafter referred to Guideline 2013), the WHO Global Report on Psoriasis(2016) [8], the Guideline for the diagnosis and treatment of psoriasis in China (2018 simplified edition) [22], etc.

Furthermore, we used TCM-related documents about psoriasis vulgaris which provide information about the classification of psoriasis, symptoms (primary symptoms, secondary symptoms and combined symptoms), syndrome types, diagnosis, treatment methods, prescriptions, drug ingredients, drug compatibility, etc. Some basic semantic types (equivalent to class in OWL) have been obtained from the guidelines and other related literature, such as disease name, basic syndrome types (III), blood heat syndrome, blood dryness syndrome, blood stasis syndrome; simultaneous syndromes; basic symptoms including main symptoms, minor symptoms; methods of treatment; recommended formulas and drugs; pharmaceutical ingredients and so on. The basic semantic types of psoriasis vulgaris are listed below:

- Health Problems: The psoriasis-related health problems are mainly divided into 3 categories, namely, disease, symptom, (incl. main symptoms, minor symptoms, accompanied symptoms), and syndrome or pattern. We hold that one could introduce a class "disease" as a subclass of process in GFO; hence, any disease, in particular PV, can be considered a process. The patient is integrated in this process, he "participates" in this process. This approach is justified by the integration law of GFO, which postulates that for any material object, in particular a patient P, there exists a process Proc(P) such that P and Proc(P) are connected in a particular way. [35-36]. Symptoms, signs, and syndromes can then be understood as properties/attributes of a disease. This approach allows a further classification in various sub-classes of disease, as functional diseases, anatomical diseases; actually, the disease classification of the ICD can be reconstructed within this framework.

- Formula: A formula or prescription usually contains some medicinal components, used for treating an illness, such as psoriasis vulgaris.

- Drug/Medicinal: Usually referring to those medicinal substances recorded in Chinese materia medica but also to some medicaments of western medicine.
- TCM Diagnose for syndrome differentiation: According to the Guideline (2013), each type of syndrome of psoriasis vulgaris has a set of corresponding symptoms, which can provide a guideline for the diagnosis of TCM syndrome differentiation.

- Method of treatment: The method of treatment is composed of the conventional therapies in TCM and western medicine, such as: TCM prescriptions and drugs, medicated bath, biological therapy, topical therapy, systemic therapy, phototherapy, etc.

- Participant/Person: Such as doctors, patients, etc.

- Compatibility and Caution: Prescribe the medicinal composition and dosage of prescriptions, special instructions and contraindications between certain medicinal or chemical ingredients.

In general, our ontology has two levels of abstraction, a core ontology, describing some basic notions of TCM domain as health problem, formula, drugs, person, etc, and a particular domain ontology for psoriasis vulgaris which specializes the basic notions as basic syndrome types, symptoms, etc. which are in this way - adapted to the disease PV. The ontology includes 99 classes, 64 properties, 1622 axioms, 285 annotation assertion, etc. Figure 2. shows the basic hierarchy of the ontology. The relevant concepts has been explicitly introduced in our former papers [19-20].

**Instantiation**

According to the instructions in the Guideline (2013), the corresponding instantiated entities are established for the basic semantic types from the classification in the ontology, such as instances for major symptoms, minor symptoms, combined symptoms, prescriptions, drugs, pharmaceutical ingredients, treatment methods, etc. These types establish the classes of the core ontology. Below the core classes there are subclasses which are associated to the disease PV, for example, PV-symptoms, PV-combined-symptoms, PV-treatment methods etc. The instances of the PV-classes are stipulated, depending on context, relevance, and usability. For example, the instances of the PV-symptoms are various concrete symptoms, being relevant and typical for PV. There is, for example, an instance “bright red lesion” of the class PV-main symptom, an instance “dry mouth” of the class PV-minor symptom. Further we can define relationships between instances of different classes by introducing object properties. Figure 3 shows a fragment of an individual Huo Xue San Yue Xiao Yin Tang (活血散瘀消炎膏) of class of drug that including several components.

