

PHD THESIS ABSTRACT

Study of epidemiological, histological and immunohistochemical aspects of non-melanocytic skin cancers

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Introduction: Skin cancers are one of the most common types of cancer in the Caucasian human population. They are represented by two large categories, depending on the pathogenesis: melanocytic skin cancers - MSC or cutaneous melanoma and non-melanocytic skin cancers (NMSC). The approach of these types of cancers within the present thesis represents the presentation on two different axes – medicine and research – of a multidimensional ideology in their management, diagnosis, and treatment.

General objectives: There were 4 research directions defined, with different objectives, but with similar impact of research and results. Thus, starting from the idea of an up-to-date study, which would reflect reality, respectively highlighting the perspectives as well as diagnostic and research trends in non-melanocytic skin cancers and at the same time aspects that were affected by the COVID-19 pandemic during the last 3 years, this thesis emphasizes the importance of continuous research in this field, regardless of the difficulties encountered, the final result being to improve the quality of life of the oncological patient, through the prism of an accurate and correct histopathological diagnosis.

General methodology: Within the 4 studies, the chosen themes were represented by topical themes with results from various research methods. Studies 1 and 3 were retrospective, descriptive studies based on data extracted from the Pathology Department of the Mureș County Clinical Hospital database. Study 2 was carried out by the scientometric research method, based on the analysis of data from the query and information extraction from the Web of Science database, and then, by using the scientometric mapping software, the interrelationships between certain analyzed parameters were studied. Study 4 provides a presentation of the main types of NMSC and the elements of differential diagnosis for them, through the microscopic analysis of the morphological and histological characters of the pathologies diagnosed in Pathology Service of the Mureș County Clinical Hospital.

Study 1 aimed to verify 3 general research hypotheses, the first having, in turn, two specific hypotheses regarding the existence of statistical values between the epidemiological parameters of the patients and the type of BCC diagnosed. To verify the veracity of the established research hypotheses, a retrospective, descriptive study was carried out in the period 2016-2020, which involved the analysis of data from the histopathological bulletins of the tissue samples obtained by surgical excision and analyzed at the Pathology Department of the Mureș County Clinical Hospital within the Dermatology, Plastic Surgery, Surgery or Ophthalmology clinics. Tissue samples came from day hospitalizations, continuous hospitalizations, or specialty outpatients. A total of 216 patients were included in the study.

Conclusions of Study 1: The study confirmed the research hypotheses that were established and that highlighted the importance of personalized treatment for each patient, through an individualized and personalized diagnosis, starting from parameters such as age before the histopathological diagnosis. The incidence of the cystic subtype of BCC was significantly higher in patients older than 71 years. From the point of view of the environment of origin, the superficial multicentric and keratotic BCC subtypes were more common in the urban environment. Patients who have been diagnosed with the superficial multicentric subtype of BCC tend to be older, unlike patients who have been diagnosed with the cystic subtype of BCC. The relationship between the statistically significant associations of diagnosed BCC subtypes and histopathological parameters showed that the nodular BCC subtype is positively correlated with ulceration, the superficial multicentric BCC subtype is associated with intra- and peritumoral infiltrate. The multicentric superficial subtype of BCC is negatively correlated with ulceration and positively associated with peri- and intratumoral inflammatory infiltrate. The cystic subtype of BCC is positively correlated with safe surgical excision. The infiltrative subtype of BCC is positively correlated with ulceration and the keratotic subtype of BCC is positively correlated with peritumoral inflammatory infiltrate.

