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Fuzzy ontology-based approach for liver fibrosis diagnosis

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ABSTRACT

The domain of the digestive system is prone to severe chronic disease in the form of liver cirrhosis, which is currently a leading cause of mortality. This article presents a new intelligent system for predicting the severity of liver fibrosis in patients with chronic viral hepatitis C. The proposed system is based on the inference capabilities of fuzzy ontology and operates on semantic rule-based techniques. A fuzzy decision tree technique was employed to generate the ontology rule base using a dataset of real fibrosis cases from the Mansoura University Hospital, Egypt. These rules were then encoded into a set of fuzzy semantic rules using the fuzzy description logic format. To evaluate the system's effectiveness, the proposed ontology was then tested on 47 chronic HCV cases, with an attempt made to see if this correctly diagnosed the patients' conditions. The performance of the proposed system was compared with that of the now-standard Mamdani fuzzy inference system; while the latter achieved an accuracy of 95.7/%, the proposed fuzzy ontology-based system demonstrated higher performance, with 97.8% accuracy. Furthermore, the proposed system also supports semantic interoperability between clinical decision support systems and electronic health record ecosystems. The positive impacts of this system on the correct prediction of liver fibrosis severity thus suggest that it has the potential to assist medical professionals in diagnosing and treating this dangerous disease.

1. Introduction

Viral hepatitis C (HCV) is a worldwide disease with a particularly high prevalence in Egypt. It has several serious effects, including cirrhosis, which commonly occurs in chronic (El-Hariri et al., 2017). Fig. 1 illustrates the stages of liver fibrosis severity that may lead to cirrhosis of the liver after recurrent or persistent liver injury; these have been traditionally evaluated by means of liver biopsies (Bucsics et al., 2018), a surgical procedure that may be accompanied by sampling errors of up to 30% (Sanai, 2010). However, the accuracy of diagnosis of hepatic fibrosis is a key aspect in managing HCV patients, especially patients in the early stages of fibrosis. In particular, early diagnosis of liver cirrhosis is important to prevent life-threatening complications (El Serafy et al., 2017). The high incidence rate of HCV infection in Egypt is also a concern, especially concerning the country's limited resources with respect to expensive diagnostic methods, which require highly experienced operators to accurately measure the hepatic stage (El Serafy et al., 2017). This has motivated researchers to develop intelligent systems, such as clinical decision support systems (CDSS) that can more affordably deliver creditable diagnostic markers for hepatic fibrosis assessment by assessing a patient's symptoms.

Electronic health records (EHRs) are repositories of patients' data; however, these are most effective where physicians can access decision support capabilities (Berges et al., 2011). EHR has several heterogeneous components, each based on its own data model (such as openEHR) with its own format, schema, and datatypes (SZhang et al., 2016). Seamless integration of distributed EHR systems and CDSS features in a unified EHR ecosystem thus requires semantic interoperability features. These allow multiple different computer systems to exchange data, with the receiving system accurately and automatically interpreting the meaning of

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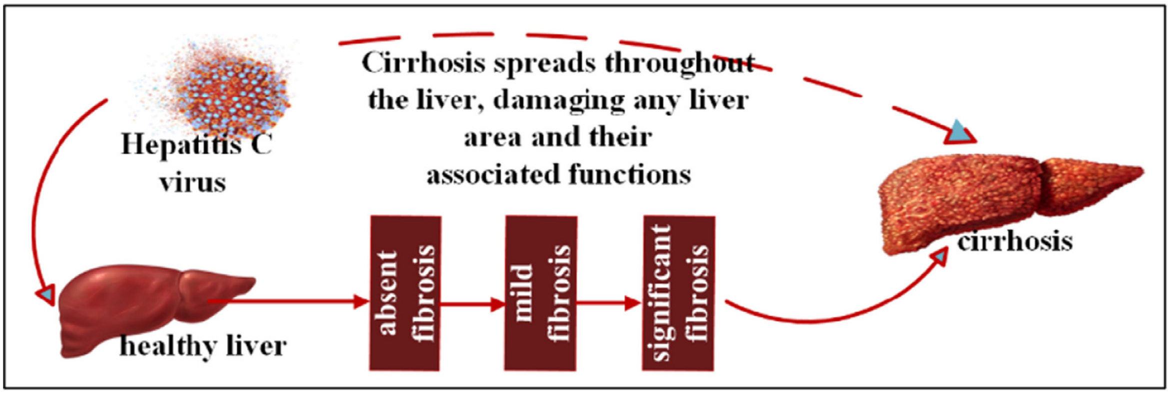


Fig. 1. Stages of liver fibrosis severity.

the data as provided by the sender (del Carmen et al., 2016). CDSS must also be capable of handling the uncertain and vague nature of medical data. Fuzzy rule-based systems (FRBSs), where properly supported by semantic capabilities, are thus preferred to handle the imprecise and vague nature of medical data, to improve CDSS performance, and to enhance interoperability between EHR and CDSS (Bobillo, 2009).

Recently, several different ontologies have been awarded crucial roles in the information retrieval process for semantic web-based search engines. This can be primarily attributed to their exceptional capacity for formalizing semantics and enabling reasoning. Such ontologies play a vital role in enhancing the effectiveness and efficiency of search engines by facilitating intelligent and context-aware information retrievalZhang et al. (2022), and by incorporating these ontologies, search engines can transcend the limitations of traditional keyword-based approaches, allowing the development of a more sophisticated understanding of concepts, relationships, and meanings. This, in turn, can facilitate more precise and relevant search results (Rajendran, 2015). The web ontology language (OWL) is now a widely accepted standard for specifying ontologies to represent knowledge in a structured manner. OWL is built upon a specific description logic (DL) that takes the form of a formal language for representing knowledge (Bobillo, 2016). Description logics (DLs) belong to the family of formal knowledge representation languages, and thus provide a systematic approach to capturing and organizing information (Bobillo, 2016); however, several classical ontologies have been used intensively in medical literature to build CDSS systems.

Alharbi et al. (2015) developed an intelligent system for diabetes diagnosis that featured a rule-based system, based on crisp ontology with 19 semantic web rules (SWRL), with the JESS inference engine used for reasoning with these rules. Bau et al. (2014) developed CDSS for diabetics undergoing surgery management using a system based on domain ontology with 31 classes, 13 properties, and 38 decision rules. They applied semantic rules integrated with the diabetes domain ontology to achieve an accuracy of 90%. However, the rules and feature selection were developed from domain expert opinion, making it harder to update the ontology's knowledge base.

Messaoudi et al. (2018) applied their methodology, based on crisp ontology and SWRL rule reasoning, to liver cancer diagnosis with a precision of 85%. The rule reasoning with SWRL was based on matching crisp sets of rules, which increased the run time of the inference process and which is not compatible with imprecise data, however. Despite the achievements of crisp ontologies, some researchers (Alharbi et al., 2015; Bau et al., 2014; Messaoudi et al., 2018; Chen et al., 2012; Torshizi et al., 2014) methodologies involving crisp ontology have thus proven ill-suited to handling imprecise and ambiguous knowledge. The reason behind this is that crisp ontology primarily represents traditional relationships between entities, which are characterized by binary outcomes, either "true" or "false". Fuzzy reasoning features may thus need to be integrated with ontology semantics in different ways to overcome this.

Chen et al. (2012) developed rule-based reasoning to infer HbA1c value, with the output values used as input to a crisp ontology reasoning system used to determine the appropriate drug regimen. Their model was based on a crisp ontology integrated with a fuzzy inference system, generating 80% accuracy. This limited accuracy was due to the fact that the methodology integrated the fuzzy logic into the reasoning system rather than into the ontology itself which led to less robust and accurate reasoning processes when dealing with complex or ambiguous information. Torshizi et al. (2014) thus followed the same methodology, applying a different tool, to develop a crisp ontology combined with fuzzy rule reasoning. Their system achieved an accuracy of 90% against 44 patient data samples in the BPH domain, as their methodology did not apply semantic approaches in the fuzzy inference system. Many studies (Alharbi et al., 2015; Bau et al., 2014; Messaoudi et al., 2018; Chen et al., 2012; Torshizi et al., 2014) have thus utilized rule-based systems; in these, the accuracy and completeness of the rule base are commonly derived from the experience of physicians, and these may thus vary from one expert to another, with the completeness and accuracy of the resulting knowledge base affecting decision support system accuracy.

Fuzzy ontology can thus be used to overcome such challenges by integrating fuzzy reasoning with ontological semantic reasoning features.

This study proposes a novel, semantically intelligent CDSS system for the prediction of liver fibrosis stage severity. The proposed system overcomes the current limitations identified from the literature by utilizing fuzzy ontology reasoning capabilities. It highlights the application of fuzzy ontology in liver fibrosis diagnosis and management. It demonstrates the effectiveness of fuzzy ontologies in handling uncertainty, integrating heterogeneous data sources, and improving diagnostic accuracy. By utilizing fuzzy ontologies, this work tries to contribute to advancing the field of liver fibrosis diagnosis and enhancing patient care. The proposed fuzzy intelligent system is based on a knowledge acquisition stage that permits both ontology construction and rule induction. In the offline phase, the most common terminologies related to the liver hepatitis domain are collated to build up a disease core ontology. This crisp ontology is then fuzzified by the application of a distinct fuzzification methodology. Then, in the online phase, fuzzy ontology reasoning is used to allow the system to determine the level of fibrosis based on the patient data received in each case.

The work presents several significant contributions, including:

- Introduction of a liver fibrosis severity prediction rule ontology (FsP): The study introduces FsP as a robust modeling framework for liver fibrosis-related knowledge and rules. This ontology enables the formal representation of diverse aspects of the disease, particularly for chronic HCV patients, providing a comprehensive foundation for further analysis and decision-making.
- Application of fuzzy logic to FsP: To address the inherent imprecision and uncertainty in liver fibrosis-related knowledge, the study incorporates fuzzy logic into FsP. This integration allows for the capture and representation of imprecise or uncertain information, resulting in the development of the Fuzzy LiverFibroOnto Ontology. This fuzzy ontology incorporates degrees of membership, facilitating gradual transitions between categories and enhancing the expressiveness of the model.
- Utilization of FsP for liver fibrosis diagnosis: Leveraging the developed FsP and employing fuzzy reasoning techniques, the study establishes an effective diagnostic approach for liver fibrosis. By utilizing fuzzy reasoning, the system can effectively handle imprecise or uncertain patient data, enabling accurate diagnoses based on the available information. This contributes to improved decision-making processes in the field of liver fibrosis diagnosis.

  These contributions collectively enhance the understanding, representation, and diagnostic capabilities related to liver fibrosis, offering valuable insights and potential advancements in the field of medical decision support systems.

The rest of this paper is structured as follows. Section 2 reviews the related works. In Section 3 we discuss the proposed methodology. Section 4 presents the fuzzy ontology reasoning process and the experimental results of our liver fibrosis diagnosis CDSS. Finally, Section 5 offers a conclusion and suggestions for future work.

