Steps That Lead to the Diagnosis of Thyroid Cancer: Application of Data Flow Diagram

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Abstract. The complete hospital information system supports the electronic patient record, which, with the history registration, its laboratory and depiction examinations through the use of expert systems, leads to the immediate and effective diagnosis and treatment of the illness. In this present study with the use of a data flow diagram, which consists of a small indication of the way an expert system based on Artificial Intelligence can be made applicable, the steps which lead to the diagnosis of thyroid cancer will be mentioned, when the patient is admitted to the outpatient Endocrinology department. With the data flow diagram, the users can visualize the way in which the system will operate and what it can achieve. Also it will present the course which the medical professional follows in order to reach the diagnosis of thyroid cancer with the slightest error percentage, using the medical information in the extensive hospital information system.

Keywords: Thyroid Cancer, Data flow diagram, Artificial Intelligence, Expert Systems.

1 Introduction

The thyroid gland derives from the embryotic endoderm and is found in the frond throat area. It is shaped like a coat of arms, its weight is 15-20 grams and it consists of two lobes which are connected to an isthmus. Thyroid cancer is a relatively rare cancer, but the most frequent endocrine gland tumor [1].

The endocrine patient arrives at the outpatient department and obtains a registration number. Following this, he is directed to the outpatient Endocrinology department. The nurse calls him into the outpatient according to her priority appointment list.

Initially, the patient's medical history is received. The patient's age, of which thyroid cancer usually appears, is between 20 and 70 years old, without excluding the other ages. Even though thyroid cancer is more frequent in women, the relative frequency (malignant to benign tumors) is larger in men and in children because in these groups, the benign thyroid nodes are relatively rare. The patient mentions whether he has been subjected to throat radiation in the past if he has a family history of thyroid cancer or multiple endocrine neoplasia, whether he has any general health problems and if he has, what medical treatment he is taking [2].

A clinical examination follows, in which the nursing staff participates. Palpation of the throat area is contacted for the examination of any node existence (the rapid node increase and the toughness of the composition) or swelling of the lymph glands is examined and the patient is examined for any chance of being euthyroid by checking his vital sings (blood pressure, pulse) and the return of the achillio is checked along with the possible existence of fear in the upper limps. In addition, the patient is examined for any chance of being euthyroid with blood tests (thyroid hormone determination) [2].

The next step after the palpation even if there aren't any sings of swelling of the lymph glands or the existence of nodes, is the ultrasound. If there are signs of nodes, their dimensions are registered to determine whether they have obvious or vague limits, if they are infrasound, ultrasound, isoichos or cystic. Also, the dimensions of the gland are registered and if it has homogeneity, non-homogeneity, echogenicity or hypoechogenicity. Moreover, any possible calcifications are observed [3].

Following this, blood samples are taken by the nurse for the blood examination conduct. More specifically, Thyroid-Stimulating Hormone (TSH), Triidothyronine (T3), Thyroxin (T4), Anti-Thyroid Peroxidase Antibodies (ABTPO), Anti-Thyroglobulin Antibobies(ANTI-TG), Calcitonin (CT) [if there is a history Ca thyroid]. If the rates are normal, the patient is observed every six months or yearly. If the rates aren't normal, a thyroid scanning is conducted, with Technetium medication (Tc 99) and g-camera or Iodine (I131) [2], [4], [5].

It is worth noting that in the presence of nodule, measuring TSH contributes to the assessment of thyroid function. At high levels of TSH, check T4, the ABTPO and ANTI-TG. If the TSH is high, the T4 (or FT4) low, ABTPO positive (+) and ANTI-TG positive (+), there is the indication of thyroiditis Hashimoto (hypothyroidism). In this case, some authors suggest that a predisposition of developing cancer of the thyroid in a territory Hashimoto, due to chronic inflammation in the area. Conversely, when the TSH is low, T4 high, T3 (or FT3) high and ABTPO (+), then there is evidence of Graves (hyperthyroidism). In both cases, the nodule should be investigated [2].

