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CADIAG-2/GALL: An experimental expert system for the diagnosis of gallbladder and biliary tract diseases*

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Abstract. The paper on hand reports on preliminary results obtained by applying the diagnostic expert system CADIAG-2 in the area of gallbladder and biliary tract diseases. The study included 71 clinical cases from a university hospital. 32 of them were multi-problem cases. The cases were tested retrospectively. The accuracy of CADIAG-2's results was determined by comparing the computer diagnoses with the clinically or, if available, anatomic-pathologically confirmed diagnoses. A total accuracy of about 90% could be reached, where the respective evaluation criterion was whether the gold standard diagnosis was either confirmed by CADIAG-2 or established as a diagnostic hypothesis at the first, second, or third place in the ranked list of proposed hypotheses. In the multi-problem cases, all discharge diagnoses were tested and evaluated separately.

Key words: diagnostic expert system, consultation system, medical information system, gallbladder and biliary tract diseases, internal medicine, fuzzy set theory, fuzzy logic, CADIAG-2/GALL, WAMIS.

1. Introduction

The paper on hand describes preliminary results obtained by applying the diagnostic expert and consultation system CADIAG-2 to 71 clinical cases with gallbladder and biliary tract diseases.[1] After discussing both the clinical aim of CADIAG-2 and its present state, an overview on CADIAG-2 is given. This overview contains brief descriptions of the components of CADIAG-2, such as its integration into the medical information system WAMIS,[2] its medical knowledge representation, its fuzzy and heuristic inference process, the medical knowledge acquisition, the medical knowledge base consistency checking, and CADIAG-2's implementation and knowledge compilation. In addition, some evaluation results obtained in other medical areas are also given. The paper then describes CADIAG-2/GALL,[3] presently working as a self-contained subsystem of CADIAG-2. It reports in detail on the present extent of CADIAG-2/GALL's knowledge base and describes the application results gained so far. A discussion about these results and about further work to be done concludes this article.

2. Clinical aim and present state

The general objective of the CADIAG-1 and CADIAG-2 projects is the development of a diagnostic expert and consultation system for differential diagnosis in internal medicine (Adlassnig et al. 1985). For this purpose, internal medicine was not taken as a whole but subdivided into its specialties cardiology and angiology, pulmonology, nephrology, gastroenterology and hepatology, hematology and oncology, endocrinology and metabolic disorders, rheumatology, neurology, and psychiatric disorders. These diagnostic groups will be all part of one program – only a small portion of this enterprise has been finished until now –, but they are and will be established and tested separately. However, given medical data of a patient, differential diagnosis can subsequently be carried out in each of these diagnostic groups. If the diagnostic results in one group are not sufficient, indications are provided by the program informing the user in which other medical areas complementary diagnoses have to be searched for.

The underlying clinical issues of the CADIAG programs are the following: (a) on the basis of the patient's findings, definitely present, definitely absent, and possible diseases should be indicated by the program; (b) in so doing, special emphasis should be laid on medically possible but rare diseases; (c) findings unaccounted for by the diagnostic outcome should be marked as such and indications to other diagnostic groups should be given whose diagnoses could explain these findings; (d) proposals for further diagnostic procedures considering their risk for the patient should be presented to the user; and, last but not least, (e) the program is intended to promote a better understanding of nosological relationships in internal medicine for the medical diagnostician.

After gaining experience with the expert system CADIAG-1 (Adlassnig et al. 1985) which was formally based on first-order predicate logic and pattern matching – the lat-

ter essentially employing precomputed unique finding patterns for hypotheses generation –, the successor system CADIAG-2 was developed and implemented (Adlassnig 1980). This system applies fuzzy set theory (Zadeh 1965, Zadeh 1973) to model inherent vagueness of medical concepts such as 'normal', 'increased', and 'decreased' (Adlassnig 1988), and fuzzy logic to infer diagnostic conclusions from given medical evidence (Adlassnig 1986). In addition, a heuristic support score that combines medical evidence being neither confirming nor excluding for the disease under consideration was devised to rank diagnostic hypotheses (Adlassnig et al. 1986a).