**2) Object- and datatype properties**

Finally, the relationship between different entities in the TCM diagnosis ontology for psoriasis vulgaris needs to be clarified. About 20 common binary object properties that relate individuals to individuals have been specified. These include: annotate (a disease can be annotated by some syndromes): according to the guideline 2013, PV can be annotated by several zheng/syndromes, including some basic zhengs and
combined zhengs, due to its different onset processes or observed symptoms. Further object properties are:

hasComponent (domain:Drugs, range:Medicinal_Substance) - that means a drug has certain components;

hasAdverseReaction (domain:Drugs, range:Drugs) - some drug components may cause adverse reaction with each other;

hasPattern (domain:Patient, range:Traditional_Medicine_Patterns) - for example, the patient's syndrome type is blood-heat;

hasPrescription (domain:Patient, range:Drugs) - some prescriptions can be proposed according to some kind of certain syndrome;

recommended (domain:Patient, range:Treatment) - some treatment methods could be recommended for a given diagnosis;

hasSymptom (domain:Patient, range:Symptom) - A patient with psoriasis_vulgaris may have some symptoms.

Through these built-in object properties, individuals which belong to different concepts in the ontology are correlated to each other and stored in the OWL ontology in the form of RDF triples as object property assertions. Then, some basic datatype properties that relate individuals to literal data are built as well, such as hasBSA(domain:Patient, data type:decimal) that means Body Surface Area, i.e. the size of body surface occupied by psoriasis; hasDLQI(domain:Patient, data type:decimal) that means Dermatological Quality of Life Index; hasTherapyPeriode (domain:Drugs, data type:string); hasDosage(domain:Drugs, data type:string); etc.

### Construction of the rules base

The rules of diagnosis-based syndrome differentiation and treatment must take into account specific regulations for diagnosis and medication in the evidence-based guidelines of TCM for psoriasis vulgaris [21]. For example, a corresponding treatment mechanism is established for the patients' observed symptoms as defined by the guidelines to ensure compliance with the standard operation required by the guidelines. In the ONTOPV related TCM diagnosis ontology, the reasoning rules are constructed for diagnosing certain syndrome types in terms of corresponding sets of symptoms. And there are further rules which are used to check the compatibility of drug components and allows to query whether some given components may cause side effects due to drug interactions. Using the rule base a reasoning process can be performed the results of which provide diagnoses and /or treatment suggestions according to the patient's symptoms. The followings are examples and explanations of some rules in the SWRL rules case.
1) Rules for the assessment of PV

\[ PV(a) \land \text{hasBSA}(a, c) \land \text{swrlb:lessThanOrEqual}(c, 0.03) \rightarrow \text{hasAssessmentOfSeverity}(a, \text{mild}) \]

A patient (a) with psoriasis vulgaris who has a skin lesions less or equal than 3% of the Body Surface Area (BSA) should be evaluated as “mild” in terms of degree of severity.

Figure 4. shows the results of the reasoning for this rule in terms of an assumed patient.

\[ PV(a) \land \text{hasBSA}(a, c) \land \text{swrlb:greaterThanOrEqual}(c, 0.1) \rightarrow \text{hasAssessmentOfSeverity}(a, \text{severe}) \]

A patient (a) with PV who has a skin lesions greater than 10% of BSA should be evaluated as “severe” in terms of degree of severity.

2) Rules for syndrome differentiation of PV

\[ PV(a) \land \text{hasSymptom}(a, \text{bright_red_lesions}) \land \text{hasSymptom}(a, \text{continuously_increased_rashs}) \land \text{hasSymptom}(a, \text{yellow_urine}) \rightarrow \text{hasPattern}(a, \text{syndrome_of_heat_in_blood}) \]

If patient (a) of psoriasis vulgaris has main symptoms of bright red lesions and continuously increased rash and has a minor symptom of yellow urine then the pattern assigned to the patient is “syndrome of blood heat”.

