

Meta Analysis

Structural carcinoma overall process: a systematic review



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ABSTRACT

Abnormalities of several oncogenes and tumor suppressor genes have been identified in carcinomas during the last decade and of pathological warfare and physiological traits, and multiple genetic changes have been demonstrated in individual carcinomas. We conducted a systematic review of studies enrolling adolescents and adults with Carcinoma, every type in which a cancer intervention was randomized, or all study designs in which there was a primary or secondary outcome. We searched Ovid MEDLINE, EMBASE, and Evidence-Based Medicine Reviews from 1990 to June 2015. Two reviewers evaluated study eligibility and abstracted data. In total, 67 studies were included and consisted of 62 randomized trials, reviews, and 5 studies. None of the studies (0/81) provided a definition. Only one randomized trial provided a definition. We were unable to identify any definitions used in studies of adolescents and adults with Carcinoma. Given that a proportion of this population may receive intensive treatment, there is an urgent need for consensus-based definitions of use across trials and review systematic and meta-analysis.

1. Introduction

The extraordinary complexity in the field of cancer stems from the fact that cancer is not a single disease, but rather a collection of many separate but related disorders that can be seen as a compromising process. 93% of cancer cases fall into the broad classification of carcinomas, or cancers of epithelial-derived cells, which make up most of the lining cells of the body. Along with cell type, the tissue or organ of origin is used to define a specific cancer further multiplying the number of sub-classifications [1-4].

Determination and documentation of carcinoma of the extent of disease in a patient is a prerequisite cellular and pathological activity in extensive epithelial tissues it starts to have a kind of structural process [5-8]. For more than more years the anatomical extent

of the disease, or cancer stage, has been classified using the tumor node metastasis classification, although, with evolving knowledge, many other factors have been recognized to also influence prognosis. Acknowledged that many factors other than the anatomical extent of disease can contribute to prognosis. Cancer staging is an evolving process that responds to developments in technology that improve diagnosis and treatment, new information about prognostic factors, and outcomes data [9-11].

The cancer is best described as unregulated cellular growth and invasion; however, the path to loss of growth regulation and the extent of dysregulation of other cellular traits can vary widely, especially with respect to the cell/tissue type(s) involved.

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Detailed molecular characterization as well as immune profiling suggests that the incorporation of prognostic and predictive biomarkers into clinical management may overcome obstacles to targeted therapies and enable prolonged survival [12-16].

More than 85% of these cases occur in developing countries. Because of the various therapeutic modalities that are available and the lack of certain knowledge concerning the proper application of these procedures, this review was undertaken with the express purpose of comparing the histopathologic aspects of the commonly occurring carcinomas as well as delineating the most appropriate treatment and reporting the results [17-19]. Due to the rarity of these features of the cell lesions, no worthwhile statistical data could be generated. We provide an overview of the types and their epidemiology, as well as the pathogenesis of each type and how this influences the management approach.

1.1. Histopathology Marker

As the individual site-specific classifications developed, it became evident that the definitions and terminology related to certain entities common to several anatomical sites were liable to vary among the different tumor panels. This problem concerned such common entities as squamous cell carcinoma, adenocarcinoma, mucinous adenocarcinoma, anaplastic and undifferentiated carcinoma, carcinoid tumors, and carcinomas in situ (Table 1) [20, 21].

However, this theory offers little explanation for the common occurrence of tumors showing an admixture of cell carcinoma and various other epithelial cell types [22, 23]. Currently, the most widely accepted theory, which does account for mixed morphology, is that CCs arise from a multipotential stem cell capable of divergent differentiation [24-26]. This possibility is suggested by rare examples of cell carcinoma arising out of a seemingly pure non-small cell carcinoma well into the course of the disease [27].


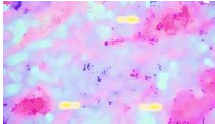
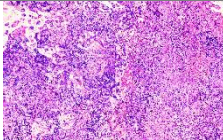
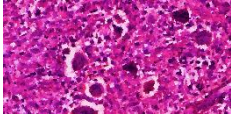
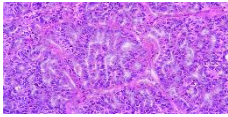
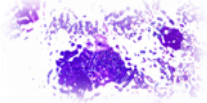
These primarily include studies of tumors with different types of composition, which

show identical molecular alterations in both the cell and non-small cell components, with additional alterations unique only to the small cell component [28, 29].