2. Related works

Fuzzy ontologies have been utilized in several different domains, including healthcare and nutrition. The authors in Khosravi and Nahavandi (2006) applied a fuzzy ontology construction in the healthcare sector to improve the quality of decision-making, while in (Wang et al., 2010), a food ontology and a fuzzy type-2 dietary ontology were applied to dietary assessment to provide personalized diets for patients with diabetes and cardiovascular diseases. That methodology achieved an accuracy of 96.9%, and analysis of the results of the study showed that fuzzy ontologies can offer a feasible and effective approach to knowledge representation for dietary assessment. Tsai (2014) introduced a methodology for medical decision support in cases of Alzheimer's disease (AD). Their methodology was based on the idea that fuzzy ontology is a useful tool for the representation of both fuzzy and crisp knowledge, and the study achieved an accuracy of 90%. In Gomathi (2015), the fuzzy ontology was employed to extract knowledge from clinical datasets on diabetes, with the goal of developing a system to predict early onset diabetes by representing the relationship between symptoms and factors. The use of fuzzy ontology in this study thus allowed for the representation of uncertain and imprecise information related to diabetes. The utilization of fuzzy ontology in (Khosravi and Nahavandi, 2006; Wang et al., 2010; Tsai, 2014; Gomathi, 2015) highlights its potential in healthcare and medicine with respect to managing knowledge representing uncertain information, However, fuzzy ontology alone can lack the ability to facilitate complex reasoning tasks, as it primarily provides a framework for knowledge organization rather than supporting reasoning mechanisms.

In El-Sappagh and Elmogy (2017), the fuzzy ontology was used to improve the performance of Knowledge-Intensive Case-Based Reasoning (KI-CBR) systems, enhancing the semantic and storage capabilities of such systems. That study proposed the use of a fuzzy ontology to represent the complex and uncertain information related to diabetes mellitus available for diagnosis. This use of fuzzy ontology thus allowed for the representation of this uncertain and imprecise information in a more flexible and nuanced manner, and the results of the study showed that this improved the accuracy and consistency of KI-CBR systems in terms of correctly diagnosing diabetes mellitus. Similarly, in Selvan et al. (2019), the fuzzy ontology was used to address the problem of uncertainty with respect to generating and recommending appropriate food and drugs for chronic disease patients. The study aimed to minimize the manual work involved in determining appropriate food and drugs for chronic patients by using IoT-generated medical records, and the results showed that the use of fuzzy ontology improved the efficiency of food and drug generation and recommendation for chronic patients in such cases. This suggests that fuzzy ontology can be used as a valuable tool for addressing some challenges of uncertainty and complexity that may arise in healthcare, particularly in terms of the management of chronic diseases.

In Fakhfakh et al. (2021), the fuzzy ontology was employed to improve the accuracy of triage systems in emergency departments. The study aimed to improve the accuracy of current triage procedures by introducing a fuzzy ontology that takes into account the complexity and uncertainty of medical data related to patient's symptoms and conditions, thus allowing for the identification of subtle differences between acuity levels, which may otherwise be difficult to identify using traditional triage systems. The researchers in (El-Sappagh and Elmogy, 2017; Selvan et al., 2019; Fakhfakh et al., 2021) thus applied case-based reasoning methodologies and fuzzy ontology to improve both consistency and accuracy; however, one of the major limitations of the process has proved to be a lack of abstraction and generalization.

In recent years, there has been an escalating interest in employing advanced computational techniques to enhance the accuracy and efficiency of medical diagnosis. One such promising avenue is the integration of fuzzy ontology into the domain of liver fibrosis diagnosis. This section reviews the existing research efforts that have explored the application of fuzzy ontology in the context of liver fibrosis diagnosis.

The works in (Zhang et al., 2018; Li et al., 2020; Wang et al., 2021) proposed a fuzzy ontology-based approach for liver fibrosis diagnosis based on clinical data. Also, the work in (Chen et al., 2019) delved into the development of a fuzzy ontology tailored for liver fibrosis staging. The constructed fuzzy ontology encapsulated linguistic variables and fuzzy rules that corresponded to various stages of liver fibrosis.

Another research direction was to build hybrid systems by combining fuzzy ontology with machine learning techniques such as support vector machines or random forests(Wang et al., 2021) for clinical records or deep learning models for liver fibrosis diagnosis to classify liver fibrosis stages from histopathological images (Chen, 2019).

Furthermore, fuzzy ontologies were utilized to generate personalized assessments of liver fibrosis severity (Smith, 2017), reason about treatment guidelines and patient preferences to generate a personalized treatment plan (Liu et al., 2022).

Despite the promising outcomes showcased by the existing works in the application of fuzzy ontology to liver fibrosis diagnosis, it is imperative to acknowledge that these studies, while insightful, are not yet sufficient to provide conclusive evidence of their effectiveness. Further validation and comprehensive testing

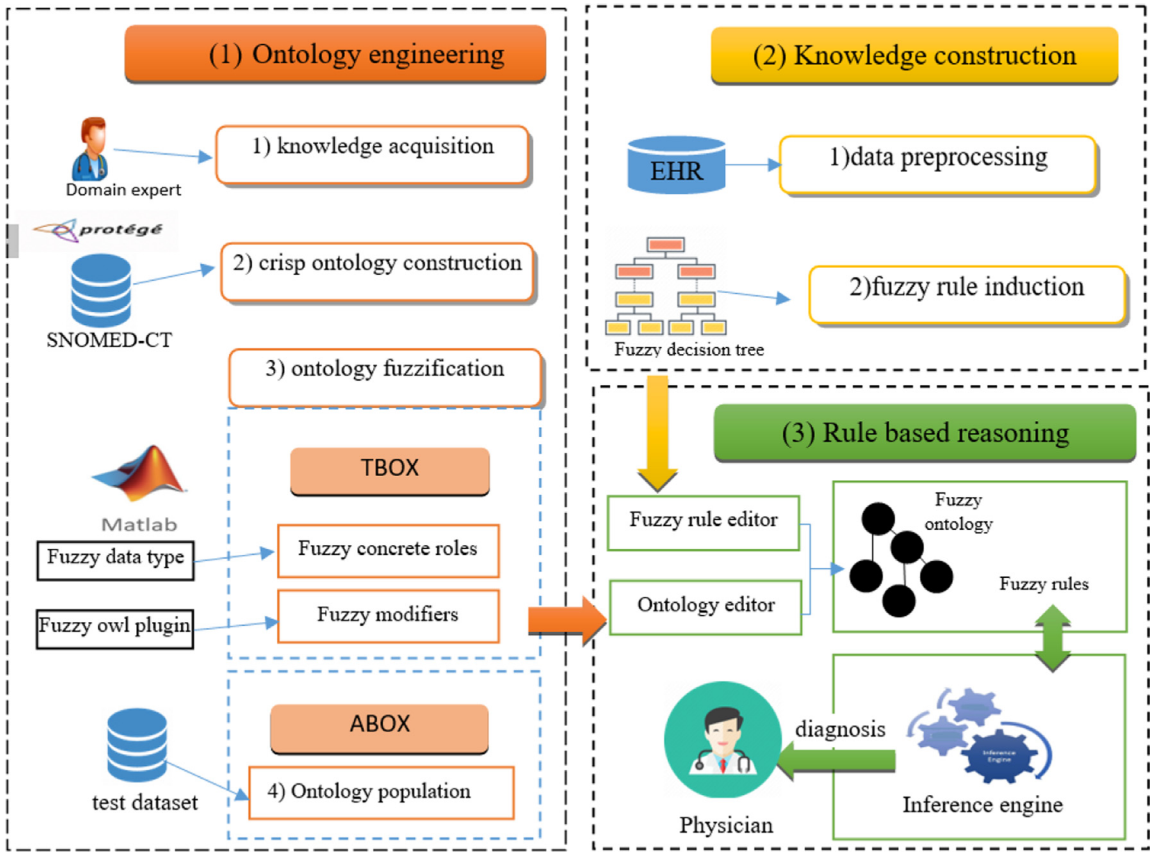


Fig. 2. : FsP: The proposed framework for a liver fibrosis diagnosis system.

are required to establish the robustness of fuzzy ontology-based systems in real-world clinical scenarios, especially with respect to chronic viral hepatitis. Additionally, the scarcity of extensive and diverse real-world patient data poses a challenge, potentially limiting the generalizability of the findings. To ensure the reliability and practicality of these approaches, future research should emphasize the acquisition of substantial and representative datasets, coupled with rigorous validation methodologies, thereby bolstering the confidence in the potential contributions of fuzzy ontology in liver fibrosis diagnosis and beyond.

3. The proposed CDSS system

This section outlines the proposed CDSS system for liver fibrosis severity prediction (FsP), based on the determination of the stage of fibrosis reached by chronically infected hepatitis C patients. The main objective of building the FsP system is to assist physicians in managing chronically infected HCV patients who need long-term personalized treatments more effectively. The system utilizes a combination of fuzzy ontological reasoning and fuzzy rule reasoning to provide semantic interoperability with expressive inference, which regular fuzzy reasoning systems are not able to provide. The framework for this FsP system is presented in Fig. 2, which illustrates two main phases, the online and offline phases. The proposed system attempts to use findings from infected patients to predict the stage of liver fibrosis. The data used thus includes personal information (age, gender, etc.), physical data (liver function, complete blood, jaundice level, etc.), and disease history, as collected from electronic health records and stored in the LiverFibroOnto ontology. Making inferences is a key feature of this system, with the various features used as independent variables for fuzzification; this process is thus discussed in greater detail in the following sub-sections. These features are all preprocessed using physician-assisted data mining tools to obtain high-accuracy diagnostic results, however.

The offline phase is essentially a process of knowledge structure formulation. Liver disease is a rich domain that necessitates various knowledge acquisition procedures to fully understand its terminology and its semantics. This phase thus involves ontology engineering, during which a crisp ontology based on standard medical ontology, the Systematized Nomenclature of Medicine Ontology Concept (SNOMED-CT), is built and extended into a fuzzy ontology [1]. The resulting ontology thus formalizes and encodes all relevant fibrosis medical terminologies, while the building process involves converting the crisp ontology into an extended entity-relationship (EER) conceptual model and adding extended fuzzy concepts.

In the online phase, users provide commands to the query engine, which consults the CDSS reasoning engine to provide personalized data. To enhance the quality of the rule-based reasoning system, a fuzzy decision tree is integrated with the CDSS to act as a machine-learning tool. The next step, therefore, involves utilizing data mining tools to improve the quality of the clinical data drawn from patients, which is then further processed to complete rule induction and ontology population. Finally, a fuzzyDL reasoner is employed to improve the inference results and provide a final decision.