From the beginning, CADIAG-1 and CADIAG-2 were designed in such a way that three modes of application in the hospital are possible (Adlassnig et al. 1986a): (a) the screening and monitoring mode based on easy-to-gather and routine data that is applicable at a very early stage of the diagnostic process; (b) the consultation mode employed after complete data collection including also results from clinical investigations; and (c) the textbook mode without connection to the central patient data base of the medical information system WAMIS used to list possible diagnoses on the basis of one or several findings given to the system.

At present, CADIAG-2's knowledge base contains 295 diseases, among them 185 rheumatic diseases (69 joint diseases, 12 diseases of the spinal column, 38 diseases of soft tissue and connective tissue system, 45 diseases of cartilage and bone, and 21 regional pain syndromes) (Kolarz and Adlassnig 1986) and 110 gastro-enterological diseases (35 gallbladder and biliary tract diseases (Akhavan-Heidari and Adlassnig 1988), 10 pancreatic diseases (Adlassnig et al. 1984), 37 colon diseases, and 28 diseases of the peritoneum). All these diagnostic groups reside in the CADIAG-2 shell and are self-contained to enable differential diagnosis.

After completing and testing the above-mentioned knowledge bases, some of the present diagnostic groups will be combined to larger ones, e.g., the subspecialties of gastroenterology will be put together to a large group of gastroenterology and hepatology. Further differential diagnostic groups will be incorporated as soon as possible, largely depending on further clinical collaborators.

3. The diagnostic expert system CADIAG-2

3.1 Integration into the medical information system WAMIS

CADIAG-2 is integrated into the medical information system WAMIS of the Vienna General Hospital (Adlassnig et al. 1986a). This integration allows the collection of the patient's findings for CADIAG-2 via the routine medical documentation and laboratory system of WAMIS. Through a data abstraction and aggregation process (Adlassnig 1988), patient data are made available to the CADIAG-2 system which tries to infer diagnoses from these abstracted findings in a data-driven manner. Patient data not routinely collected in WAMIS can be added to CADIAG-2 through a man-machine interface which processes medical terms given in natural language. A word segmentation algorithm allows usage of medical synonyms and abbreviations; moreover, it accepts various orthographic variants and takes different medical suffixes into account (Adlassnig and Grabner 1985).

3.2 Medical knowledge representation

CADIAG-2's diagnostic process is primarily based on both stored disease profiles containing findings associated with the disease under consideration from all areas of investigation (e.g., the complete disease profile of *pancreatic cancer* can be found in [Adlassnig et al. 1986b]) and diagnostic decision rules which are often very complex such as the ARA criteria for rheumatic diseases (Arnett et al. 1988, Kolarz and Adlassnig 1986). The disease profiles contain all those findings that are either definitely confirming (pathognomonic), definitely excluding, obligatory, or associated with the disease under consideration. A complex rule is established if a well-known combination of findings is either a definitely confirming (pathognomonic), definitely excluding, obligatory, or strongly indicating criterion for the considered disease.

The degree of association between findings and diseases in these profiles and between rule antecedents and disease consequents in the rules is expressed by two separate relationships: (a) by the necessity of occurrence of a certain finding or a rule antecedent with a disease, and (b) by the sufficiency of the finding or the rule antecedent to infer the disease. In the context of CADIAG-2, these two relationships are called frequency of occurrence and strength of confirmation, respectively (Adlassnig et al. 1986a).

From the statistical point of view, the necessity relationship may be interpreted as sensitivity of the finding or the rule antecedent with the disease. Conversely, the sufficiency relationship is interpreted as positive predictive value of the finding or the rule antecedent for the disease (Adlassnig and Kolarz 1986).