Please refer to Figure 4.

\[ PV(a) \land \text{hasSymptom}(a, \text{pink_lesions}) \land \text{hasSymptom}(a, \text{dry_scales}) \land \text{hasSymptom}(a, \text{dry_mouth_and_throat}) \rightarrow \text{hasPattern}(a, \text{syndrome_of_blood_dryness}) \]

If patient (a) of psoriasis vulgaris has main symptoms of red lesions and continuously increased rash and has a minor symptom of dry mouth and throat, then the pattern assigned to the patient is “syndrome of blood dryness”.

This example is shown as in Figure 6

3) Rules for prescription:

\[ PV(a) \land \text{hasPattern}(a, \text{syndrome_of_heat_in_blood}) \rightarrow \text{hasPrescription}(a, \text{decoction_of_cooling_blood_and_toxin_resolving}) \]

A patient (a) of psoriasis vulgaris who has been ascribed to has a syndrome of heat in blood would be prescribed a recipe named "blood-cooling and toxin-resolving decoction ".

Please refer to Figure 4.
PV(?a)∧hasPattern(?b,syndrome_of_blood_dryness) -> hasPrescription(?b, decoction_of_nourishing_blood_and_toxin_resolving)

A patient (a) of psoriasis vulgaris who has been ascribed to a syndrome of blood dryness would be prescribed a recipe named "blood-cooling and toxin-resolving decoction" (凉血润燥汤).

Please refer to Figure 6.

PV(?a)∧hasSymptom(?a, gastric_acid_regurgitation)∧hasPattern(?a, syndrome_of_blood_dryness)->hasPrescription(?a,Compound_Capsules_of_Qing_Dai)∧hasPrescription(?a,Compound_aluminium_hydroxide_tablets)

A patient of psoriasis vulgaris and with symptom “gastric acid regurgitation” who has been identified with syndrome of blood dryness could be prescribed the drugs combination of compound capsules of qing dai which has main component of danshen and compound aluminium hydroxide tablets. (As shown in Figure 7.)

4) Rules for treatment of psoriasis:

PV(?a)∧hasAssessmentOfSeverity(?a, mild) -> recommend(?b, Corticosteroids)

A patient of psoriasis who has been evaluated as “Mild” in terms of severity of skin lesions should be recommended to receive some topical therapies (e.g. corticosteroids or Vitamin D3 analogues, etc.) [8].

Please refer to Figure 4.

PV(?a)∧hasAssessmentOfSeverity(?a, severe)∧hasDLQI(?a, ?d)∧swrlb:greaterThan(?d, 20) -> recommend(?a, Infliximab)

A patient of psoriasis who has been evaluated as “Severe” in terms of the severity of skin lesions, and has a Dermatology Life Quality Index (DLQI), which is greater than 20, should be recommended to receive some biologic therapies, e.g. infliximab, ustekinumab, etc [30].

Please refer to Figure 5.

5) Rules for drugs adverse reaction

Drugs(?a)∧Drugs(?b)∧hasComponent(?a, danshen_root)∧hasComponent(?b,aluminum_hydroxide)->hasAdverseReaction(?a, ?b)

Two drugs containing danshen_root and aluminum hydroxide may cause adverse reactions. The Figure 8 shows the result of this rules triggered

Case-based reasoning using fuzzy logic
As mentioned above, a diagnosis of TCM is usually based on the comprehension of manifestation of pulse, tongue coating, complexion, physical constitution and other signs and symptoms, some of which are certain while more of them are fuzzy, ambiguous, nonlinear and uncertain. Hence, in the process of diagnosis, TCM doctors often more rely on their own knowledge and experience rather than logical reasoning to find solutions. Therefore, the difficulty of establishing a TCM expert system lies in the uncertainty of knowledge representation, data acquisition and logic reasoning. The complexity and fuzziness of knowledge faces new challenges and requirements to knowledge representation and reasoning mechanism.