The process of creating the inference system begins with the use of fuzzy logic to map crisp inputs to outputs. The resulting mappings or fuzzy rules take the form of conditional IF-THEN

[1] Available at https://www.snomed.org

statements, which establish the relationships between fuzzy inputs and outputs, thus serving as the foundation for decision-making. During the defuzzification phase, the fuzzy inference results can be transformed into a crisp output by the application of a fuzzy set. In this case, the output is a percentage indicating the predicted severity of liver fibrosis, calculated by identifying values associated with liver fibrosis intervals in the domain discourse. This process is facilitated by the use of LiverFibroOnto, a fuzzy HCV domain ontology. A detailed discussion of this ontology's construction and the rule-based reasoning applied is therefore provided in the ensuing subsections.

3.1. Ontology engineering

3.1.1. Knowledge acquisition

The primary aim of the knowledge acquisition phase is to acquire a comprehensive understanding of the knowledge required for the accurate diagnosis of liver fibrosis. The dataset collected during this phase in this instance was overseen by physicians with expertise in this matter. Fig. 3 represents the steps of this phase, from identifying the appropriate medical experts to the development of the conceptual model of the knowledge base. To gather medical expertise on the crucial variables, ranges of values, and correlations associated with chronic HCV-infected patients' liver fibrosis, a team of physicians at the Hospital of Mansoura University in Mansoura, Egypt, was put together. These experts then provided input on the relevant variables represented in the study. In addition, written materials on liver diseases, including a literature review across this medical field, were consulted. As shown in Fig. 3, the data analysis process then used these elements to model knowledge within the HCV medical domain across the following classes:

- Human: This class includes patients and physicians. Patients were defined as those with chronic HCV infections, aged between 16 and 90. Physicians were then defined as those responsible for the diagnosis and treatment of HCV patients.
- Disease: Diseases in this model include not only liver fibrosis but also its comorbidities such as obesity and diabetes mellitus.
- Demographic: Patient demographic data (e.g. age, gender).
- Laboratory test: Laboratory tests in the HCV medical domain include all specific tests for liver fibrosis disease such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum bilirubin level (SB), white blood cell count (WBC), and platelet count (PLT).
- Symptom: This class covered patient symptoms, including hepatocellular jaundice, diarrhoea, dyspnoea, fatigue, vomiting, and appetite changes.
- Sign: This class covered fibrosis signs such as hepatic associates, spleen enlargement, portal veins, and lesions of the liver.
- Diagnosis: This referred to the nature of the liver fibrosis severity stage. Fibrosis stages vary from one infected patient to another, based on clinical data, though they may be used to describe the severity of the liver fibrosis to a certain extent: absent fibrosis means no fibrosis, liver fibrosis stage 2 is mild fibrosis, liver fibrosis stage 3 is significant fibrosis, while liver cirrhosis refers to extensive liver damage.

This step allows initial analysis of the data required to organize the knowledge base structure. In the next step, a crisp ontology

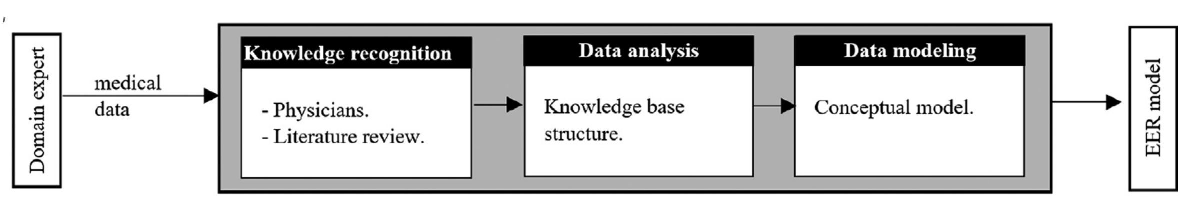


Fig. 3. Knowledge acquisition phase.

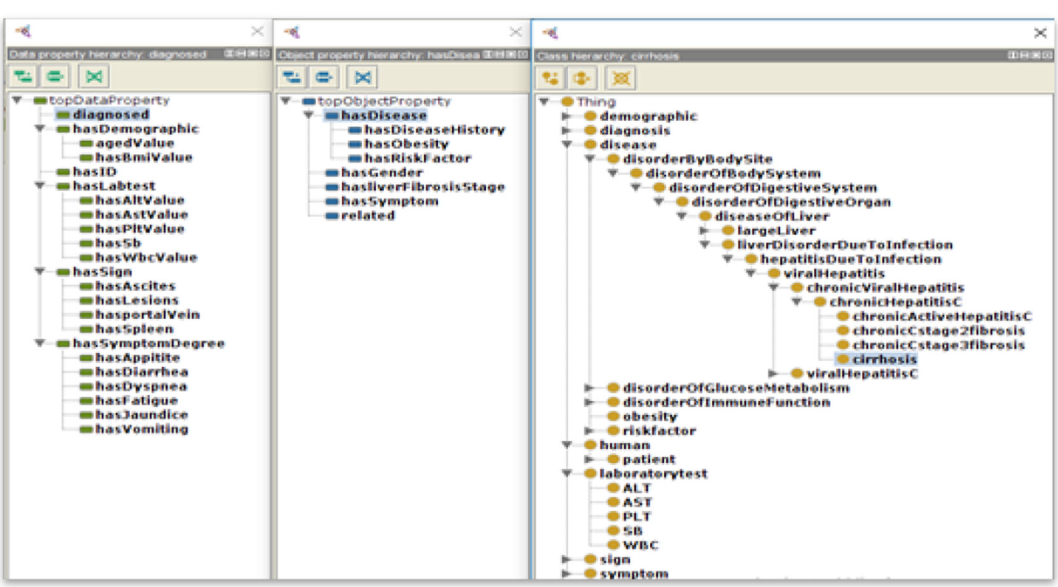


Fig. 4. Class hierarchy of the proposed ontology.

Table 1
Fuzzy datatype definition.

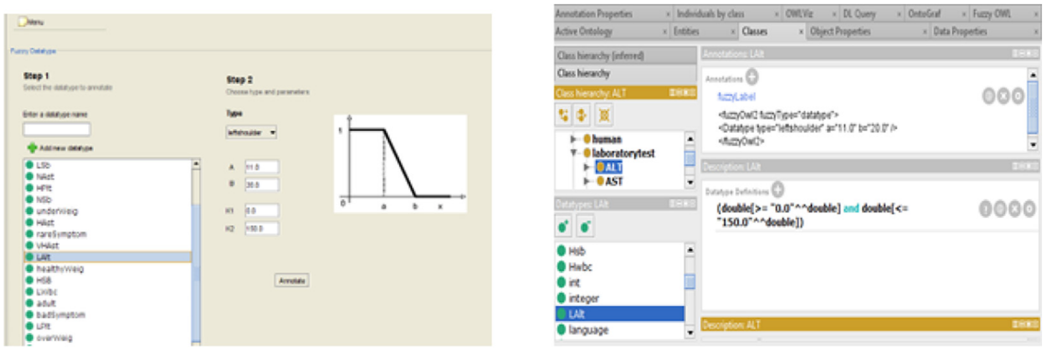
Fuzzy concept	Fuzzy datatype (FDT)	Fuzzy concrete predicate	Concrete role
Lowsb	LSb	Left-shoulder(0.0,4.0, 0.4, 0.8)	*hasSb*
normalSB	NSb	Trapezoidal(0.0, 4.0,0.4, 0.8, 2.0, 2.4)	
HighSB	HSb	Right-shoulder(0.0,4.0,2.0, 2.5)	
lowAlt	LAlt	Left-shoulder(0.0,150.0, 11.0, 20.0)	*hasAlt*
normalAlt	NAlt	Trapezoidal(0.0, 150.0, 11.0, 20.0, 35.0, 45.0)	
highAlt	Halt	Trapezoidal (0.0,150.0, 35.0, 40.0, 50.0, 56.0)	
vhighAlt	VHAlt	Right-shoulder(0.0,15.0, 50.0, 60.0)	
lowAst	Last	Left-shoulder(0.0,150.0, 10.0,18.0)	*hasAst*
NormalAst	Nast	Triangular(0.0,150.0, 10.0, 20.0, 30.0)	
highAst	Hast	Triangular(0.0, 150.0, 23.0, 33.0, 43.0)	
vhighAst	VHAst	Right-shoulder(0.0,15.0, 35.0, 50.0)	
vlowWbc	VLWbc	Left-shoulder(0.0,20.0, 2.0,4.0)	*hasWbc*
lowWbc	LWbc	Trapezoidal(0.0, 20.0, 2.0,4.0,6.0,8.0)	
normalWbc	NWbc	Trapezoidal(0.0, 20.0, 6.0,8.0,12.0,15.0)	
highWbc	HWbc	Right-shoulder(0.0,20.0, 12.0,15.0)	
vlowPt	VLWbc	Left-shoulder(50.0,500.0, 128.0, 175.0)	*hasPlt*
lowPlt	LPlt	Triangular(50.0, 500.0, 140.0, 190.0, 240.0)	
normalPlt	NPlt	Trapezoidal(50.0, 500.0, 190.0, 240.0, 340.0, 390.0)	
highPlt	HPlt	Right-shoulder(50.0,500.0, 12.0,15.0)	
Absent	Absent	Left-shoulder(0.0,10.0, 1.0,3.0)	*Has symptom*
raresymptom	Rare	Triangular(0.0,10.0, 3.0,5.0,7.0)	
badSymptom	Bad	Right-shoulder(0.0,10.0,7.0,9.0)	
youth	Young	left-shoulder(16.0, 90.0, 20.0, 35.0)	*aged*
middleage	Adult	trapezoidal(16.0, 90.0, 30.0, 35.0, 50.0, 55.0)	
oldage	Old	right-shoulder(16.0, 90.0, 50.0, 70.0)	

was modeled to gather concepts from the different basic sub-domains. The resulting common conceptual data model (e.g., the Entity Relationship (ER) model) graphically represents data as distinguishable entities that represent real-world factors and the relationships that connect these different classes to each other. Both the factors and their relationships may thus be identified as having different attributes and constraints (Sweidan et al., 2020). The authors in (Sweidan et al., 2020) illustrated in detail the process of mapping the EER model to allow expansion of the specification of such factors within the hierarchical structure.