In the context of CADIAG-2's inference process, the necessity and sufficiency relationships between findings and diseases are employed as fuzzy binary relationships. This allows the mathematical composition of fuzzy membership degrees of findings in the patient under consideration with the relationships frequency of occurrence and strength of confirmation to obtain fuzzy membership degrees of diseases in the patient (Adlassnig 1986). This composition is CADIAG-2's basic operation for fuzzy inference and the chaining process. It is also applied to relationships between rule antecedents and diseases contained in CADIAG-2.

In addition, CADIAG-2 allows the inclusion of hierarchical and excluding relationships among findings and among diseases. They are expressed by means of the above-mentioned necessity and sufficiency relationships and employed

by the same compositional rule of inference which was applied to finding-to-disease and decision rule-to-disease relationships (Adlassnig 1986).

3.3 Fuzzy and heuristic inference process

The inference process of CADIAG-2 aims at generating one or more differential diagnoses and, at the same time, at excluding some or all remaining diagnoses (Adlassnig 1986, Adlassnig et al. 1986a).

Diagnoses are indicated as definitely confirmed if pathognomonic findings were found in the patient or confirming rules were triggered by patient's findings. Because of the hierarchical relationships among diseases in CADIAG-2, diagnoses at a higher level in the disease hierarchy are confirmed as well if subdiagnoses are indicated as being confirmed.

Excluded diagnoses are established by either present excluding criteria or absent obligatory criteria. Excluding criteria may be single excluding findings, excluding rules or other, already established diagnoses which exclude other diagnoses. Findings and rule criteria which are defined to be obligatory present in the patient to establish a certain diagnosis but are definitely absent consequently exclude the respective diagnosis. Definitely excluded disease categories in the disease hierarchy cause also the exclusion of the entire set of the respective subdiagnoses, if any.

Diagnoses being confirmed and excluded at the same time – which might happen due to contradictory patient data and/or knowledge base errors – are termed diagnostic contradictions. They are displayed stating the reason of being established.

Diagnostic hypotheses are generated if a diagnosis is: (a) neither confirmed, nor excluded, nor a contradictory result, and (b) the strength of confirmation of at least one present finding, one triggered rule, or one already established subdiagnosis is equal or higher than a given threshold.

Since the application of fuzzy set theory allows for mathematical modeling of borderline findings, the degree of presence of a finding (degree of membership in a fuzzy set) is combined with its strength of confirmation. If the resulting value, which is a measure of certainty of the concluded disease, lies between the threshold and unity (unity means definite confirmation), the respective disease has to be taken into consideration as a diagnostic hypothesis.

In addition, diagnostic hypotheses are ranked according to a heuristic score of support. This score is calculated on the basis of: (a) the number of single findings present or present to a certain degree and having a relationship to the disease under consideration; (b) the degree of presence of these findings; and (c) the degrees of the frequency of occurrence and the strength of confirmation between these findings and the respective disease. This support score reflects the combined evidence for a certain disease.

Diagnoses which are neither confirmed, nor excluded, nor diagnostic hypotheses, nor contradictory results are put into a category denoted 'not generated diagnoses'. This enables the physician to obtain a complete survey of all diseases included in CADIAG-2's knowledge base. An example of a CADIAG-2 inference process in the area of pancreatic diseases can be found in (Adlassnig et al. 1986b).

3.4 Medical knowledge acquisition

In CADIAG-2, two forms of knowledge acquisition have been applied: (a) elicitation of medical knowledge from human experts, and (b) semiautomatic acquisition of medical knowledge from a patient data base with already diagnosed patients.

Medical experts provide definitional and judgmental knowledge from textbooks and their own practical experience. The estimation of appropriate values for the frequency of occurrence and strength of confirmation degrees is assisted by an automatic procedure which calculates the respective values from patient records with known diagnoses stored in the WAMIS system (Adlassnig and Kolarz 1986). Here, the possible statistical interpretation of the necessity and sufficiency relationships mentioned in Section 3.2. is employed.

3.5 Medical knowledge base consistency checking

Due to the large number of medical relationships contained in CADIAG-1 and CADIAG-2, intense efforts have been made to verify consistency and completeness of the respective knowledge bases.