In the case of psoriasis vulgaris, for any possible diagnosis and treatment in view of syndrome differentiation, TCM doctors must firstly identify the patient’s symptoms, in order to obtain the corresponding diagnosis results. This could be considered as a kind of pattern recognition. According to M. Friedman and A. Kandel[2,3], a pattern is an abstract object which is inspected for the recognition process. And we usually regard a pattern as a schematic description of an object which we want to recognize. A schematic description can be understood as a type which can be instantiated, and this type can be specified by some selected features. Thus, recognizing an object Obj with respect to a pattern P means to capture/understand Obj as an instance of P. We may introduce a number of standard patterns P1, ..., Pn and recognize an object Obj as being an instance of one of the standard patterns P1,..., Pn. If the patterns are exhaustive then we achieve a classification procedure: given an object we determine to which pattern or type the object Obj belongs.

To achieve a clinical diagnosis of psoriasis vulgaris, a doctor acquires symptoms, being subjective chief complaints, reported by the patient, and signs which can be objectively observed by the doctor. Sometimes, there are cases that these gathered information does not allow to exactly determine to which standard pattern the patient belongs. To treat such cases we must introduce a degree of belonging to a standard pattern. This procedure is called fuzzy pattern recognition. We took an example from the evidence-based clinical guidelines for psoriasis vulgaris in TCM (2013), according to the diagnostic criterion of blood-heat syndrome(血热证), which may have two main symptoms of bright red lesions, continuously increased rashes, and four minor symptoms, including irritability and upset, yellow urine, red tongue, rapid pulse. As long as the patient has all major symptoms and at least one minor symptom, the syndrome of blood-heat can be determined. The same principle could be applied to the identification of blood dryness syndrome (血燥证), except that the latter symptoms can be expressed as major symptoms of pink lesions, dry scales and minor symptoms of dry mouth, pale tongue, thready pulse. If the patient is observed with some symptoms of blood heat syndrome, combination with some symptoms of blood dryness syndrome, the question is how to identify this patient. This case can be observed quite often in practice, because the onset of this disease is a gradual process according to the theory in TCM. In the early stage of this disease, it is mostly manifested as blood heat syndrome, and mostly blood dryness syndrome in the middle stage, but mostly blood stasis syndrome(瘀血证) in the late stage. It can also be manifested as other types of combined syndrome simultaneouly. In TCM sometimes decisions cannot be easily made on the basis of two-valued logic. Hence, the problem about pattern recognition
in a process of syndrome differentiation can be considered as a more-or-less type rather than yes-or-no type which pertains to the topic of fuzzy pattern recognition.

Some methods of the current paper are inspired by Zadeh's fuzzy set theory \cite{25-27}, which is a generalization of crisp set theory. A fuzzy set consists of objects and their respective grades of membership in the set. The grade of membership of an object in the fuzzy set is given by a subjectively defined membership function. The value of the grade of membership of an object can range from 0 to 1 where the value of 1 denotes full membership, and the closer the value is to 0, the weaker is the object's membership in the fuzzy set.\cite{23}

A mechanism of information retrieval is proposed, which integrates ontology and CBR using fuzzy pattern recognition. This integration provides automatic reasoning and semantic retrieval in line with the norms of TCM evidence-based clinical guidance for psoriasis vulgaris, and, additionally, also simulates the thinking mode of experts based on fuzzy logic. Meanwhile, a solution is carried out to find a similar case from the case base using the proposed method of lattice degree of nearness \cite{28}[23]. In the ONTOPV prototype, the user can input data, collected from patients as input parameters into the system. Examples of such data are: main symptoms, minor symptoms, personal information (age, gender, past history, family history, etc.), chief complaint (which means subjective description of the patient), etc.

