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Original Article

A new standardized data collection system for interdisciplinary thyroid cancer management: Thyroid COBRA☆

Luca Tagliaferri[a], Carlo Gobitti[b], Giuseppe Ferdinando Colloca[a], Luca Boldrini[c,*], Eleonora Farina[d], Carlo Furlan[b], Fabiola Paiar[e], Federica Vianello[f], Michela Basso[f], Lorenzo Cerizza[g], Fabio Monari[d], Gabriele Simontacchi[h], Maria Antonietta Gambacorta[c], Jacopo Lenkowicz[c], Nicola Dinapoli[a], Vito Lanzotti[i], Renzo Mazzarotto[j], Elvio Russi[k], Monica Mangoni[h]

[a] Polo Scienze Oncologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy
[b] RT Department, Aviano Cancer Center, Italy
[c] Polo Scienze Oncologiche ed Ematologiche, Istituto di Radiologia, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy
[d] Department of Experimental, Diagnostic and Specialty Medicine - DIMES, University of Bologna, S. Orsola-Malpighi Hospital, Bologna, Italy
[e] Department of Translational Research and New Technologies in Medicine, University of Pisa, Pisa, Italy
[f] Radiotherapy Unit, Istituto Oncologico Veneto, Padua, Italy
[g] Radiotherapy Unit, Ospedale di Circolo, Varese, Italy
[h] Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence, Italy
[i] KBO Labs - Fondazione Policlinico Universitario "A. Gemelli", Università Cattolica del Sacro Cuore, Rome, Italy
[j] Radiotherapy Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[k] Radiotherapy Unit, Ospedale S. Croce e Carle, Cuneo, Italy

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ABSTRACT

The big data approach offers a powerful alternative to Evidence-based medicine. This approach could guide cancer management thanks to machine learning application to large-scale data. Aim of the Thyroid CoBRA (Consortium for Brachytherapy Data Analysis) project is to develop a standardized web data collection system, focused on thyroid cancer.

The Metabolic Radiotherapy Working Group of Italian Association of Radiation Oncology (AIRO) endorsed the implementation of a consortium directed to thyroid cancer management and data collection. The agreement conditions, the ontology of the collected data and the related software services were defined by a multicentre ad hoc working-group (WG).

Six Italian cancer centres were firstly started the project, defined and signed the Thyroid COBRA consortium agreement. Three data set tiers were identified: Registry, Procedures and Research. The COBRA-Storage System (C-SS) appeared to be not time-consuming and to be privacy respecting, as data can be extracted directly from the single centre's storage platforms through a secured connection that ensures reliable encryption of sensible data. Automatic data archiving could be directly performed from Image Hospital Storage System or the Radiotherapy Treatment Planning Systems.

The C-SS architecture will allow "Cloud storage way" or "distributed learning" approaches for predictive model definition and further clinical decision support tools development.

The development of the Thyroid COBRA data Storage System C-SS through a multicentre consortium approach appeared to be a feasible tool in the setup of complex and privacy saving data sharing system oriented to the management of thyroid cancer and in the near future every cancer type.

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* Corresponding author.
E-mail address: luca.boldrini@unicatt.it (L. Boldrini).

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1. Introduction

The last decade has seen huge advances in the amount of data that are routinely generated in the world, as well as our ability to use technology to analyze and understand that. Currently the intersection of these trends is what is called “Big Data” and it is helping businesses in every industry to become more efficient and productive [1]. In medicine, the “big data” approach seems to offer a powerful alternative to the Evidence-based Medicine (EBM). With the world's population increasing and longer life expectancy, models of treatment delivery are rapidly changing, and many of the decisions behind those changes are being driven by data. Big data system is centred on the application of machine learning algorithms do large-scale data. The best example is in the cancer care, where clinics and hospitals generate huge amounts of electronic health record (EHR), the big data systems is able to combine all of this data, published literature and EHR by algorithms and to guide the cancer management [2]. We could call it “learning healthcare system”.

In our project we decided to start with thyroid cancer, since this tumor and its treatment, appear to be very varied, and the use of a big data system could be extremely useful in helping physicians to make decisions.

The incidence of thyroid cancer (TC) has progressively increased in high-income countries since the '70s a large proportion of these cancers are likely to be due to diagnostic changes, namely the wide use of ultrasonography, computed tomography and magnetic resonance, which are used for a variety of medical conditions not always related to the thyroid gland [3]. At present, TC can no longer be considered a rare disease and its incidence is likely to continue increasing in the future. In contrast to the rise of the incidence rates, TC mortality trends appear to be stable or even declining [3]: the possible harm resulting from overdiagnosis and overtreatment is therefore a hot topic of debate among the involved medical specialties.