3.1.2. Ontology construction

This process is concerned with developing a crisp ontology to create a formal and structured representation of domain knowledge, in this case, with reference to defining the concepts, relationships, and properties that describe the chronic HCV domain. The construction of a crisp ontology typically involves several steps, including domain analysis, concept identification, relationship modeling, and knowledge representation. It may also involve incorporating existing ontologies or knowledge sources, refining and validating the ontology, and iteratively improving its structure and content (Alexopoulos et al., 2012). LiverFibrosisOnto, a crisp ontology, was modeled using a semantic framework that covers all relevant concepts related to the HCV domain, with particular reference to liver fibrosis domain knowledge. The proposed ontology was built on a taxonomy model, and the main concepts were designed to cover both clinical and demographic aspects, with each having its own subclasses to interact with the etiological mechanism. Clinical classes included laboratory tests, symptoms, signs, diseases, and diagnoses, while age and gender were identified as non-clinical (demographic) classes. The etiological mechanism used in the diagnosis process is rule-based, while the disease class is built on SNOMED-CT. The latter was imitated in the ontology hierarchy to generate terms with concept identification (encoding) and synonym terms. The interactions among classes were then modeled using objects and data properties capable of specifying a diagnosis. A sample list of crisp ontology axioms in the DL syntax was also provided.

patient ⊑ human	patient ≡ (∃hasID. integer) ⊓ (∃haslabtest. laboratorytest) ⊓ (∃hasSymptom. symptom) ⊓	
human ⊑ Thing	(∃hasSign. sign) ⊓ (∃hasDisease. disease) ⊓ (∃hasDemoghraphic. demographic)	
demographic ⊑ Thing	demographic ⊑ ∃hasDemographic. (age ⊔ gender)	
laboratorytest ⊑ Thing	laboratorytest ⊑ ∃haslabtest. (ALT ⊔ AST ⊔ SB ⊔ PLT ⊔ WBC)	
symptom ⊑ Thing	symptom ⊑ ∃hasSymptom. (jaundice ⊔ appetites ⊔ dyspnea ⊔ diarrhea ⊔ fatigue ⊔ vomiting)	
sign ⊑ Thing	sign ⊑ ∃hasSign. (hepaticAscites ⊔ portalVein ⊔ lesionsOfLiver ⊔ spleenEnlarged)	
diagnosis ⊑ Thing	patient ⊑ ∀hasliverFibrosisStage. diagnosis	sign = {yes, no}
female ⊓ male ⊑⊥	diagnosis = {absentFibrosis, mildFibrosis, significantFibrosis, cirrhosis}	
disease ⊑ Thing	disease ⊑ (∃hasRiskFactor. instance) ⊓ (∃hasDiseasehistory. instance) ⊓ (∃hasObesity. instance)	
patient ⊑ ∀hasID. integer	⊥⊑ age ⊓ gender ⊓ laboratorytest ⊓ symptom ⊓ sign ⊓ disease	



(a) (b)

Fig. 5. Example of a fuzzy datatype LAlt.

As an example, the patient class is a subclass of the human class and its instances are related to the instances of the other classes (laboratorytest, symptom, etc.) through properties. The axiom "demographic ⊆ ∃hasDemographic. (age ∪ gender)" implies that every instance of the concept "demographic" must have at least one associated property, "hasDemographic", that is related to "age" or "gender" (or both). Fig. 4 illustrates the hierarchy classes and the object and data properties of the developed ontology.

3.1.3. Ontology fuzzification

As noted, crisp ontology is a special case of a fuzzy ontology in which all relation and property degrees are held in the range d=[0,1] (Yaguinuma et al., 2013). In the case of the liver fibrosis fuzzy ontology in this case, LiverFibrosisOnto, the crisp ontology thus generated includes several fuzzy datatypes, concepts, and properties. In OWL2, the concrete domain allows representation of a range of datatypes including strings, Booleans, doubles, or integers, while in fuzzyDL, the concrete domain is, in fact, a fuzzy concrete domain (EBobillo, 2011). The Zadeh fuzzy logic (Zadeh, 1965) was specified in this case, with the default semantics for the fuzzy operators used (define-fuzzy-logic Zadeh). A sample list of ontology axioms in fusil syntax, where d defines the fuzzy data type for the linguistic term for every fuzzy variable, was then created.

certain degrees of membership or association then denoted by the level of "d".

Following (Sweidan et al., 2020), the fuzzification of each element in the ontology was done as follows:

- Fuzzy datatypes and fuzzy concrete roles (data properties): Data properties in the crisp ontology can be defined with fuzzy data types where their ranges are delimited by means of data range expressions such as [double min, double mix]; for example, (double [>=0.0] and double [<=150.0]) for the hasAlt input property data range was used in this case. The associated membership functions are then defined over the referential data range. The fuzzy concrete role was defined in Fuzzy OWL2 by setting the range data type to a defined fuzzy data type. An annotation example in OWL2 for the fuzzy datatype LALT, as seen in Fig. 4(a), shows that a fuzzy data type is created for each of these fuzzy rough concepts (lowAlt,normalAlt,highAlt), and then a fuzzy concrete role is defined for all of its linguistic values (e.g., hasAlt(patient, lowAlt), where Alt is a crisp concept and lowAlt is a fuzzy concept). Example 1: Where previous knowledge about a patient is encoded as the fuzzy TBox:

SB ⊑ (∃haslowSb. d) ⊓ (∃hasnormalSb. d) ⊓ (∃hashighSb. d)	jaundice ⊑ (∃hasAbsentJaundice. d) ⊓ (∃hasRareJaundice. d) ⊓
ALT ⊑ (∃haslowAlt. d) ⊓ (∃hasnormalAlt. d) ⊓ (∃hashighAlt. d)	(∃hasBadJaundice. d)
AST ⊑ (∃haslowAst. d) ⊓ (∃hasnormalAst. d) ⊓ (∃hashighAst. d)	appetites ⊑ (∃hasAbsentAppetites. d) ⊓
PLT ⊑ (∃haslowPlt. d) ⊓ (∃hasnormalPlt. d) ⊓ (∃hashighPlt. d)	(∃hasRareAppetites. d) ⊓ (∃hasBadAppetites. d)
WBC ⊑ (∃haslowWbc. d) ⊓ (∃hasnormalWbc. d) ⊓ (∃hashighWbc. d)	dyspnea ⊑ (∃hasAbsentDyspnea. d) ⊓ (∃hasRareDyspnea. d) ⊓
age ⊑ (∃hasYoungage. d) ⊓ (∃hasAdultage. d) ⊓ (∃hasOldage. d)	(∃hasBadDyspnea. d)

All axioms thus represent an exact meaning, though interpretation may depend on the specific context and domain of the crisp ontology. For example, the axiom "$SB \subseteq (\exists haslowSb.d) \cap (\exists hasnormalSb.d) \cap (\exists hashighSb.d)$" implies that SB is characterized by having connections to a range of fuzzy concepts representing "lowSb", "normalSb", and "highSb", with

$$patient \sqsubseteq \exists hasSb.SB$$
$$lowSb \sqsubseteq SB$$
$$lowSbPatient \equiv patient \sqcap \exists hasSb.lowSb$$

The facts about the specific patient p_1 are encoded with the following fuzzy ABox: $\langle p_1 : patient \sqcap \exists hasSb.lowSb, 0.9\rangle$. So, p_1 is a patient having lowSb with a degree of 0.9. Here, the ontology contains seven fuzzy input variables: age, ALT, AST, WBC, SB,

```
(implies (and patient (some hasSb LSb)(some hasJaundice absentSymptom)(some hasVomiting absentSymptom)
        (some hasPortalVein no))(some diagnosed absentFibro))
(implies (and patient (some hasAlt NAlt)(some hasSb LSb)(some hasPlt NPlt)(some hasWbc NWbc)
        (some hasJaundice absentSymptom)(some aged old))(some diagnosed mildFibro))
(implies (and patient (some hasAst HAst)(some hasSb HSb)(some aged old)(some hasGender female))
        (some diagnosed cirrhos))
(implies (and patient (some hasAst LAst)(some hasSb HSb)(some hasWbc NWbc)(some aged adult))
        (some diagnosed signFibro))
(implies (and patient (some hasAst VHAst)(some hasSb HSb)(some hasWbc LWbc)(some hasGender male)(some aged adult)
        (some hasVomiting badSymptom))(some diagnosed cirrhosis))
(implies (and patient (some hasAst VHAst)(some hasSb HSb)(some hasWbc LWbc)(some aged adult)
        (some hasAppetites badsymptom))(some diagnosed cirrhosis))
(implies (and patient (some hasAst VHAst)(some hasSb HSb)(some hasAlt HAlt)(some hasJaundice badSymptom)
        (some aged adult)(some hasGender male))(some diagnosed cirrhosis))
```

Fig. 6. Sample of the implicative rules.

```
(define − concept rule1 (and patient (some hasSb LSb)(some hasJaundice absentSymptom)(some hasPortalVein no)
(some hasVomiting absentSymptom)(some diagnosed absentFibro)))
(define − concept rule2 (and patient (some hasSb LSb)(some hasAlt NAlt)(some hasPlt NPlt)(some hasWbc NWbc)
(some aged old)(some hasJaundice absentSymptom)(some diagnosed mildFibro)))
(define − concept rule3 (and patient (some hasAst HAst)(some hasSb HSb)(some aged old)(some hasGender female)
(some diagnosed cirrhosis)))
(define − concept rule4 (and patient (some hasAst LAst)(some hasSb HSb)(some hasWbc NWbc)(some aged adult)
(some hasRiskFactor hypertension)(some diagnosed signFibro)))
(define − concept rule5 (and patient (some hasAst VHAst)(some hasSb HSb)(some hasWbc LWbc)(some aged adult)
(some hasVomiting badSymptom)(some hasGender male)(some hasRiskFactor arthritis)(some diagnosed cirrhosis)))
(define − concept rule6 (and patient (some hasSb HSb)(some hasAst VHAst)(some hasWbc LWbc)(some aged adult)
(some hasAppetities badSymptom)(some diagnosed cirrhosis)))
(define − concept rule7 (and patient (some hasSb HSb)(some hasAst VHAst)(some hasAlt HAlt)
(some hasJaundice badSymptom)(some hasGender male)(some aged adult)(some diagnosed cirrhosis)))
(define − concept RuleSet (or rule1 rule2 rule3 rule4 rule5 rule6 rule7 ... ... ... rule74))
(defuzzify − mom? RuleSet p8 diagnosed)
```

Fig. 7. Examples of the developed Concept definition rules.

PLT, and symptom in the class of 'patient.' These variables are important in the diagnosis process. Table 1 represents the membership functions used for fuzzy classes:

As an example, the fuzzy concept definition of $C_1 \equiv \exists\ property_1.\ FDT$ such that $C_1 \equiv \exists\ property_1.\ FDT$ this, along with as assertion highAst(patient5), indicates that individual patient5 has highAst with respect to property hasAst. The inferred values from the fuzzy ontological reasoning can thus be either crisp (0,1) or have a fuzzy degree of truth [0,1], depending on the fuzzy concrete predicate "d". The concept "highAst" can thus be represented as a fuzzy concept, seen in the form "patient5" is an instance of highAst(patient) with membership degree "0.14". In FuzzyDL, this is represented as (instance p5 highAst 0.14).

- Fuzzy abstract roles (fuzzy object properties).