Then the system processes these data by searching for rules, included in the SWRL rules base. If the given preconditions are met, one or more rules are triggered, and subsequently the corresponding standard diagnosis results and treatment scheme will be obtained. At the same time, it can also be compared with the past cases stored in the case database. If there is a matching case record, the case with higher similarity will be extracted as the reference case and provided to the user for comparative analysis. The workflow of case retrieval in ONTOPV is shown in Figure 9.

We consider an example to illustrate this workflow. Let P a patient who satisfies some symptoms, say "continuously increased rashes, pink lesions, dry scales, yellow urine, dry mouth, red tongue, rapid pulse", whereas "continuously increased rashes, yellow urine, red tongue, rapid pulse" are typical symptoms of blood heat syndrome, and "pink lesions, dry scales, dry mouth" are typical symptoms of blood dryness syndrome, in the meantime "red tongue, rapid pulse" can also be interpreted as symptoms of the combined syndrome of heat-toxin according to the guideline 2013. In order to determine which type/syndrome this patient should be ascribed to, we put all the data as parameters into the system Ontopv, for the purpose of diagnosis. If there is a SWRL rule matching one of the standard criteria for the blood dryness syndrome then this rule can be triggered. From this we know the basic syndrome of this patient is \textit{blood dryness}. But the question is still open for the doctor, how he can interpret the combined symptoms of blood heat and of heat-toxin? And what is the most adequate prescription, he may recommend for this patient? Thus, we can search the case base, looking for some cases of patients with similar symptoms. If the doctor succeeds, he may find at least one case, similar to the patient, then he could extract this case as a comparable reference for the clinical diagnostic decision making. Finally, the updated case can also be stored in the case base if the doctor agrees with the extracted case, or the
extracted case may be ignored if the doctor disagrees with the case record. However, we emphasize that the system only provides some auxiliary decision support; in any case, the final clinical decision must be made by the doctor.

Below we will further elaborate on how the above process of case retrieval is performed. Firstly, the cases of patients can be considered as a pattern space $A = (a_1, a_2, ..., a_m)$, where $a_i, 1 \leq i \leq m$ are vectors in $\mathbb{R}^n$, i.e. each pattern is characterized by $n$ features. For example, each case can be characterized by gender, age, patient's chief complaint, symptoms, Western medicine diagnosis, TCM diagnosis, syndrome type, treatment method, recommended medication, and quantitative score of each syndrome type based on the comprehensive score according to the membership function defined.

Suppose the universe of discourse $U = \{\text{several patient cases}\}$, the diagnostic features of the patient-cases include several symptoms, which need to be diagnosed and classified according to the color of the lesion, the nature of the lesion, tongue- and pulse manifestation, urination, complexion, and chief complaint. Thus, we can get the pattern space of syndrome $S= \{\text{blood heat syndrome, blood stasis syndrome, blood dryness syndrome, combined syndrome}\}$, and the combined syndromes can be further divided into wind, dampness, and heat toxin, etc. according to guideline 2013. Among them, the pattern of blood heat-, blood stasis-, blood dryness-, and combined syndrome can be considered as fuzzy sets. To determine which type syndrome the patient exhibits, a TCM doctor must firstly determine which features, say symptoms go to this classification. This problem can be measured by using the degree of membership and of similarity between two fuzzy sets $A$ and $B$, which is discussed below.

Using the principle of maximum membership in fuzzy set, a simple membership function can be firstly established to determine which basic syndrome type a patient has. According to the guideline, a basic syndrome type can be defined. If a patient exhibits two major symptoms and at least one minor symptoms, then the diagnosis is true, which means the patient's symptoms have full membership degree with this syndrome type. Accordingly, a simple membership function can be established.