Thyroid cancer is the 18th most common cancer in Europe, with the highest world age-standardized incidence rates for TC recorded in Italy for men and in Lithuania for women. Thyroid cancer incidence rates are highest in Northern America and lowest in Western Africa, even if it is important to bear in mind that variations among countries may reflect not only a different prevalence of risk factors but also differences in the use of screening protocols and diagnostic methods. The incidence shows a predominance in females with a male:female ratio of about 1:1.5 to 1:3 in most countries [4].

The etiology of TC still remains unclear, out of a small proportion of forms probably directly linked to previous radiation exposure for benign or malignant diseases of the neck or of the mediastinum (mainly lymphomas treated during childhood or patients exposed to nuclear disasters).

Other possible causes of TC include an excess of body mass, either an insufficient or an excessive intake of iodine [5] and some nutritional particularities [6,7].

Most TCs are well differentiated papillary and follicular carcinomas, which show an excellent prognosis. Ten-year overall survival of 93% for papillary carcinoma and of 85% for follicular carcinoma shows that the prognosis of these entities is one of the best among all cancers.

High 10-year overall survival rates are also observed in patients with Hürtle (76%) and medullary carcinoma (75%) [8]. Only a small proportion (about 2%) of TC is undifferentiated (or anaplastic) carcinomas, which grow very rapidly and have a high mortality rate.

In spite of the excellent prognosis about 20% of well differentiated carcinomas relapse locoregionally or at distant sites and late recurrences can also occur after decades from the first diagnosis and primary treatments [9].

The most important prognostic factors in differentiated TC are age, tumor size, tumor extension beyond the thyroid capsule, and the presence of distant metastasis. A number of prognostic scoring systems have been introduced which take into account these variables; however, the 2009 American Thyroid Association guidelines recommended an Initial Stratification System that can better predict the risk of disease recurrence and/or persistence [10].

The latest version of the guidelines (2015) introduced the concept of the “dynamic risk stratification” that should be continuously modified during the follow-up [11]. Clinical and histopathological factors remain to date the only reliable elements for prognostic stratification in TC patients. Despite recent advances in the knowledge of the genetics of TC, there are few new markers, which may be useful as prognostic factors. BRAF mutations have some value when associated with the classical parameters or in the particular setting of iodine refractory tumors [12], but additional studies are needed to confirm the potential impact of other biomarkers. In a future perspective, new data and indications are expected from radiomics, which allows qualitative and quantitative performance analyses with high-output-extraction of numeric radiologic-data in order to obtain prognostic information from patients treated for cancer.

Advances in TC treatment now include the evidence that thyroid remnant ablation can be achieved using low doses instead of high doses of radioiodine and that ablation can be achieved by the administration of recombinant TSH instead of thyroid hormone withdrawal [13,14]. Both result in a lower radiation exposure and fewer side effects for patients.

Because of the slow growth and the very indolent behavior of well-differentiated TC, it is difficult to demonstrate a beneficial effect of diagnostic or therapeutic options unless very large cohorts of patients are observed over decades.

However, a number of questions remain open regarding TC treatment, such as optimal therapy for local or regional relapse, treatment of tumors that have become refractory to radioiodine, role of the inhibitors of the tumoral growth, treatment of aggressive anaplastic carcinoma that to date show an ominous prognosis.

Treatments' choice is oriented by evidence based medicine (EBM) guidelines, mainly based on prospective Randomized Clinical Trials (RCTs).

These trials often have limiting factors as they represent a small subgroup of the general population, far from daily clinical practice reality and this represents one of the main reasons for which small benefits observed in highly selected patients cohorts could also disappear if applied in daily clinical activity [15].

In this context, observational studies are gaining an always more important role in the evaluation of RCTs' impact on clinical practice highlighting treatments results and describing their side effects on a wider and more heterogeneous population [16].

Observational studies lie on big data collection and accurate data management which require time and resources: a significant optimization of these procedures can be reached using Standardized Data Collection (SDC) protocols that improve data quality through the definition of variables that have to be collected and their relative measurements.

Following other similar experiences [17], the main objective of the Thyroid COBRA Project was the creation of a scientific consortium working on thyroid cancer through a robust system for SDC. The validation of the most recent treatments and clinical management technologies through the setup of Decision Support Systems (DSS) represents the long-term aim of this project which will allow an always more accurate treatment individualization in the frame of modern personalized medicine.

2. Methodology

The Metabolic Radiotherapy Working Group of Italian Association of Radiation Oncology (AIRO) has firstly agreed the structure of the project and defined the consortium agreement text, the ontology of the considered data set and the minimal requirements for each aspiring centre to be admitted in the project.