For CADIAG-1, a program was developed that verifies the internal consistency of the stored medical knowledge and – in case of inconsistencies – provides the line of reasoning for subsequent correction (Barachini and Adlassnig 1987). Because of the possible homomorphic mapping of CADIAG-2's finding-to-disease relationships into the finding-to-disease relationship categories of CADIAG-1, this program has partially been applied to CADIAG-2's knowledge base as well (Adlassnig and Kolarz 1986).

3.6 Implementation and knowledge compilation

The on-line consultation system CADIAG-2 was programmed in CICS/VS command level language and PL/1. It is embedded in the time-sharing environment of the medical information system WAMIS, which runs on an IBM 3090/180S under MVS controlled by VM. At most of the screens, input is entered by using light-pens. The knowledge base of CADIAG-2 is contained in several VSAM/KSDS index-sequential files. These records contain the medical knowledge of CADIAG-2 in a compiled and redundant form that guarantees optimal performance.

A complete on-line consultation session includes: (a) access and transfer of patient data from the central patient database of WAMIS to CADIAG-2; (b) abstraction and aggregation of patient data from WAMIS by the patient data fuzzy interpreter; (c) review of patient data by the consulting physician who may add, update, or delete data; (d) the diagnostic fuzzy inference process establishing confirmed and excluded diagnoses as well as diagnostic hypotheses; (e) display of the diagnostic results and their explanations; and (f) input of some further patient data according to the examination proposals of CADIAG-2. Two to three iterations of the consultation session takes between 2 and 10 minutes. The inference process with about 30.000 inference steps (CADIAG-2 application in rheumatology [Kolarz and Adlassnig 1986]) takes only about 10 to 25 seconds depending on the general load of the WAMIS time-sharing system.

CADIAG-2 is also available as a batch-PL/1 program, which accesses the respective VSAM/KSDS files. This program is employed for a number of tests to validate and improve both CADIAG-2's methodology and its knowledge base.

3.7 Previous evaluation results

Results were obtained by applying the system to 544 clinical cases (426 rheumatic cases [Adlassnig et al. 1985], 47 pancreatic cases [Adlassnig et al. 1985], 71 gallbladder and biliary tract cases [Akhavan-Heidari and Adlassnig 1988]). Among them, there were about 180 multi-problem cases with two or more final diagnoses. For each of the rheumatic cases, about 800 findings were available, which were either present (positive), present to a certain degree (borderline), or definitely absent (negative). This large number of findings per patient is the result of the structured data collection in the associated rheumatological department. Each of the pancreas, gallbladder, and biliary tract cases included about 200 positive, negative, and borderline findings.

4. The CADIAG-2/GALL system

CADIAG-2/GALL attempts to establish differential diagnoses in the area of gallbladder and biliary tract diseases. In using this system, it is presently assumed that the patient under consideration is suffering from one or more diseases in this area only.

4.1 CADIAG-2/GALL's knowledge base

Table I shows the 20 gallbladder and biliary tract diagnoses contained in CADIAG-2/GALL's knowledge base. The disease profiles established for these diagnoses contain findings from all areas of medical investigation. Altogether, 597 different findings were included in the 20 disease profiles.

Table I. Diagnoses contained in CADIAG-2/GALL's knowledge base. 20 gallbladder and biliary tract diseases.

carcinoma of gallbladder
polyp of gallbladder
gallbladder calculus
acute cholecystitis
chronic cholecystitis
atonic gallbladder
Mirizzi syndrome
postcholecystectomy syndrome
choledocholithiasis
stone of Vater's papilla
hypertonia of the ductus cysticus
extrahepatic cholangiocarcinoma
polyp of the bile ducts
acute cholangitis
chronic cholangitis
sclerosing cholangitis
hypertonia of the sphincter of Oddi
hypotonia of the sphincter of Oddi
biliary dyskinesia
hemobilia

The number of findings from the different investigation areas is as follows: 137 history items, 78 signs from the physical examination, 151 laboratory test results, 136 X-ray and 19 CT-scan findings, 35 findings from ultrasonography, 22 findings from endoscopy, and 19 biopsy and histology findings.