We have assigned a weight value to each symptom, including the main- and the minor symptom, for example, there are altogether 2 main symptoms and 4 minor symptoms in the blood-heat syndrome. Then a weight value of 0.3 is assigned to each main symptom and 0.1 to each minor symptom. Similarly, we assign a weight value to each symptom in every syndrome type, so that we can establish a simple membership function to judge a given case of a patient, membership degree of this patient's syndrome type. Then we only need to add the weights of the patient's symptoms to estimate the degree of membership in the class of a syndrome type he may have.

Suppose we have a fuzzy set of symptoms and syndrome of a patient in the case database $P= \{\text{blood fever, bright red lesions, dry scales, slow pulses, pale tongue, yellow urine, heavy head}\}$ corresponding to each basic syndrome of blood heat, blood dryness, combined syndrome wet due to the defined membership function above, a fuzzy vector of the patient $p = (1, 0.5, 0.3)$ which may be interpreted that
the patient’s symptom set has respective grade of membership: 1 (true) for blood heat syndrome of and 0.5 (possible) for blood dryness syndrome of and 0.3 (less possible) for combined syndrome wet.

Let us assume there are two reference cases A and B in the case base, and both correspond to the above-mentioned three syndrome types in terms of a grade of membership:

Given as fuzzy vector $a = (0.6, 0.4, 0.2)$, with the symptom set {Qi deficiency, bright red lesions, upset, red tongue, string pulse, dry scales, dry mouth, dizziness}

And fuzzy vector $b = (0.7, 0.1, 0.1)$ with the symptom set {blood heat accumulation, white scales, red skin lesions, thin and white tongue fur, dry mouth, slippery pulse}

Using the method of lattice degree of nearness proposed by P.Z. Wang[25], the similarity between two fuzzy sets can be defined by the following expression:

$$\sigma_0(A, B) = \frac{1}{2} [A \cdot B + (1 - A \oplus B)]$$

Where $A \cdot B$ and $A \oplus B$ are the inner and outer products of A and B, i.e.

$$A \cdot B = \max \{\min [X_A(x), X_B(x)], x \in X\}$$

$$A \oplus B = \min \{\max [X_A(x), X_B(x)], x \in X\}$$

Then the inner product and the outer product of $p$ and $a$ are 0.6 and 0.3 respectively; while the inner product and the outer product of $p$ and $b$ are 0.7 and 0.3 respectively. The lattice distance between the two is 0.65 and 0.7. Obviously, the case of $p$ and $b$ is closer. Therefore, $b$ can be taken as an approximate case.

**Results**

The ONTOPV prototype can graphically display the knowledge, related to psoriasis vulgaris which includes: knowledge of the disease, syndrome types, related symptoms, diagnosis and treatment methods, prescription, drugs component, which all have been built in the ontology. Then, some practical functions, such as ontology reasoning, case retrieval, semantic query, and medication alert can be implemented.

1) **Ontology reasoning**

According to the patient input information, including main symptoms and minor symptoms, etc., evaluation and analysis can be performed. If the input symptoms can meet the diagnostic criteria of the syndrome type, the system will prompt the user with the corresponding diagnosis suggestion for
reference. For example, as shown in Figure 10, after imputing the main symptoms to a patient, including bright red lesion, continuously increased rashes, and the minor symptoms, including irritability and upset, yellow urine, the system obtains the inferred results of a blood-heat syndrome (血热证) through reasoning over ontology, and output the corresponding medication recommendations: blood-cooling and toxin-resolving decoction (清热解毒汤) .

2) Case retrieval

In the case database of the ONTOPV prototype, by using the above-mentioned method of fuzzy pattern recognition, the input symptoms and signs of a patient can also be used to find a similar case in the case database. For example, we take the same input symptoms as an example for ontology reasoning, as a consequence, the no.16-case is matched with maximal similarity and output as query results which is shown in Figure 11.

3) Semantic query and visualization

In the ONTOPV prototype we can perform a semantic query over the knowledge base that is built in the ontology.