The objective of **study 2** was to investigate the new trends in research related to histopathological and immunohistochemical diagnosis in cutaneous squamous cell carcinoma, so that the importance of research, but also the need for continued research in this type of pathology, could be identified and emphasized. In order to achieve the established objective, a scientometric study was carried out, based on the direct and indirect analysis

of literature through the Web of Science (WoS) database. The WoS database was queried by establishing key query terms. As key query terms there were established: "squamous cell carcinoma", "skin" and "immunohistochemistry". To facilitate the WoS query, we used the special Advanced Search function, and the key terms used for our list were selected for all domains, by marking the "All fields" option, respectively using the Boolean variable "AND". The query scheme was: "((ALL=(Squamous cell carcinoma)) AND ALL=(skin)) AND ALL=(immunohistochemistry)". After the initial database query, a total of 983 articles were retrieved according to the established criteria. The inclusion criteria of the articles in the study were based on the years in which they were published (2017-2022), access policy (Open Access), research field (Oncology, Pathology, Dermatology and Molecular Biology), as well as the type of article (Original Research). A total of 76 articles were included and analyzed based on the keywords used. The data obtained from the WoS were transformed into numerical data files and loaded into the VOS Viewer.

Conclusions of Study 2: Interest and trends in the research of cutaneous squamous cell carcinoma remain high, by targeting new methods of diagnosis and treatment of these pathologies. The scientometric research method highlighted the need for a multidisciplinary approach for the best evolution of the patient. Research in the field of squamous cell carcinoma is continuous, thus succeeding in emphasizing the importance of developing new diagnostic and treatment methods for these lesions. Limitations of the study are represented by the fact that only the Web of Science database was queried and analyzed, and only Open access articles were analyzed.

The objective of **study 3** was to analyze the differences between the histopathological diagnoses of dermatopathology from the Pathology Department of the Mureş County Clinical Hospital one year before the COVID-19 pandemic, respectively during the COVID-19 pandemic in order to highlight the changes that the COVID-19 pandemic brought them to diagnose these pathologies. To achieve the established objective, a retrospective and descriptive study was carried out by analyzing diagnostic data from the Pathology Department of the Mureş County Clinical Hospital, between April 2019 and February 2020 (before the COVID-19 pandemic) and between April 2020 and February 2021 (during the COVID-19 pandemic).

Conclusions of Study 3: During the COVID-19 pandemic, a decrease in the number of histopathological diagnoses of dermatopathology in Pathology Department of the Mureş County Clinical Hospital was observed for both benign and malignant lesions, particularly NMSC and melanoma, compared to the same period one year before the pandemic.

The objective of **study 4** was to present the main microscopic types of non-melanocytic skin cancers and precursor lesions diagnosed in SAP. A descriptive, iconographic morphological study was carried out, in which representative cases for the studied pathology were selected from the Pathology Department of the Mureş County Clinical Hospital database. Microscopic images are from Hematoxylin-Eosin (HE) and immunohistochemistry (IHC) stained preparations.

Conclusions of Study 4: To establish the histopathological diagnosis, it is necessary that all the histopathological parameters of the tumor formations are analyzed, both by Hematoxylin-Eosin staining and by immunohistochemical reactions. Thus, a definitive histopathological diagnosis can be formulated, with a direct impact on the appropriate treatment for each patient. The differential diagnosis of NMSC must be made correctly, based on the morphological characteristics and immunohistochemical profile of each individual lesion.

General conclusions: For basal cell carcinoma, young age and the absence of ulceration are predictive factors for the multicentric superficial subtype, and advanced age and ulceration are predictive factors for the nodular and adenoid-cystic subtype. Scientometry and keyword mapping for squamous cell carcinoma showed strong discriminative value for: cancer, skin, immunohistochemistry, and expression. During the COVID-19 pandemic, a decrease in the number of histopathological diagnoses in dermatopathology, especially NMSC and melanoma, was observed, falling to less than a third compared to the same period one year before the pandemic. Due to the measures imposed during the COVID-19 pandemic, patients did not have had access to adequate diagnosis and treatment and this led to the development of tumors in advanced stages, both for NMSC and melanoma. The histopathological and differential diagnosis of NMSC must be done correctly, by using Hematoxylin-Eosin and special stains, but also by immunohistochemical or molecular biology tests. The patient with NMSC should benefit from a personalized diagnosis, based on a multidisciplinary team and a holistic approach.