Object properties in a crisp ontology can be extended to fuzzy abstract roles by the imputation of fuzzy membership values. A fuzzy object relation connects instances at their membership degree and thus allows fuzzy role assertions, such as "patient1-hasRiskFactor- hypertension at degree 08", represented as (related patient1 hypertension hasRiskFactor 0.8). Here, the property hasRiskFactor connects the instances "patient1" and "hypertension", and this can be used to infer the severity of the disease risk factor. To represent the fuzzy entities used in the developed liver fibrosis ontology, the methodology procedures for IKARUS-Onto (Alexopoulos et al., 2012) were applied to convert the crisp ontology into fuzzy cases. This abstract and complete methodology focuses on ontology fuzzification, allowing the resulting ontology to be represented in the OWL2 ontology using Fuzzy OWL2 2.1.1 plug-in in Protégé 4.3, Java 1.8, and Gurobi 6.5, all of which provide support in terms of creating Fuzzy OWL2 ontologies, as shown in Fig. 5a. The plug-in allows specification of the type of fuzzy logic used, along with fuzzy datatype definition, fuzzy modified concepts, fuzzy modified role, fuzzy modified datatype, and fuzzy axioms; however, it cannot translate fuzzy representations directly into the OWL2 ontology (Bobillo, 2016).

The fuzzy linguistic variables and fuzzy sets (ranges and shapes) used were modeled from the domain experts' knowledge and the most recent clinical practice guidelines (Sweidan et al., 2019). The plugin was then used to define the fuzzy components by means of annotations for the various concepts and relationships to be coded (FuzzyLabel annotation), delimited by start and end tags tags fuzzyOwl2, \fuzzyOwl2 as seen in Fig. 5b. Based on this, crisp ontology reasoners such as pellets were available for use.

3.1.4. Ontology population

An ontology has the ability to store a range of knowledge in a machine-readable format; as such, there are many options for ontology population, including FEER2FOnto (Cross and Kandasamy, 2011). This option was used to store instances with the structure of the resulting ontology, to help ensure consistency. Using the constructed fuzzy ontology, it was possible to map the relationships between various fuzzy properties such as "age" and attributes of fuzzy age, such as "youth", "middleAge", and "oldAge". Object properties such as "hasDisease" were then used to connect the instances of classes of patient and disease, and the OWL axioms were used to identify patient cases, as seen in the following example:

ClassAssertion(:patientpatient1)

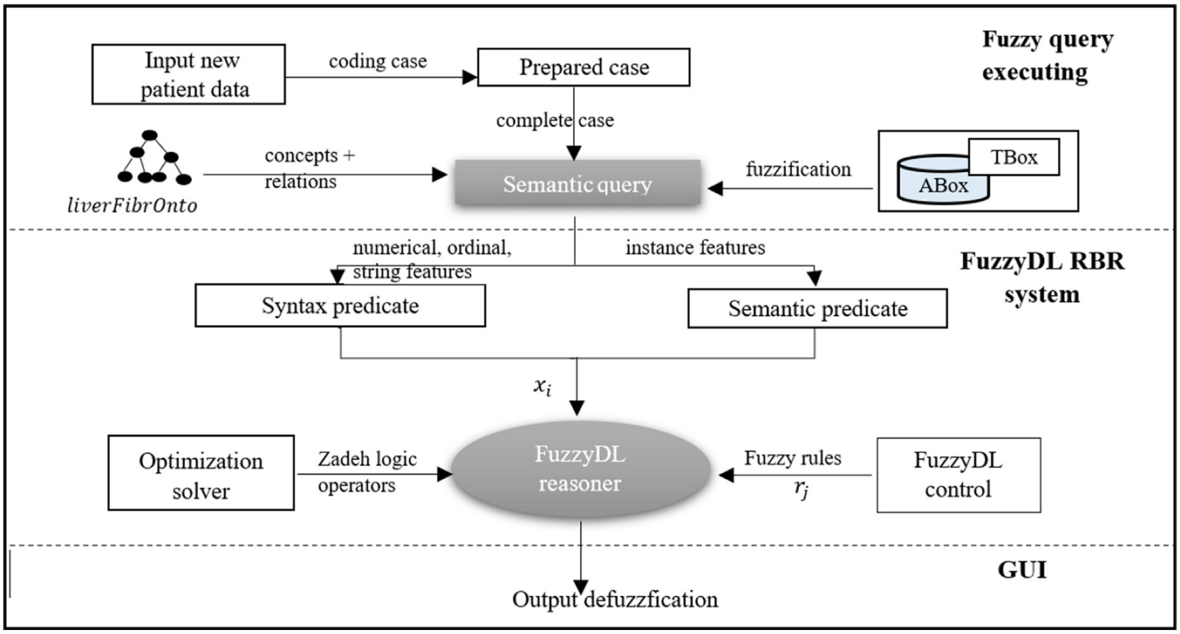


Fig. 8. FuzzyDL reasoning.

ObjectPropertyAssertion(:hasDiseasepatient1414916001)
DataPropertyAssertion(:agedp1 "57.0" sd:double)
DataPropertyAssertion(:hasIDp1 "17" sd:integer)
DataPropertyAssertion(:hasJaundicep1 "2.0" sd:double)
DataPropertyAssertion(:hasSbp1 "0.6" sd:double) continue......

The translation rules from Zhang et al. (2008) were used for mapping the ontology instances "concept, data property, instance, axioms, and object property" from the relational database instances "table, attribute, tuple, primary key, and foreign key", respectively, for the whole database. The resulting ontology after population contained 47 instances in the "patient" class.

3.2. Knowledge construction

3.2.1. Knowledge base

Full ontology population requires a significant amount of time and effort; however, this may be minimized by the use of external resources such as fuzzy rules, which decrease the need for expert input and increase the possible level of automation of the system (Cross and Kandasamy, 2011). As discussed in (Sweidan et al., 2019), a set of 74 fuzzy rules was generated through machine learning for this study in a form

$$if\ A^1\ is\ \ a_i^1\ and\ A^2\ is\ a_i^2\ and \ldots and\ A^n\ is\ a_i^n\ then\ C\ is\ c_i \tag{1}$$

The diagnosis rule base thus captures input variables for the relevant conditions for a relevant patient sample to generate liver fibrosis severity stages for each that can act as a control system for the output diagnosis. Liver fibrosis diagnosis requires a set of conditional features, many of which do not occur simultaneously during infection. For instance, some patients may have a "cirrhosis stage" while other conditions remain in normal status. In contrast, other patients may have "absent fibrosis" accompanied by poor general condition. As there is no single way to diagnose each patient case, predicting the stage of liver fibrosis requires a flexible set of diagnosis rules composed of a range of medical conditions related to liver fibrosis. These rules must specify the etiological features corresponding to the diagnosis, and the membership function that ties each feature to the relevant patient case. The fibrosis level predicted is then based on these features and the membership function of the target variable. Hence, when fibrosis is diagnosed, it is assigned a degree of "truth" that ties it to a diagnosis class with a detected membership value $\beta \rightarrow [0, 1]$. For instance, a cirrhosis patient could be identified as (instance patient1 cirrhosis, 0.7).

To facilitate clinical diagnosis across the entire domain of liver fibrosis, FsP can utilize a powerful fuzzy DL reasoner. The acquired knowledge is represented in the form of if-then rules, which can be expressed in various ways, such as a Mamdani structure, implication rules, or concept definition and defuzzification (Yaguinuma et al., 2013). These rules are then mapped as a control system (Cross and Kandasamy, 2011). An example of a rule fuzzy axiom may be defined as (if dataProperty 1 is low and dataProperty 2 is normal, then dataProperty 3 is mild), where the data Properties 1 and 2 are rule inputs and dataProperty 3 is the output property. All of these properties are defined by linguistic terms *(low, normal, mild)*, and both properties and linguistic terms are defined in the fuzzy ontology LiverFibrosisOnto. The inferred output value thus depends on both the fuzzy operators and linguistic terms.

a. Definition of fuzzy rules as implication rules:
FuzzyDL implications can be used to define fuzzy rules; these then become implicative rules, and they can serve as the building blocks of fuzzy logic systems, providing a framework for reasoning in situations where precise and crisp logic may not be applicable. Figure]6 presents a sample of generated fuzzy rules as defined with fuzzyDL implications (Sweidan et al., 2019). Here, rule 1 means "if the patient has low SB and has absent jaundice and has absent vomiting and has not portal-vein, then the liver fibrosis should be set to absent fibrosis". This approach is not based on the output fuzzy set shape, instead generating a numerical output corresponding to the minimum value α: thus, the implementation of this approach alone offers a highly faulty diagnosis.
Fig. 6 illustrates the use of specific conjunction $\otimes$*andimplication* $\Rightarrow$ *operators*. The semantics of the rules is determined by the minimum degree of truth, based on the conjunction operator and the conjunctive combination of

rules (Yaguinuma et al., 2013). By default, if $0 << 1$, the numerical value of the consequent β is inferred to be 1.0 when $\alpha \Rightarrow \beta$, and $if = 0$, then $0 << 1$. However, such a semantic structure is not suitable for the liver fibrosis diagnosis system as it does not yield optimal performance.

b. definition of fuzzy rules as concept definition and defuzzification:

An alternative approach to defining fuzzy rules in fuzzyDL involves using concept definitions and fuzzy operators, encompassing the role of the latter as concept definitions, to specify the relationships between fuzzy variables, and their contributions to the defuzzification process. This converts fuzzy outputs into crisp values for decision-making or further processing (Bobillo, 2016). A sample of generated fuzzy rules, defined using fuzzyDL concept definition (Sweidan et al., 2019), is presented in Fig. 7. In this approach, the minimum is used for conjunction and the maximum for disjunction in terms of the rule semantics and aggregation. The fuzzyDL thus reasoner offers three defuzzification methods (LOM, SOM, MOM) that follow these fuzzy rules (Bobillo, 2016). However, the knowledge base may require additional information to be added to improve the accuracy of diagnosis in such cases. Based on medical expert knowledge, additional information related to the patient's health status, such as semantic antecedents for risk factor diseases related to liver fibrosis severity diagnosis, was added in this case.

Implication rules and concept definition approaches differ mainly in terms of the defuzzification methods they employ. In particular, the former does not take into account the shape of the fuzzy set, while the latter's numerical output is implicitly based on the shape of the output fuzzy set, as seen in COA (Yaguinuma et al., 2013). As the output property in the liver fibrosis diagnosis system has an interval overlap, while each interval corresponds to a fuzzy linguistic term with its own fuzzy set shape, the concept definition approach may be assumed to be more suitable for representing and reasoning with fuzzy rules in FuzzyDL. To measure the degree of satisfiability and to infer the crisp values of fuzzy concepts, the command (defuzzily-mom? RuleSet p8 diagnosed)) was used after the rules were executed. The output terms (absentFibro,mildFibro,signFibro,cirrhosis) and their properties within the range [k1,k2] was thus modeled using fuzzy ontology. The MOM defuzzification method was used to calculate their means, as, where $[0.0, 5.0].]$. The concept definition approach was applied to employ the fuzzyDL reasoner to infer the relevant satisfaction values, based on the firing accuracy of the fuzzy rules, which were in the range $\in [0.1]$ for all diagnosed individuals.