The scanning examination will show whether the node is non-functional or functional. The non-functional node is barely visible because it doesn't absorb a large quantity of the radioactive medicine compared to the salivary glands, while the functional node is more obvious because it absorbs a large quantity of the radioactive medicine. Initially, the functional node is treated with medication when the patient has hyperthyroidism. If the hyperthyroidism cannot be treated with medication, a small dosage of radioactive Iodine is given (I131) (approximately 20mci). A condition for giving RAI (radioactive Iodine) is the absence of cold regions on the scanning because they might cause cancer in the future. If the node continues to be functional, then surgery is conducted. We avoid giving radioactive Iodine (I131) to patients when they are at reproduction age [5].

In the case where the node is non-functional, we examine whether it has calcifications, whether it is larger than 1 cm and whether it is infrasound or solitary. Following this, we proceed to fine needle aspiration with the guidance of an ultrasound. The cytology liquid nature techniques which have been used in the last few years, have significantly increased the accuracy of FNA because they provide higher sufficiency and sample quality and easier application of more techniques like immunocytochemistry. If the result doesn't show malignancy, the patient is observed every six months to a year. However, if it shows malignancy, the patient is operated on in the following six months, a biopsy of the sample is conducted and according to the result, the type of thyroid cancer is determined. The biopsy sample is analyzed microscopically, histologically, immunohistochemically and pathologically, so that the type of cancer will be found. The carcinoma of the thyroid gland in its majority (95%) is diversified carcinoma from follicular cells and constitutes papillary and medullary carcinoma, while anaplastic carcinoma constitutes undifferentiated cells and the medullary shows differentiation towards c-cells [6], [7].

2 The Types of Thyroid Cancer

2.1 Papillary Carcinoma

It is the most frequent type of thyroid carcinoma (80%) in regions with sufficient Iodine and it often appears after throat irradiation. It has decreased mortality and it affects middle aged women more frequently (40 years of age). Macroscopically, it is usually rough, grayish outbreaks with irregular margins. Histologically, the tumor architecture may be papillary, half papillary-follicular or exclusively follicular. Vascular connected axis appears which is covered with monostivo cube shaped epithelium. Today, the pathological-anatomical diagnosis of papillary carcinoma is mostly based on cellular characteristics [8]. The cells are polygonal with eosinophil cytoplasm and with relatively irregular nuclei which throng together in pseudostivadosi. To the naked eye, they are nuclei with a thick nuclear membrane. The mitosis is absent. The cellular atypia is average or even small. Lymphocyte cellular filtration is often observed in the tumor as well as in the remaining thyroid [9]. Immunohistochemical findings are: Thyroglobulin (Tg)+, TTF1+, CK19+, Ker34bE12+, Galestin-3 and HBME-1+ (nonspecific indicators), Panker+, CK7+, CK20-, RET+, synaptophysin-, chromogranini-. The immunohistochemistry is very useful for the identification of the metastasis but less useful for the differential diagnosis. The metastatic papillary carcinoma displays positive immunostaining for thyroglobulin and TTF-1, from the lungs positive immunostaining for TTF-1 and negative thyroglobulin [10].

2.2 Follicular Carcinoma

It is less frequent malignant (10-15% of thyroid carcinoma), in the 5^{th} decade, more frequent in women and in regions with iodine deficiency [10]. Macroscopically, it appears as a solitary, compacted tumor with a capsule and a variety of morphology.