For example, if we query the prescription of blood-cooling and toxin-resolving decoction in the knowledge base, the system will display its ingredients, dosage and usage as Figure 12 shown.

4) Medication alert

In the ONTOPV prototype, the user is allowed to input some prescription. If there are two drugs containing some ingredients that may cause adverse reactions, the system will alert the users to the adverse reactions of the drug to the patient. For example, if a doctor prescribes a combination drug product of zidanyinxie capsule (滋阴养血片) with ingredients of danshen root (丹参) and Gatropin for a patient suffering from indigestion, the system will prompt that the two drugs due to having ingredient of aluminum hydroxide may bring about adverse reactions and should be used cautiously. (shown as in Figure 13)

Discussion

In the current paper we presented a detailed report about a designed and implemented prototype for psoriasis diagnosis, based on syndrome differentiation. The system realizes the basic functionalities of data collection, querying, browsing, and navigation, but also supports rule-based knowledge reasoning and integrates approximative reasoning, based on CBR through fuzzy logic. The system is intended to provide users with clinical decision support for TCM syndrome differentiation in diagnosis of psoriasis. In addition, it comprises a domain knowledge base of psoriasis, which is developed in the GFO framework with good extensibility. Through visualization of the knowledge graph and the query interface, doctors can quickly retrieve the needed information from the knowledge base. Furthermore, the system also provides a module for detection of medication conflicts, based on knowledge-based reasoning, which can assist doctors to ensure drug-use safety and reduce drug-induced risks. However, we are still in the early
stages of project planning. Although we have implemented a preliminary prototype system, the existing case library can only support fuzzy matching of some basic types of syndromes of PV. One of the important reasons of this situation is that up to now we cannot obtain a large number of clinical cases and EHR data. Hence, we need more adequate cases to be added into the case base in order to support the requirement to retrieve all combinations of basic types and combined types of the syndromes of PV.

**Conclusions And Future Research**

The domain experts (medical staff of the Guang’an men Hospital, China Academy of Chinese Medical Sciences, Beijing) have tested the functionality and usability of the system based on ontology and practice-relevant test data. According to the interviews with domain experts, the system currently meets all specified requirements for the clinical syndrome differentiation of the psoriasis vulgaris according to the guideline 2013. The future works will include collecting more electronic medical records and cases, extending query and reasoning for all syndromes of psoriasis, as well as integrating the clinical diagnosis and treatment knowledge of TCM and Western medicine. These methods will be extended to other TCM syndromes, and for this purpose we need an ontology of Zheng-types and tools to organize and compute syndromes/Zheng and to extract semantic information from EHR (electronic health care records), according to [29]. Additionally, a module of adverse drug reaction (ADR) has been implemented, and we are planning to use this ADR-module for further research in the future. In particular, we want to develop a knowledge base of comorbidities, caused by ADR. Such a module is an important and valuable contribution for clinical decision support.

**List Of Abbreviations**

CBR: Case Based Reasoning; GFO: General Formal Ontology; PV: psoriasis vulgaris; QoL: quality of life; TCM: Traditional Chinese Medicine;

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The data that support the findings of this study are available from the corresponding author on request.
Competing Interest

The authors declared that they have no competing interests.

Funding

This work was supported in part by grants from by National Key R&D Program of China (2019YFC1710400; 2019YFC1710401) which provide financial support in the design of study, collection of data and writing the manuscript, and the Fundamental Research Funds for the Central Public Welfare Research Institutes (ZZ13-YQ-126, ZZ13-YQ-127) which provide financial support in analysis and interpretation of data.

Authors’ Contributions

HL wrote the main manuscript text. HL and YZ conceived the idea and designed the study. ZW contributed to the visualization. YC, BG, JW and CC participated in case gathering and interpretation. HH guided the study and revised the manuscript.

Acknowledgments

Not applicable.

Supplementary Materials

Not applicable.

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