The following histological types: the ICD-O morphology code is provided in square brackets [30]:

- a) Adenocarcinoma [M 8140/3]
- b) Well moderately differentiated.
- c) Poorly or undifferentiated
- d) Squamous cell carcinoma [M 8070/3]
- e) Undifferentiated neoplasms
- f) Not specified carcinoma
- g) Neuroendocrine tumors [M 8246/3]
- h) Lymphomas [M 9590/3]
- i) Germ cell tumors [M 9064/3]
- j) Melanomas [M 8720/3]
- k) Sarcomas [M 8800/3]
- l) Embryonal malignancies [M 9070/3]

Table 1. Types of carcinomas from the microscopic view of histopathology (evidence is copied).

Histological types	photo
Adenocarcinoma	
Squamous cell carcinoma	
Adenosquamous carcinoma	
Anaplastic carcinoma	
Large cell carcinoma	
Small cell carcinoma	

Immunohistopathological studies can be utilized to further characterize undifferentiated neoplasms, poorly differentiated carcinomas, neuroendocrine tumors, lymphomas, germ cell tumors, melanomas, sarcomas, and embryonal malignancies [31]. The issue has not been extensively investigated on a molecular basis, and the limited information available is still controversial and inconclusive.

1.2. Molecular Abnormalities

Abnormalities have been detected in chromosome 1 including deletion of 1p, translocations with a breakpoint at 1p, isochromosome 1q, and evidence for gene amplification. Abnormalities have been found in the short arm of chromosome 12. The isochromosome 1(12)p or a deletion in 12p – a germ cell chromosomal marker – was observed in 25% of patients with poorly differentiated carcinoma and predominant lymph nodal disease [32-34]. Chromosomal instability (aneuploidy) was found in 70% of patients with metastatic adenocarcinoma or undifferentiated carcinoma [35, 36].

Overexpression of c-myc, ras, and c-erbB2, as demonstrated by immunohistochemistry, was reported in 96%, 92%, and 65% of cases, respectively [37]. No differences in angiogenesis, as measured by microvessel density, were detected between [38]. Suggesting an essential role of proteolysis in these tumors [39].

1.3. Clinical Behavior

Patients must have a histologic diagnosis of cell carcinoma, a normal plain radiograph and computed tomography scan of the chest, and a normal sputum cytology or negative bronchoscopy [40]. Mainly affects patients middle-aged or older, with more than 70% of patients being older than 50 years. An association between cigarette smoking and alcohol consumption has been suggested. Although long-term survival and complete responses have been reported [41, 42], the clinical course is generally aggressive, with median survival ranging from 3 to 27 months [43] and an overall 5-year survival rate of 13% [44].

1.4. Structure Diagnosis

Cell carcinomas are uncommon and malignant with a reported incidence of 0.1% to 0.4% in the United States [45, 46]. They account for 2.5 to 5.0% of all small cell carcinomas [40, 44, 47]. In general, they resemble their pulmonary counterparts in morphology, behavior, and purported histogenesis. Here, we focus on the pathology with a review of histogenesis, sites of occurrence, diagnosis, differential diagnosis, molecular features, and clinical behavior.

The architecture is generally solid; however, irregular organoid groupings, trabeculae, and rosette-like patterns may be present. The cells are generally two to three times the diameter of a mature lymphocyte with finely dispersed chromatin, inconspicuous nucleoli, and scant cytoplasm. Nuclei frequently conform around the nuclei of adjacent cells (nuclear molding). The cells are quite fragile and crush artifact is a common feature in biopsy specimens. Supporting the contention that cell carcinomas arise from a multipotential basilar epithelial cell, these tumors are often associated with an in situ and/or invasive carcinoma more typical for the site of origin [48-50]. Tumor cells show scant cytoplasmic organelles with occasional elongated cytoplasmic processes, sparse neurosecretory granules, and scattered poorly formed intercellular desmosomes [51, 52].

Despite extensive work-up, less than 20% of patients at the primary site of their cancer identified ante mortem. Autopsy studies have reported that 70% of cases remained undiagnosed. Sample of tumor tissue is essential for carrying out light microscopy examinations, immunohistochemical investigations, evaluating other markers or receptors as well as performing more specific investigations such as electron microscopy or genetic/molecular studies [53, 54].

Immunohistochemical studies are of paramount importance. Several cell components can be the Immunoperoxidase technique using a series of monoclonal or polyclonal antibodies to enzymes, structural tissue components (i.e. cytokeratin),

hormonal receptors, hormones, oncofetal antigens, or other substances [55]. These markers are CA 125, CDX2, cytokeratin's 7 and 20, estrogen receptor, gross cystic disease fluid protein 15, lysozyme, mesothelin, PSA, and transcription factor 1 [56].

Results in the detection of a primary site for cancer in 30–35% of patients [57]. It is very important to classify into established clinicopathological sub-sets to guide diagnostic approaches and to be able to offer optimal therapeutic management [58]. Some favorable sub-sets require specific treatment approaches and have the potential for an excellent treatment outcome.