3.3. Fuzzy reasoning

The ontology in this work was built using fuzzy datatypes defined with fuzzyDL. The performance of the related reasoning system thus heavily relies on the effectiveness of the employed reasoner. While the fuzzyDL reasoner (Bobillo, 2016) can reason with fuzzy logic for OWL2 ontologies, it has several limitations such as not enforcing symmetry or reflexivity restrictions, as well as not supporting cardinality constraints (Rodríguez et al., 2014). However, these limitations are not critical for the current work. The online phase of the system receives input data samples from HCV patients, which are applied to the architecture of the reasoning system, as depicted in Fig. 8.

The reasoning system thus consists of two phases: the user query input management procedure and a fuzzyDL rule-based reasoning procedure. Using fuzzy ontology, the user query is converted into a semantic query that can be processed by the inference engine. Then, as described in Algorithm 1, a set of fuzzy rules r_j is inferred for each input vector x_i using the fuzzy inference engine. The fuzzyDL reasoning algorithm is based on fuzzy inference rules and an optimization solver is thus used to perform approximate reasoning and infer the output.

3.3.1. Fuzzy queries executing

The query is fuzzified based on the corresponding fuzzy set with respect to numerical features, while other ordinal and categorical features remain the same. The query is defined in a semantic form as conjunction of predicates, such as $Q_J = p_1 \sqcap p_2 \sqcap \ldots \sqcap p_i$, where each p_i contains fuzzy concept assertion $(a : C_i,\ n)$. Here, the fuzzy object property assertion is $(a, b : R_i,\ n)$, the fuzzy data property assertion is $(a, \upsilon : T_i,\ n)$, and the fuzzy datatype for υ linguistic terms (Bobillo, 2016). In order to facilitate reasoning, the query vector for asserting individual *'p18'*, could be $Q = < wbc = 5.3,\ ast = 46,\ fatigue = 6,\ age = 50,\ gender='male',\ disease = \text{“}lichenPlanus\text{”}, \ldots >$, for example, with a semantic representation of the query encoded as ABOX in fuzzyDL.

(instance p18 (= hasID 118)1.0)	(instance p18 (= hasWbc 5.3) 1.0)	(instance p18 (= hasDyspnea 1.0) 1.0)	(related p18 no hasEnlargedSpl 1.0)
(instance p18 (= hasAlt 37.0)1.0)	(instance p18 (= aged 50.0) 1.0)	(instance p18 (= hasAppetite 9.0) 1.0)	(related p18 no hasPortalVein 1.0)
(instance p18 (= hasAst 46.0)1.0)	(instance p18 (= hasDiarrhea 1.0)1.0)	(instance p18 (= hasFatigue 6.0) 1.0)	(related p18 no haslesions 1.0)
(instance p18 (= hasSb 2.9)1.0)	(instance p18 (= hasJaundice 9.0)1.0)	(instance p18 male hasGender 1.0)	(related p18 lichenPlanus hasDiseas1 .0
(instance p18 (= hasPlt 189.0)1.0)	(instance p18 (= hasVomting 1.0)1.0)	(related p18 no hasHepaticAscites 1.0)	(*instance* p18 (= *diagnosed* 2.5) 1.0)

Algorithm 1: fuzzyDL approximate reasoning

Input: inference rules r_j, Fuzzy propositions $D^k \to D, D = [0,1]$, input variable,

Begin

Step 1: For each variable x_i Of rule r_j,

- Compute the weight $\mu_{Ci}(X) = w_i,\ w_i \in [0,1],\ \sum_i^k w_i = 1$

  $\mu_{Ci}(X): X \to [0,1]$, each fuzzy concept $C_i \in \{X_1, \ldots, X_k\}$,

  $\mu_{C1}(X) \geq \mu_{C2}(X) \geq \cdots \geq \mu_{Ck}(X)$

- Select max w_i

Step 2: For each rule $r_j, r_j \in \{r_1, r_2, \ldots, r_p\}$,

- Aggregate r_j Clauses by selected fuzzy operator @ // a function $@^I : D^k \to D$ //
- Aggregate the related consequence into firing degree using inference mechanism

  $\oplus_{j=\{1,\ldots,p\}}(x_{j1} \otimes x_{jn} \otimes y_o)$ // Weighted maximum-weighted minimum- weight sum//

Step 3: Defuzzified the output variable τ // LOM, SOM, MOM//

Step 5: next iteration,

Go to Step 1

End

The next step is thus the fuzzification of numerical data, while categorical and ordinal data remain the same, which involves encoding the instance structure of the data. Thus, the resulting query vector will be $Q =< lowWbc = 0.2,\ normalWbc = 0.8,\ highWbc = 0.0,\ \ gender ='male',\ \ disease = \prime 4776004 \prime, . >$. The fuzzified query then needs to be transformed into a semantic query, or a conjunction of a set of predicates based on the interval defined for each output class.

3.3.2. FuzzyDL RBR system

As illustrated, a fuzzy rule-based system consists of a set of fuzzy rules r_j, Algorithm 1 illustrates the inference mechanism used to perform an approximate reasoning process. For every clause in the antecedent of the rule, the satisfiability degree of a current value of the variable and the linguistic label in the rule are typically computed using $t - norm\otimes$ and implication $\Rightarrow$, then the developed rule clauses are aggregated into a firing degree using a fuzzy logic operator $t - conform\oplus$, before aggregation operators (AOs) aggregate the k values of O different consequences related to the fuzzy output variable y. Finally, the output variable is defuzzified by using a defuzzification method such as largest of maxima (LOM), smallest of maxima (SOM), and middle of maxima (MOM) (Rajendran, 2015).

The developed reasoning system thus infers the output property, "diagnosed", for patient satisfaction β using the fuzzy rule set and the MOM defuzzification method using a Gurobi optimizer. The obtained values are then passed back into the fuzzy ontology for diagnosis using fuzzy ontology reasoning tasks. As an example, where the approximate reasoning infers the output value $\beta = 2.5$ as in $(instance\ p18\ (= diagnosed\ 2.5)\ 1.0))$, an output conceptualizing the degree of satisfiability, the system computes the maximal entailment degree for the "diagnosis" concept assertion axiom by applying the reasoning task (instance oCn), where $n \geqslant 0.0$. Patient case 'p18' is an instance of 'cirrhosis' with a degree of n = 0.714. However, the degree for other output classes, such as: 'liverFibrosis3', 'liverFibrosis2', and 'absentFibrosis', is at least $n \geqslant 0.0$ in all cases. As this work aims to predict the severity of fibrosis in each case, particularly cirrhosis, that may affect the long-term treatment process, the query $(all - instance?\ cirrhosis)$ is thus also used to check the satisfiability for individuals with cirrhosis.

This research thus proposes a new approach to fuzzy inference mechanisms based on semantic similarity and fuzzy set theory. Semantic approaches have been applied in fuzzyDL reasoning in order to measure medical concept similarity semantically using constructed ontologies. Semantic similarity defines how similar the meaning of concepts is based on "IS-A" relationships (Elsappagh et al., 2015). Semantic similarity thus depends on defining the ontological structure to infer a level of similarity between two concepts (Elsappagh et al., 2015). The semantic similarity between concepts $sim_{path} = 1$, where C1 = C2 in the same class (e.g. disease instances) is strong; elsewhere, the semantic similarity $sim_{path} \in [0, 1]$. For example, the antecedent of fuzzy rule '(-some hasPortalVein yes)' when inferred by the previous query vector $Q\ =<\ disease = \text{"}lichenPlanus\text{"}, \ldots >$ for emph'p18', we can say, Sim (lichenPlanus, portal vein) =1, as these diseases are very specific instances of one concept. Finally, the aggregation of antecedents for every rule r_j is based on the fuzzification of numerical data and the identification of semantic similarity among the structured data.

4. System evaluation

The FsP system proposed in this study is a rule-based system that aims to predict the severity of liver fibrosis in patients with chronic HCV infection. The central component of this system is a fuzzy ontology. The evaluation of the system was conducted in several phases, based on a full analysis of the obtained results and a comparison of the performance of the proposed system with that of the Mamdani inference system (Sweidan et al., 2019). Additionally, a general discussion of the overall efficiency of the proposed system against other similar systems is offered.

4.1. Ontology evaluation

This section focuses on the comprehensive evaluation of the fuzzy LiverFibrosisOnto ontology, taking into account its syntax, semantics, and coverage. The evaluation process involved assessing the ontology by defining a set of desirable qualities and requirements, such as conciseness, correctness, intelligibility, and adaptability against which to compare it. Creating an ontology that is widely accepted is an iterative process, involving use, critical analysis, and continuous updating and reimplementation over an extended period. Based on the lack of universally accepted evaluation mechanisms (Fakhfakh et al., 2021), alternative methodologies were also required to evaluate the ontology's quality. According to El-Sappagh and Elmogy (2017), conventional evaluation metrics such as precision and recall are not suitable for ontologies, which require a comparison with a standard ontology, which may not always be available. Consequently, several different evaluation methodologies may be employed, and in this study, an evaluation method based on classifying quality evaluation methods for ontologies was employed. By following this approach, a comprehensive and robust evaluation of the fuzzy LiverFibrosisOnto ontology was thus enabled.

4.1.1. Ontology consistency

The use of this approach in the HCV medical domain and liver fibrosis diseases presents a valuable opportunity to improve the diagnosis and treatment decisions for chronic HCV-infected patients through the inclusion of ontology in automatic clinical decision support systems. The developed LiverFibrosisOnto ontology has 189 semantic classes, 48 fuzzy classes, 10 fuzzy object properties, 23 fuzzy datatype properties, 24 fuzzy datatypes, a 437 logical axiom count, a 216 subclass axioms count, a 58 equivalent class axioms count, a 68 individual count, and an 86 entity annotation axioms count, all based on 47 real patient cases. To validate the ontology, the OWL reasoners HermiT 1.3.6, Pellet 2.3.0, and Fact++ were applied to check consistency between the crisp ontology, while the fuzzyDL 1.1 reasoner was used to check consistency and the ability to reason using fuzzy concept definitions. The Ontology Pitfall Scanner (OOPS!) and the Manchester ontology validation tool were also used to ensure that the overall outcomes were free of common ontology development pitfalls. To ensure the ontology's correctness, a medical domain expert manually checked this, while to further increase accuracy, the expert's comments on the fuzzy inference in the diagnosis process were incorporated. The expert thus reviewed all fuzzy components and confirmed that the overlap between the functions of each fuzzy variable ranged from 25% to 50%. In terms of ontological completeness, as the crisp ontology may be assumed to be complete, the entire fuzzy ontology is thus complete, containing a comprehensive set of medical terminology related to the diagnosis of the disease of interest, as verified by an expert. Finally, the expert also confirmed that the fuzzy ontology met all necessary requirements for diagnosis.

4.1.2. Criteria-based evaluation

Due to the lack of existing benchmark ontology to assess the proposed ontology against, it was important to nevertheless compare it with other ontologies within the same domain. As in the

Table 2
Comparative evaluation between LiverFibrosisOnto and other ontologies.