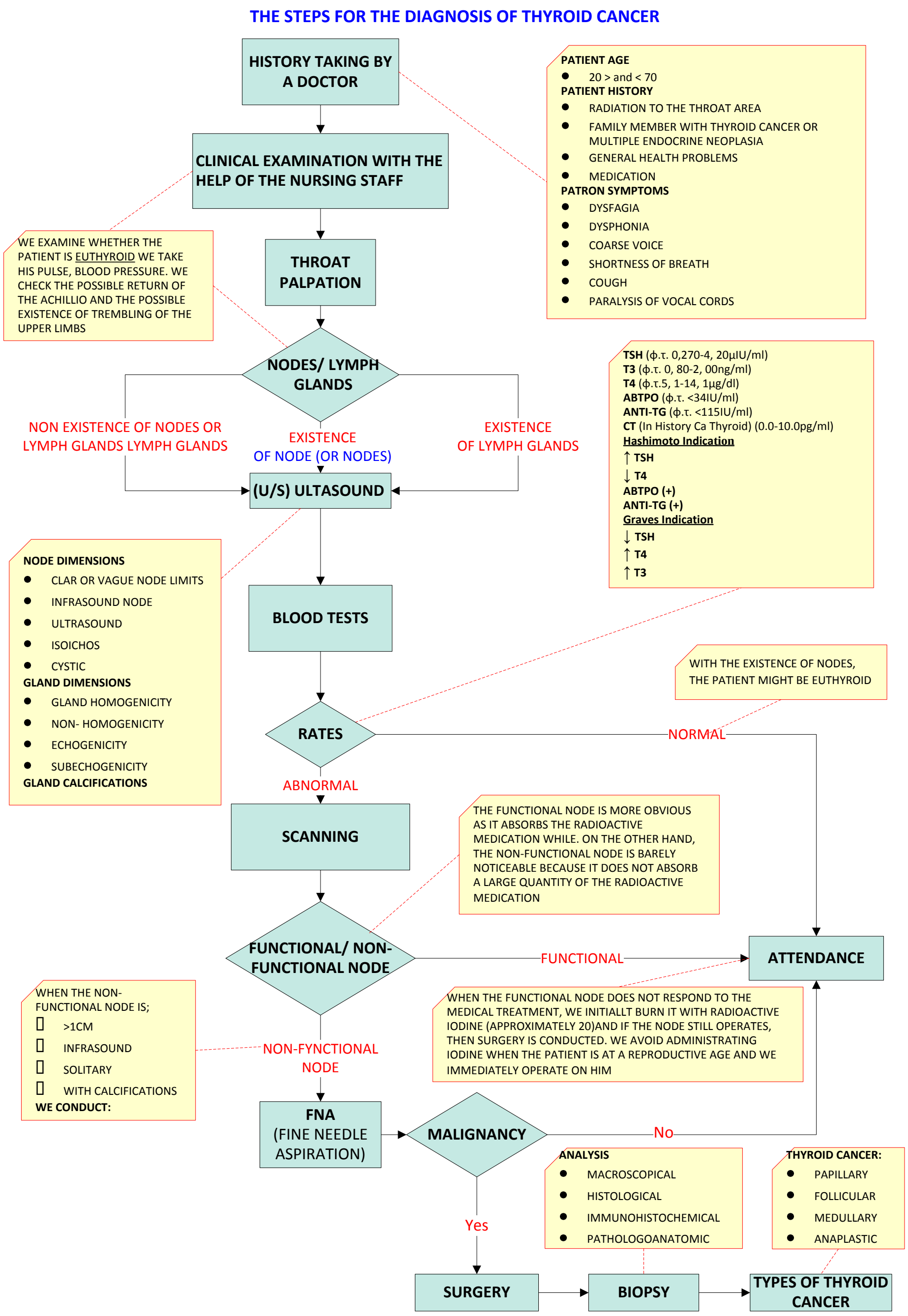

Fig. 1. The steps for the diagnosis of thyroid cancer.

Immunohistochemical findings are: Thyroglobulin (Tg)+, TTF-1+, LMWKer+, Galestin-3 and HBME-1+, CD15+, CD44V6+, BCL-2+, E-cadherin+, beta-canin+. Pathological-anatomical, it is characterized as follicular carcinoma. There are two kinds of follicular carcinoma: a. Follicular carcinoma with a capsule and infiltration and b. widely infiltrated follicular carcinoma. Infiltrated development is observed in the thyroid tissue and in the blood vessels, possibly with a complete absence of a capsule. Histologically, it comprises small follicles but also nests, beams and compact aggregates of neoplastic cells, which resemble morphologically the follicular cells, present small, medium or large atypia and not rare mitosis [11].