Accumulation of these alterations can endow carcinoma cells with greater proliferative, invasive, and survival propensities in a cell-autonomous fashion addition to carcinoma cells, tumors contain large numbers of various non-transformed cells [59]. Recent evidence also suggests that tumorigenesis is dependent upon contextual signals received from the closely apposed [60, 61]. Recent reports of giant cell carcinoma contradicted the original definition by including tumors with clear-cut glandular or squamous features, implying that it could be derived from either an adenocarcinoma or a squamous cell carcinoma [62-64].

2. Material and Methods

2.1. Data sources and searches

We developed a protocol for review and followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [65]. We performed comprehensive searches for relevant trials using Ovid MEDLINE and EMBASE from 1990 to June 2015 and Evidence-Based Medicine (EBM) reviews-Cochrane Central Register of Controlled Trials from 1990 to the second quarter of 2015, without the restriction of language or publication status. The search strategy included the following medical subject heading terms: "Carcinoma", "Molecular Pathology", "treatment-related mortality", "Various types", and "Invasive Carcinoma type". We also included multiple synonyms, abbreviations, and related keywords for each of these terms. The search

strategy can be found in Additional file 1. We focused on two types of studies, namely: (1) trials in the existing evidence on every variety of Carcinoma of primary and secondary; and (2) any type of study with molecular pathology of invasive carcinoma. We also examined the reference lists of retrieved original and review articles. As this study was a systematic review of primary studies, no ethical approval was required.

2.2. Study selection

Inclusion and exclusion criteria were defined as a priori. Randomized trials were included if: (1) the study was comprised solely of adolescents or adults (age defined by each study but generally included patients up to 20 years of age); (2) the population consisted of carcinoma. Exclusion criteria were as follows: (1) no randomized intervention; (2) randomized intervention related to the process of forming carcinoma; (3) study included adult subjects above the age of 20; (4) report contained results of more than one, separate randomized controlled trial (RCT) (ie. a review); (5) phase 1 trial; (6) duplicate publication; (7) published before 1990; (8) non-English publication; and (9) abstract form only. When duplicate studies were identified, the publication with the longest follow-up was chosen. For studies in which Carcinoma was an outcome, they were included if: (1) the study was comprised solely of children, adolescents, and adults up to the age of 20; (2) the population consisted of all types of carcinomas (3) Carcinoma was a primary or secondary outcome; (4) treatment did not consist solely of HSCT. Exclusion criteria were like those of therapeutic randomized trials except that randomization was not required.

One reviewer (AAN, SNI, or BD) screened the titles and abstracts of publications identified by the search strategy. Articles thought to be potentially eligible were retrieved in full and each of these articles was independently assessed for eligibility by two reviewers (AA and AAN). Final inclusion of studies into the systematic review was by agreement of both reviewers and discrepancies were resolved by consensus. The reviewers were not blinded to study authors or outcomes. Data abstraction was

performed by two reviewers (AAN and SNI) using a standardized data collection form.

2.3. Outcome measures and definitions

The outcome of interest was the presence of Carcinoma definitions in studies of adolescents and adults with Carcinoma and if present, to describe how these definitions were defined. We also looked at the reporting of the following variables of interest when considering Carcinoma: whether Carcinoma over entire self-growth and reproduction was described, reporting of deaths before the production process and deaths from unknown causes and histopathological changes in the growth process of patients' cells.

3. Results

It has been illustrated (Figure 1) the flow diagram of trial identification and selection. A total of 4,733 titles and abstracts were reviewed; 131 full articles were retrieved for detailed evaluation, and 67 satisfied eligibility criteria to be included in the systematic review. Of these studies, 62 were randomized studies, a study of the overall structure, and 5

were studies in which Carcinoma type was a primary or secondary outcome. The reasons for exclusion are detailed in Figure 1.

Summarizes the data related to Carcinoma definitions among the types of studies. None of the randomized trials or Carcinoma studies define Carcinoma for this population. Of these studies, one study did refer to the concept of early death.

This multicenter randomized review from the International the general effect and general function of the Carcinoma, of initiation.

This practice guideline has depicted the status regarding the staging. The diagnosis of cell carcinoma by light microscopy is made not by excluding other types of lung carcinomas that Hal pen to manifest areas of large, atypical cells but rather by positively identifying the features of the characteristic cells. As discussed, there are several areas where active research is needed, ranging from molecular pathogenesis to detection.