The extent of the disease profiles, i.e., the number of findings which have been reported to occur in patients with the respective disease, ranges from 20 to 97 with an average of

Table II. Interpretation of the necessity and sufficiency relationships in CADIAG-2.

value	**necessity relationship** (frequency of occurrence)	**sufficiency relationship** (strength of confirmation)
1.00	in all cases	pathognomonic
0.90	very often	very strong
0.75	often	strong
0.50	in half the cases	medium
0.25	seldom	weak
0.10	very seldom	very weak
0.00	never	exclusion

38 findings. Altogether, 1235 necessity and 1119 sufficiency relationships have been included in CADIAG-2/GALL's knowledge base. They are expressed as numbers between zero and unity and represent a shorthand for judgmental information, as their suggested interpretations in Table II indicate. Some findings, such as patient's sex and age, are included in the respective disease profiles but with a necessity relationship only.

Many of the diseases contained in CADIAG-2/GALL cannot be directly confirmed by pathognomonic criteria: they can only be established as hypotheses in the diagnostic inference process.

At present, complex diagnostic decision rules are not defined in CADIAG-2/GALL; however, several rules with high degrees of confirmation have been already devised and will be included in the knowledge base in the near future. Nevertheless, the majority of knowledge in CADIAG-2/GALL will still consist of finding-to-disease relationships contained in the disease profiles.

In addition, 3 hierarchical and 192 mutually exclusive relationships among findings and 18 mutually exclusive relationships among diseases are contained in CADIAG-2/GALL's knowledge base as well.

4.2 Patient data

For this study, 71 clinical cases from the 2nd University Clinic for Gastroenterlogy and Hepatology were tested with a total of 103 gallbladder and biliary tract diagnoses (32 patients had two different diagnoses in this area). The study group consisted of 23 male and 48 female patients, with an age means of 56 ± 20 years (see Table III). There was a lack of cases with the other diagnoses contained in CADIAG-2/GALL; however, it is planned to completely test all included diagnoses on the basis of real patient cases from our hospital and on the basis of cases described in the literature.

Table III. Number of tested cases with gallbladder and biliary tract diseases.

14	cases with	gallstone and acute cholecystitis
9	cases with	gallstone and chronic cholecystitis
9	cases with	extrahepatic cholangiocarcinoma and extrahepatic cholestasis
11	cases with	gallstone
9	cases with	carcinoma of gallbladder
6	cases with	extrahepatic cholangiocarcinoma
5	cases with	acute cholangitis
5	cases with	chronic cholangitis
3	cases with	postcholecystectomy syndrome
a total of		
71	cases with	103 gallbladder and biliary tract diseases

The findings used in CADIAG-2/GALL's inference process were abstracted from the available hospital records. The average number of findings per patient used in this study was 30 positive and borderline findings and 170 negative findings.

4.3 Results

The accuracy of the diagnostic results was determined by comparing CADIAG-2/GALL's diagnostic results with clinically or, if available, anatomic-pathologically confirmed diagnoses, which acted as gold standard diagnoses (see Table IV). Confirmed diagnoses were established in nine cases due to present pathognomonic histology findings. Excluded diagnoses were not obtained.

Diagnostic hypotheses were established if at least one finding with a high degree of confirmation was present in the patient. The respective degree of confirmation is checked against a threshold that can be changed by the user interactively. In this way, the extent of the hypothesis generation can be controlled by the consulting physician. The subsequent ranking of the hypotheses is done according to CADIAG-2's computed heuristic support scores. In most of the tested cases several diagnostic hypotheses were established and the reasons were given correctly.