Criteria	Metrics	The proposed ontology	FOTS ontology (Fakhfakh et al., 2021)	Diabetes ontology (El-Sappagh and Elmogy, 2017)
Complexity	An average number of paths to reach a class from root	3	3	3
	Average number of object properties per class	1.4	1.2	1.3
Abstraction	The average depth of the ontology	2	3	2
Cohesion	The average number of the connected classes	27	54	27
Conceptualization	Semantic Richness	0.6	0.46	0.49
	Attribute Richness	0.9	1.61	2.26
	Inheritance Richness	4.2	8	5
Completeness	There are no standard fuzzy ontologies to compare	Not applicable	Not applicable	Not applicable
Vagueness Spread	rating the amplitude of imprecision determination in the ontological structure.	0.35	0.55	0.67

case of fuzzy ontologies for liver fibrosis, no specific counterparts were available for comparison, the ontology proposed by El-Sappagh and Elmogy (2017) for diabetes diagnosis and that developed by Fakhfakh et al. (2021) was used as reference points. In evaluating the quality of the proposed ontology, multiple metrics were utilized, with evaluation criteria that encompass a range of aspects such as complexity, cohesion, conceptualization, abstraction, completeness, and comprehension (Fakhfakh et al., 2021) (see Table 2). Upon comparing the proposed ontology with the ontologies noted, LiverFibrosisOnto was found to exhibit the characteristics of being complete, functional, and semantically rich.

4.2. Proposed system performance

In this section, the relative benefits of the applying resulting fuzzy rule-based system for the prediction of fibrosis severity with respect to crisp approaches are discussed. The satisfiability degree is thus considered as an evaluation parameter, in terms of whether the fibrosis stage is predicted and its influence on the diagnosis accuracy. Liver fibrosis severity ratings from the 47 real patient samples (40% dataset) were thus grouped into four categories: absent, mild, significant, and cirrhosis as presented in 9.

These results are illustrated in 3. The input variables for each sample were then added to the developed system and the output results were derived as represented. As in Fig. 10, the horizontal axis represents the predicated fibrosis severity stage for each patient case, with the results classified into four overlapping categories. To improve readability, the horizontal axis was divided into four zones according to the fuzzy output intervals defined in Section 3.1.3. Based on this, 15 patients were placed in the absent zone, 13 in the mild zone, 9 in the significant zone, and 10 in the cirrhosis zone.

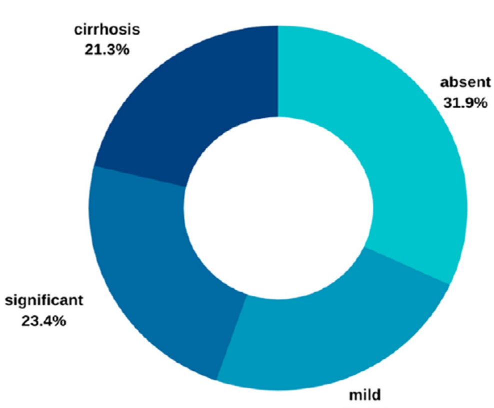


Fig. 9. Distribution of patients by fibrosis stage.

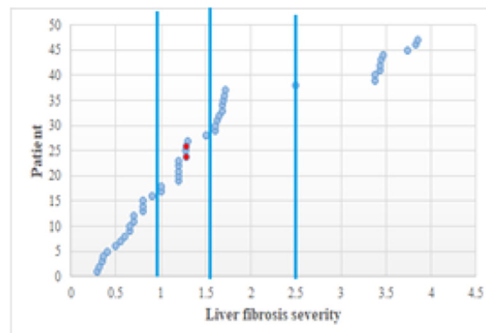


Fig. 10. Results based on defuzzification values.

To evaluate the outcomes from the system, a statistical comparison was made between the expert diagnoses and the system diagnoses. The results for the given dataset showed an agreement of 0.957, with the Cohen Kappa statistic (Smeeton, 1985) used to measure the agreement between the system and the expert as follows:

$$k = \frac{Pr(a) - Pr(e)}{1 - pr(e)} \tag{2}$$

where Pr(a) is the actual observed agreement, and Pr(e) is the hypothetical probability of chance agreement. The relevant statistics were thus calculated as follows: $Pr(a) = \frac{15+11+9+10}{47} = 0.957$, and $pr(e)_{FsP:f0} = \frac{15}{47} = 0.319, Pr(e)_{expert:f0} = \frac{15}{47} = 0.319$.

Therefore, $Pr(e)_{f0} = Pr(e)_{FsP:f0} \times Pr(e)_{expert:f0} = 0.319 \times 0.319 = 0.1018$. The other classes were then calculated as follows:

$Pr(e)_{f1} = 0.0647, Pr(e)_{f2} = 0.0448, Pr(e)_{f3} = 0.0452, finally Pr(e) = Pr(e)_{f0} + Pr(e)_{f1} + Pr(e)_{f2} + Pr(e)_{f3} = 0.256$.

Thus, $k = \frac{0.957-0.256}{1-0.256} = 0.942 = 94.2\%$.

This highlights that the FsP results have a 94.2% correspondence with the medical expert's decisions.

Fig. 11 illustrates the confusion matrix for the system results. The measuring terms used were drawn from (Sweidan et al., 2019); with true positive (TP) counting the cases of correctly identified cirrhosis; true negative (TN) counting the cases correctly identified as non-cirrhosis; false negative (FN) counting the cases incorrectly identified as non-cirrhosis; and false positive (FP) counting the cases incorrectly identified as cirrhosis. These measuring terms were used in measuring performance across all four output diagnosis classes, indicating that the outcome of the system

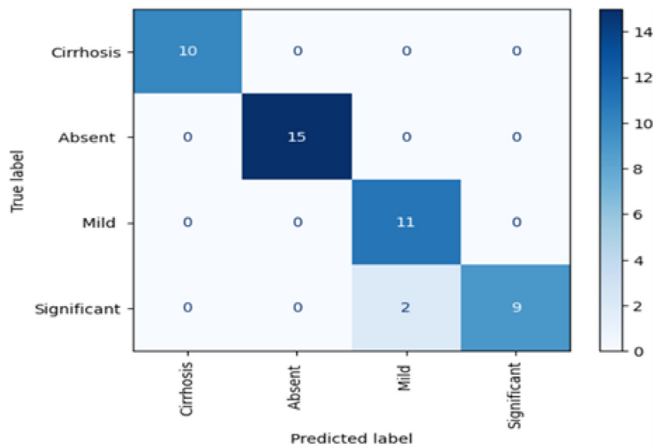


Fig. 11. Confusion matrix for results evaluation.

offers remarkable performance, as shown in Fig. 12. Overall, the system achieved an accuracy of prediction of 97.8%. Thus, the proposed system is expected to be highly useful in supporting physicians specializing in liver diseases.

To determine the statistical significance of the proposed system versus Mamdani, Friedman test was conducted to compare the proposed model's performance and Mamdanie's performance. The test yielded a statistically significant result (${}^{2}(1)$ = 5.000, p = 0.0150), indicating significant differences in the performance of the two models. Post-hoc analysis using the Wilcoxon signed-rank test with Bonferroni correction revealed that the proposed system (Mdn = 4) performed significantly better than Mamdanie (Mdn = 2, Z = −2.828, p = 0.0047)."

4.3. Comparison between the proposed system and the other fuzzy systems.

This study aimed to help solve the prediction problem for liver fibrosis stages for HCV patients using a set of biomarkers implemented in an FsP system, creating a medical fuzzy semantic system for liver fibrosis stage diagnosis. A prediction model was constructed based on fuzzy rules developed by applying a fuzzyDL reasoning method to experimental datasets, and functions for both input and output parameters. The study thus utilized a real dataset in an appropriate semantic framework. A training dataset of 60% of the full dataset was used to generate the knowledge base (Sweidan et al., 2019), and a fuzzy decision tree was then implemented to generate 74 fuzzy rules for use in the prediction model within the semantic framework. The generated fuzzy rules were defined using the Mamdani fuzzy inference system (Sweidan et al., 2019), with the same fuzzy rules generated in the form of fuzzyDL concept definitions to be used as the knowledge base for the semantic fuzzy system. Fuzzy rule-based systems develop fuzzy if-then rules using fuzzification and inference methods, and the resulting fuzzy output is usually converted into crisp output through defuzzification (Van Leekwijck and Kerre, 1999). The remaining 40% of the dataset was then used in an evaluation process for both systems: the dataset overall contained 47 real data samples, with patients across all stages of fibrosis.

The study compared the results of a standard fuzzy rule-based system without any semantic capabilities against the results of the developed fuzzy semantic system FsP using pre-defined terms. The proposed system was thus found to be an improvement on the previous system (Sweidan et al., 2019); the liver fibrosis diagnosis system developed based on Mamdani fuzzy inference system was used to evaluate the developed linguistic variables based on membership functions and the fuzzy rules. The numerical output was thus generated by using Mamdani FIS corresponding to the aggregated rules value in the domain of discourse (Van Broekhoven and De Baets, 2006). In defuzzification, the center of gravity (COG) function is used to defuzzify output variables in a manner not based on the shape of the output fuzzy set (Van Broekhoven and De Baets, 2006). Thus, existing fuzzy expert systems cannot extract membership values for liver fibrosis stages. In contrast, the FsP uses the MOM defuzzification method to produce the mean value of the maximum membership values based on the shape of the output fuzzy set, which offers membership capability (Van Leekwijck and Kerre, 1999). Table 3 illustrates the results obtained by the FsP expert system for 10 samples from the dataset, with the output values passed into fuzzy ontology and thus available to other reasoning tasks, such as instance, check queries for output classes with user authorization. In each class, the prediction results were compared with the actual diagnoses by a medical expert. Eqs. (3)–(6) were then used to calculate the relevant metrics Sabbeh and Fasihuddin (2023), Zamzami et al. (2023).

$$precision\ (Pre) = \frac{TP}{TP + FP} \tag{3}$$

$$Recall\ (Re) = \frac{TP}{TP + FN} \tag{4}$$

$$Accuracy\ (Acc) = \frac{TP + TN}{TP + TN + FP + FN} \tag{5}$$

$$F1 - measure = \frac{2 * precision * recall}{precision + recall} \tag{6}$$

Fig. 10 10 shows a comparison of the performance metrics for Mamdani FIS (Sweidan et al., 2019) and the fuzzy rule-based ontology. This illustrates that the average rates increased in the case of

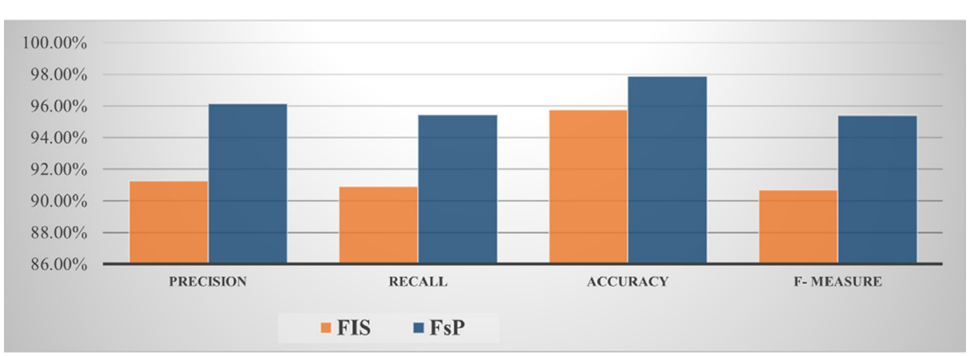


Fig. 12. Comparison between Mamdani FIS and fuzzy ontology.

fuzzy ontology in all cases. The average precision rate increased from 91% to 96%, accuracy increased from 95.7% to 97.8%, and function measure increased from 90% to 95%. Moreover, the precision and recall rate increased for the fuzzy ontology as compared to Mamdani FIS; in one instance, the FsP result (patient29, significant) had a satisfaction value of 1.6, thus matching the expert opinion, while the instance (patient29, cirrhosis) had a satisfaction value of 3.34 under Mamdani FIS, thus not matching the expert opinion. The proposed system thus appears able to predict fibrosis at high levels Significant, cirrhosis, and the achieved results suggest that liver fibrosis severity prediction is both more precise and accurate than existing systems.