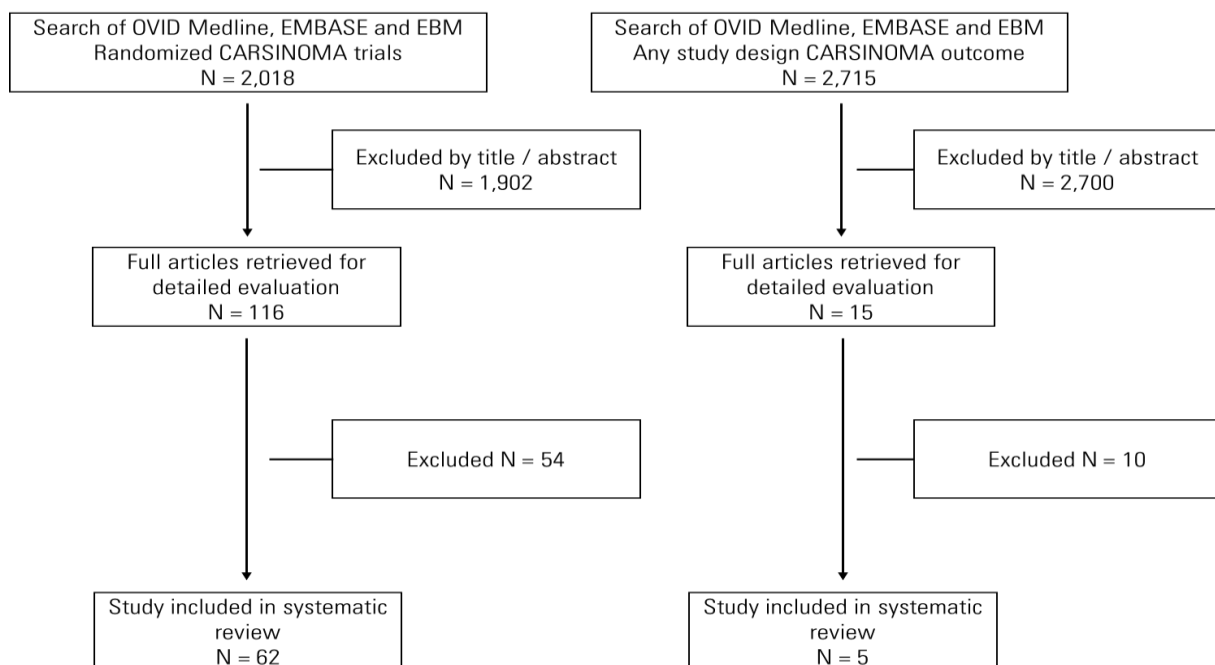


Fig. 1. Flow diagram illustrating the flow of studies identified by search strategy and reasons for exclusion

4. Discussion

The carcinomas are classified based on the presence or absence of a component as either

mixed or pure carcinomas, respectively. Cases displaying only a cellular carcinoma component are extremely rare and comprise

0.043% to 0.19% of all cases of cancer. The annual age-adjusted incidence per 100,000 population in the USA is 7–14 cases, in Australia 17–19 cases, in the Netherlands 5.4–7.1 cases and in Asia 7.4 cases. The median age for occurrence is around 60 years and Cs is marginally more frequent in males [66-71]. The elucidation and organizing of the molecular steps that determine the transition from nonmalignant to malignant should allow the stratification of patients according to the distinct pathways that led to carcinoma and provide for new preventive and therapeutic strategies.

The overall definition of carcinoma of histologically confirmed in whom a detailed medical history, complete physical examination including pelvic and rectal examination, full blood count and biochemistry, urinalysis, and stool occult blood testing, histopathological review of biopsy material with the use of immunohistochemistry, chest radiography, computed tomography (CT) of the abdomen and pelvis and, in certain cases, mammography fail to identify the primary site [72-76]. In this heterogeneous group of tumors, an aggressive biological and clinical course, there are no obvious etiological or risk factors that contribute to the pathogenesis of this syndrome.

This study used case data available in electronic research networks and available clinical evidence. They were also classified as avoiding or not avoiding the use of studies related to carcinoma and common cancers in the past year. Data were statistically analyzed for this systematic review.

5. Conclusion

In conclusion, this systematic review reports the absence of definitions among studies of adolescents and adults with Carcinoma. As a better understanding is crucial in choosing specific strategies to improve the survival of adults with carcinoma, further work should prioritize the development of a consistent definition that can be used across different diagnosis categories. A consensus approach is likely the best approach to create such a definition.

Conflict of Interests

All authors declare no conflict of interest.

Ethics approval and consent to participate

No human or animals were used in the present research.

Consent for publications

All authors read and approved the final manuscript for publication.

Informed Consent

The authors declare not used any patients in this research.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

All authors had equal role in study design, work, statistical analysis and manuscript writing.

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