2.3 Medullary Carcinoma

It consists of 5-10% thyroid carcinoma. It is the most aggressive diversified cancer with a percentage of survival of a decade since the diagnosis, 40-50%. It derives from the parathylakiodi or c-cells of the thyroid and excretes calcitonin [12]. The medullary carcinoma separates into sporadic or hereditary. The hereditary carcinoma are divided into simple hereditary, hereditary medullary with a combination of pheochromocytoma or/and hyperparathyroidism, in multiple endocrine neoplasia type MEN IIa, into hereditary with other relative disorders in MEN IIb. Macroscopically the sporadic medullary carcinoma most often appears as a solitary, rough, grayish hob. The familiar carcinoma is often multifocal and bilateral and consists of 25% of medullary carcinoma. Pathological-anatomical, the c-cells have an indescribable shape with a grayish lesion of 1 cm and over [2]. They are contralateral or multiple and bilateral tumors. Histologically, sporadic and familiar present a wide variety of shapes. The typical type is characterized by nests and beams of neoplastic cells. The cells are small, plasmokytoeidi or fusiform and many are binuclear. Immunohistochemical findings are: Calcitonin+, Chromogranini A+, CEA+, Synaptophysin+, NSE+, XMB Keratin+, TTF-1, Somatostatin+, Thyroglobulin [2].

2.4 Anaplastic Carcinoma

Anaplastic carcinoma is also called undifferentiated. The average survival does not exceed 6 months. It usually appears in the 7th decade of a person's life and in young children [13]. Macroscopically, cancerous masses are observed, some of which are rough and others are dead, which are usually inherently fixed to the surrounding gland tissue. Histologically, we observe diffusion in the development of the cancer cells, which are mainly fusiform or primarily gigantic with many cores. The cells present large atypia, diversity, large cores, much mitosis, while in many positions they are dead [14]. Immunohistochemical findings are: Epithelial immunohistochemical indicators [Keratin+ (40-100%), EMA+ (30-50%), TP53, CEA+ (10%)]. Thyroglobulin expression and TTE-1 factor are very rare. Pathological-anatomical large cell types appears (epithelial, spindle shaped, gigantic cells, a mixture) and microcellular type cells [15], [2].