In multi-problem cases, very good results were obtained in cases with the following two discharge diagnoses: *extrahepatic cholangiocarcinoma* and *extrahepatic cholestasis*. Both diagnoses were in 100% of the cases either confirmed or among the first three hypotheses. Similarly, in cases with *gallstone* and *acute cholecystitis* the computer diagnoses were in 71.4% of the cases on the first place; they were in 92.9% either on the first, the second, or the third place in the ranked list of hypotheses, i.e., both diagnoses were ranked at a high position in the diagnostic process.

In those cases where a single disease was diagnosed, very good results could be obtained with the diagnoses *gallstone*, *gallbladder carcinoma*, and *acute cholangitis*. In all 25 cases tested the correct diagnosis was at least among the first three hypotheses indicated by CADIAG-2/GALL. Unsatisfactory outcome was obtained in some cases with a treatment history that had led to improved clinical patterns and normalized laboratory test results, and in cases with ill-defined diseases such as *chronic cholangitis* and *postcholecystectomy syndrome*.

5. Discussion

We are currently in the process of an extensive clinical evalu-

Table IV. Results obtained by applying the diagnostic expert system CADIAG-2/GALL to 71 cases with 103 clinically or anatomic-pathologically confirmed gallbladder and biliary tract diagnoses.

			CADIAC-2/GALL's diagnoses			
clinical diagnosis	**tested cases**	**tested diagnoses**	**confirmed**	**1st hypothesis**	**1st, 2nd, 3rd hypothesis**	**confirmed, 1st, 2nd, 3rd hypothesis**
gallstone	**14**	14	–	10	13	13 (92,9%)
and acute cholecystitis		14	–	10	13	13 (92,9%)
gallstone	**9**	9	–	4	8	8 (88,9%)
and chronic cholecystitis		9	–	2	7	7 (77,8%)
extrahepatic cholangiocarcinoma	**9**	9	1	6	8	9 (100%)
and extrahepatic cholestasis		9	–	8	9	9 (100%)
gallstone	**11**	11	–	7	11	11 (100%)
carcinoma of gallbladder	**9**	9	7	–	2	9 (100%)
extrahepatic cholangiocarcinoma	**6**	6	1	–	4	5 (83,3%)
acute cholangitis	**5**	5	–	2	5	5 (100%)
chronic cholangitis	**5**	5	–	1	2	2 (40,0%)
postcholecystectomy syndrome	**3**	3	–	2	2	2 (66,7%)
total	**71**	103	9	52	84	93 (90,3%)

ation of the accuracy and acceptance of the CADIAG-2 system (Kolarz and Adlassnig 1986, Adlassnig 1987, Akhavan-Heidari and Adlassnig 1988). As reported above, good results have been obtained in cases with acute diseases and in cases where specific investigations such as X-ray, CT-scan, ultrasonography, endoscopy, biopsy, and histology provide sufficient medical evidence to confirm or to hypothesize a present disease. Reasons for not being successful with CADIAG-2/GALL were the following: (a) some cases did not represent the first hospitalization of the patient; (b) patients often had a treatment history that had improved clinical patterns and laboratory test results; and (c) in some cases only an uncertain or incomplete patient record was available.

The presently obtained total diagnostic accuracy of about 90% is considered acceptable, though further improvement has to be achieved. The next steps aim at enhancing the overall performance of the system. They include: (a) revising the medical knowledge base, (b) carrying out further clinical tests including also prospective case analyses, and (c) performing more complex evaluations of the diagnostic results such as the determination of not only sensitivity rates but also specificity rates and ROC curves (Adlassnig 1987).

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Notes

* This is a revised and extended version of the paper: M. Akhavan-Heidari and K.-P. Adlassnig (1988) quoted in the References below.

1 'CADIAG' stands for *C*omputer-*A*ssisted *DIAG*nosis.

2 'WAMIS' is the German acronym of *W*iener *A*llgemeines *M*edizinisches *I*nformations-*S*ystem (Vienna General Medical Information System).

3 'CADIAG-2/GALL' denotes the CADIAG-2 application in the area of gallbladder and biliary tract diseases.

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