Discussion. In this work, knowledge of the medical domain was integrated into a fuzzy ontology with a fuzzy rule base to generate a fuzzy expert system. The resulting FsP system can handle imprecision and uncertainty at both input and output levels. The system can thus be used to process medical terminological knowledge in a clinical domain to represent both patient cases and rules and thus interpret fibrosis diagnoses. Within this approach, 17 concepts and 74 diagnosis rules were elicited to meet the system requirements. The derived model was then evaluated against a dataset featuring 47 real HCV patients who were clinically and pathologically diagnosed by medical experts. Machine learning was used to construct a fuzzy rule knowledge base that offered interoperability across complete coverage of the diagnosis domain. There are two approaches to describing and modeling fuzzy rules in fuzzyDL: the implication rules, and concept definition and defuzzification. In terms of the obtained satisfaction values during the development of the initial approach utilizing implication rules, certain sample cases emerged where satisfaction could not be inferred, leading to inconsistencies in the resulting knowledge base. As a result, the system achieved an accuracy rate of only 64.5% when fuzzy rules were developed using this approach. For the available dataset, however, the system developed using the alternate method gave the correct diagnosis for nearly 98 of the patients. The system faults tended to the diagnosis of cases (patient24, patient25) diagnosed by physicians with significant fibrosis as having mild fibrosis, as seen in Fig. 9. Overall, however, the concept definition and defuzzification approach was deemed more suitable for use in a diagnosis system than the implication rules approach provided by the fuzzyDL reasoner. The RBR system layer is the core layer in the proposed system, as this contains the whole RBR cycle. In this layer, the fuzzy ontology, fuzzy rules, and the set of queries are all coded by fuzzy description logic and syntax through a sublime text editor to facilitate interactions with the fuzzyDL syntax (Parry and MacRae, 2013a).

FuzzyDL is characterized by an environment that provides a representation of object descriptions using only linguistic information (Bobillo, 2016). The fuzzy ontology was thus used to predict fibrosis severity using a fuzzyDL reasoner based on the available data objects (Parry and MacRae, 2013b). The fuzzyDL reasoner supports expressive logic with elements that no other fuzzy reasoner utilizes, such as the aggregation of fuzzy concepts, fuzzy implications for fuzzy hierarchy structures, and defuzzification (Bobillo, 2016). One of its functions is a fuzzy ontology reasoner, which permits inference-related fuzzy concepts, and another supports fuzzy rule inference. Thus, in this context, the fuzzyDL reasoner may be considered a hybrid reasoner (Bobillo, 2016). Various researchers have thus used the fuzzyDL reasoner in inference mechanisms to infer outcomes in several domains, including cardiovascular (Parry and MacRae, 2013b), Alzheimer's disease (Tsai, 2014), diabetes (Elsappagh et al., 2015), and obesity-related cancer (Elhefny et al., 2015). Table 4 illustrates the empirical analysis of methodologies developed in rule-based systems in different medical domains based on semantic frameworks. Chen et al. (2012) developed their model based on a crisp ontology integrated with

Table 3
Results obtained using the FuzzyDL approaches.

P#	Laboratory test					Symptom						Sign				Age	Gender	Disease	FuzzyDL Concept Definition Satisfiability [0.0,5.0]	Liver Fibrosis Stage
	ALT	AST	SB	PLT	WBC	Jaundice	Diarrhea	Dyspnea	Vomiting	Fatigue	Appetite	Hep. Ascites	spleenEnlrg	Portal vein	Liverlesions					
10	41	37	1.4	416	9.5	5	2	2	1	6	9	0	0	0	0	58	M	N/A	0.65	absent, 0.8
39	67	125	1.7	78	5.6	9	9	5	1	7	5	1	1	1	1	59	F	Obesity	3.375	cirrhosis, 1.0
13	48	44	0.7	158	4.5	3	1	6	2	5	6	0	1	0	0	60	M	N/A	0.8	mild, 0.4
41	86	84	2.8	61	6.2	9	4	1	8	5	9	1	1	1	1	62	M	Portal hypertension	3.437	cirrhosis, 1.0
20	54	65	2.0	416	10.1	8	1	1	4	5	9	0	0	0	0	39	M	Diabetes	1.2	mild, 0.83
8	22	25	0.6	194	4.91	1	1	1	1	6	5	0	0	0	0	40	M	N/A	0.60	absent, 0.83
37	53	92	1.3	110	6.0	6	1	2	2	5	1	0	0	1	0	62	M	Portal hypertension	1.72	significant, 0.43
2	18	23	0.3	230	5.3	1	1	1	1	6	9	0	0	0	0	23	M	N/A	0.31	absent, 1.0
29	85	46	2.4	155	5.3	6	1	1	1	6	9	0	0	0	0	68	M	N/A	1.6	significant, 0.39
47	37	61	2.6	44	6.0	1	1	5	1	9	1	0	0	1	0	65	M	Portal hypertension	3.85	cirrhosis, 1.0

Table 4
Empirical analysis of other rule-based ontology approach.

Reference	Technique	Domain	Year	Accuracy
(Chen et al., 2012)	Crisp ontology + fuzzy rules	Anti-diabetic drugs recommendation	2012	80 %
	Crisp ontology + SWRL	Diabetic patients undergoing surgery	2014	90 %
(Torshizi et al., 2014)	Fuzzy ontology + fuzzy rules	Benign prostatic Hyperplasia	2014	90 %
(Alharbi et al., 2015)	Crisp ontology + SWRL	Diabetes Mellitus	2015	89 %
(Messaoudi et al., 2018)	Crisp ontology + SWRL	Liver cancer	2018	85 %
	Crisp ontology + SWRL	Breast cancer	2021	67.36%
	Fuzzy ontology + fuzzy rules	Liver fibrosis	2023	98%

a fuzzy inference system, which offered 80% accuracy: the fuzzy mapping rule provided a functional mapping between fuzzy input and fuzzy output, yet the crisp ontology that represented the relationship between input and output became very complicated when developed in the fuzzy system. Torshizi et al. (2014) built on this to develop a clinical decision support system using another tool. They developed their methodology by adding fuzzy ontology and fuzzy rule reasoning in the BPH domain; however, they did not apply semantic capabilities to their fuzzy inference system. This study thus took a very different approach to integrate semantic approaches with fuzzy inference systems to ascertain system output using fuzzyDL, which appears to speed up the run time and allow the generation of more accurate results.

The proposed system is based on a set of features related to liver fibrosis disease that includes routine blood laboratory tests, patient physical examinations, demographic data, and risk factors for such diseases in semantic terms. The experimental results for the system confirm the applicability of the approach to diagnosing such diseases: the average precision rate of the existing system is just 91.2% (Sweidan et al., 2019), whereas that of the proposed system is 96.1%, an improvement of nearly 5%. The results of a comparative analysis between systems also confirmed that supplementing the fuzzy rules with an ontology-based approach is more efficient in terms of diagnostic processes in ascertaining liver fibrosis severity. Integrating fuzzy ontology with a crisp ontology that follows crisp logic and reasoning approaches can be challenging due to the differences in semantics, reasoning mechanisms, and representation methods between these approaches. Interoperability issues must thus be carefully addressed to ensure effective integration and seamless communication between fuzzy and crisp systems. Overall, while fuzzy ontologies have advantages in terms of handling uncertainty and imprecision, they also have limitations related to computational complexity, subjectivity, interoperability, and development and maintenance effort. Addressing interoperability challenges often requires developing mapping mechanisms, and translating between fuzzy and crisp representations, and established approaches to creating common ground that enables communication between fuzzy and crisp ontology were thus applied in this work (Sweidan et al., 2020). However, these can add complexity and introduce additional layers of translation or interpretation, which may impact the overall efficiency and effectiveness of an integrated system.

5. Conclusion and future work

Liver fibrosis is a resistant disease found in chronically infected HCV patients. The nature of this disease means that it requires long-term treatment, yet despite the importance of addressing it, it has been overlooked by many data scientists. In this paper, an intelligent system FsP is thus proposed to predict liver fibrosis severity among chronically infected HCV patients.

The proposed approach has a competitive advantage, being the first method to achieve liver fibrosis diagnosis using fuzzy ontology integrated with fuzzy rule reasoning. Soft computing methods have been implemented in most existing research studies on liver fibrosis disease, while the FsP system achieves an increase in average precision over the existing system. The proposed approach thus makes several further contributions: it uses standard medical terminologies to build a formal ontology and uses data mining tools to build fuzzy rules for prediction from the available dataset. Using FuzzyDL reasoning allows inference of the output properties to be available to other fuzzy ontology reasoning tasks, while the integration of fuzzy rules with fuzzy ontology enhances the accuracy of prediction. The proposed system achieved an accuracy of 97.8%, and the results were also independently deemed reliable by physicians specializing in the diagnosis of liver fibrosis severity.

The study can be expanded in terms of three main aspects. The first addresses heterogeneity by emphasizing the matching between "fuzzy" and "crisp" structures. The second requires incorporating Fuzzy Rules and Fuzzy Ontology into a decision support system, which could assist medical communities in conducting analysis and providing explanations. Finally, the third emphasizes the design of a Fuzzy Knowledge Base (FKB), which could further enhance system capabilities.

In the future, treatment procedures will be further enhanced by making the field of chronic patient monitoring more effective in terms of precipitating and supporting long-term treatment. Future work in this area should thus be based on the use of fuzzy service ontology structures to represent knowledge about standard cloud services, including PaaS, IaaS, and SaaS, as a way to build semantic technology-based systems.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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