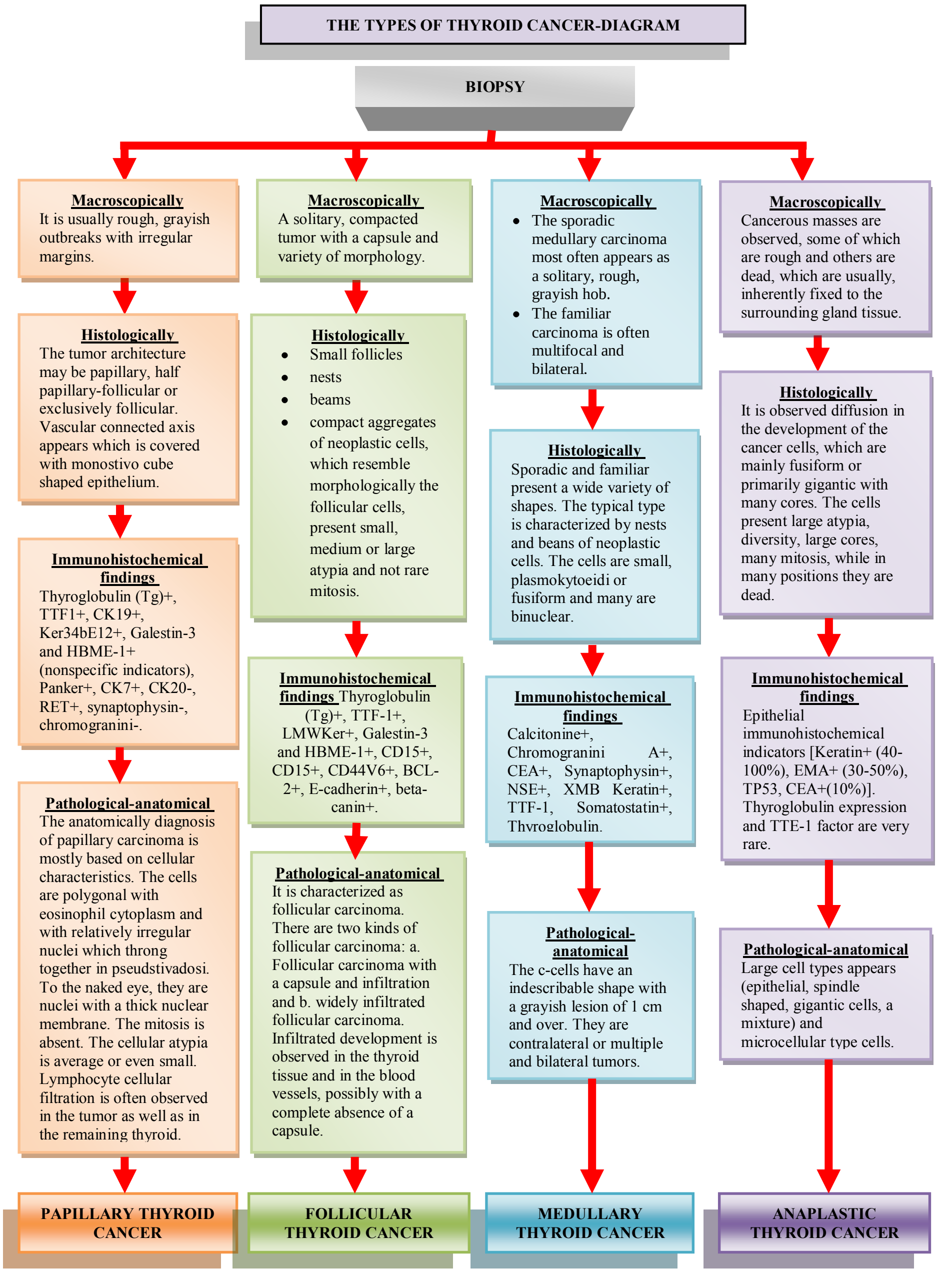

Fig. 2. The types of thyroid cancer diagram.

3 Description of the expert system

The data flow diagram, as follows from the above, is a graphical presentation of "flow" of data which derives from external bodies into an information system and it presents the way in which data is entered affects the overall system by orders, in the handing and reporting to the final user [16]. This is an expert system that uses Artificial Intelligence, the field of computer science that is concerned with designing intelligent computer systems, which contributes to the prediction of individual disease and specifically here, the prediction of thyroid cancer [17].

A doctor, in order to make a diagnostic decision, can be assisted by an automated diagnostic system. In medical diagnosis, Database Management Systems are used for storing, retrieving and manipulating patient data. The automated diagnostic system analyzes large databases of such historical patient data, in order to discover relations buried in the data, by using database analysis and pattern recognition techniques. The aim should be to assign a patient to either a benign, or a malignant group, a data classification problem, more accurately than the low identification rate achieved by widely adopted methods, due to considerable variation in interpretations.

A system for automated thyroid cancer diagnosis can be built, based on artificial intelligence techniques [17], such as artificial neural networks [18], [19], decision trees, probabilistic neural networks, association rules, expert systems, in the aim to predict and classify thyroid cancer patterns.

A knowledge based expert system is an intelligent computer program using knowledge and inference procedures to emulate the process through which a physician uses his knowledge and information presented by a patient and test results, to infer diagnosis. The expert system provides organization and successful handing of the medical data of patients with a history of thyroid cancer, whether they are numbers, texts or binary files. It also uses neural networks, depending on the circumstances existing in the system, leading to the potential diagnosed existence of thyroid cancer [18]. Neural networks are mimicking the biological processes of groups of neurons in the human brain. They can be trained with datasets and generalize past experiences to produce new results, when unknown inputs are applied. They are used for classification purposes. All data that concerns the patient (history, laboratory and imaging tests), is stored in a database, which authorized users have a right to, depending on their role in the system (doctors, nurses, programmers), to intervene and modify the contents of the database. The expert system should be trained through the huge set of data available for many diseases [19], offer the possibility retrieved from the database, the elements that will lead to the prediction of disease and hence the user in the diagnosis of thyroid cancer [20] [21].

Moreover, all above information should be available to authorized users via the Internet and without breaking down any confidentiality so that they can at any time from their mobile phone, check the details on each patient. This possibility makes the system more efficient and friendlier to users [22].

The expert system function and effectiveness is based on a combination of technologies and basic principles. At first, digitization technologies for medical data and the patient's electronic file is being used. The digitization process involves the use of international technological standards and good practices aiming at an interoperable digital medical content which could be further used to the expert system.

For data access and exchange the use of metadata standards is supported in the expert system. The metadata standards used are focusing on the following three categories:

a. Patient identity - data elements about a patient, which includes a patient's full name, previous names with associated date ranges (as an optional element), date of birth, address, zip code and one type of patient identification (ID) data along with the origin of that ID; The metadata standards adopted include Health Level 7 version 2 (HL7 V2) messages and Health Level 7 Clinical Document Architecture Release 2 (HL7 CDA R2) [23].
b. Provenance - data elements about the source of the clinical data, which provides information on the "who, what, where and when" and includes a tagged data element (TDE), a time stamp, and digital signatures used to ensure the data has not been altered since its creation; the HL7 CDA R2 and the Clinical Data Interchange Standards Consortium (CDISC) standards are used to provide the information on provenance.
c. Privacy - data elements include a privacy policy pointer and content elements descriptions such as data type and sensitivity. The Clinical Document Architecture Release 2: and Patient Consent Directives (CDA R2 PCD) standards are used for privacy.

At a second stage, mapping of the metadata already being collected to international metadata standards for bio and medical informatics is implemented. The mapping process is being implemented in a fully automated way within the databases used [24]. The database design is primarily based on the aforementioned metadata standards. The database is structured and implemented in a way which supports the full documentation of the patient's data in line with the international metadata standards. The number of entries is until now strictly restricted as the system is at its early implementation stages. The entries selected represent a typical set of data preserved, accessed and exchanged for its patient. [24].

Expert system's technologies which facilitate decision support during the diagnosis and treatment of thyroid cancer. The system is using both current and history patient data to support doctor's decisions. Depending on the data flow analyzed above the system use: A neural network algorithm based on a Bumptree Network [25] which combines the advantages of a binary tree with an advanced classification method using hyper ellipsoids in the pattern space instead of lines, planes or curves. The arrangement of the nodes in a binary tree greatly improves both learning complexity and retrieval time. A fuzzy logic algorithm, which if necessary, is used to determine or predict the maximum or minimum values of certain biometric data under examination [26], [27]. Web user interfaces for the doctor and medical personnel, which allow data insertion, search, editing and support through the diagnosis and treatment stages of the thyroid cancer. The services can be offered through the internet, at a distributed and geographically dispersed way.

Both neural network and fuzzy logic algorithms are being implemented as black boxes for input data and output results. They are transformed from programming languages to dynamic link libraries which can be integrated to the whole information system. The web user interfaces which are implemented in web scripting languages are able to can and execute the algorithms based on the data inserted by the final user. The results are also integrated to the web applications. The integrated system support doctors and medical personnel to at first diagnose effectively the thyroid cancer and at a second stage to offer personalized treatment to the patient [28].

The system is in the phase of its mid- implementation. The two algorithms have been completed and evaluated, the database on which the overall system relies has been designed and implemented and the web user interfaces are at their early implementation.

In the next stage, the decision support subsystem should be fully completed and evaluated. The evaluation should focus on algorithmic performance measures for the decision making process, statistical data and an evaluation study of the whole performance of the expert system. Based on the evaluation study the expert system should be finally optimized.

4 Conclusions

An important factor in the doctor's correct and timely diagnosis of thyroid cancer with a minimum error percentage and as an extension of the data flow diagram is the creation of an expert system which medical professionals can utilize and which will lead them to decision making and their justifications. The reliability of the programme can be adjusted with the analysis of decision tree results so that we can accelerate the accuracy percentage. For the system to be effective and to support the correct decision, it must be utilized so that it acts like a human (Artificial Intelligence), user friendly, have immediate and effective data entry, while it is equally important to have quick access to the internet at any moment, from any geographical location.

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