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CARCINOMA OF THE UTERINE CERVIX INCIDENCE AND INFLUENCE OF AGE

A STATISTICAL STUDY

BY

ARNE LINDELL

STOCKHOLM 1952

FROM THE GYNECOLOGICAL DEPARTMENT (DIRECTOR: HANS-LUDVIG KOTTMEIER)
OF THE RADIUMHEMMET, STOCKHOLM

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PREFACE

Docent HANS-LUDVIG KOTTMEIER, M.D., the present chief of the Gynecological Department of the Radiumhemmet, gave me the idea for this study while I had the privilege of working under him in 1948 and 1949. His unfailing interest and encouragement, both during those years and thereafter, have been of inestimable value to me.

Professor JAMES HEYMAN, M.D., was the head of the Gynecological Department throughout the three decades covered by this investigation. With his profound knowledge of the material and his long experience in the field of gynecological radiotherapy, Professor Heyman has been of invaluable assistance to me. I am deeply indebted to him for his generous interest and for his sound advice and criticism.

Professor AXEL WESTMAN, M.D., head of the Women's Clinic of the Karolinska Sjukhuset and my present chief, has greatly facilitated my work by his interest and understanding.

Docent CARL-OTTO SEGERDAHL, Ph.D., has, in numerous profitable conversations, given me invaluable advice and help on statistical problems.

I am much indebted to the chiefs of the radiological institutions, whose kind assistance made it possible to assemble the material on which my study is based.

The staff members of the Central Bureau of Statistics gave generously of their time and interest in helping me to collect the population data I needed for my work.

I welcome this opportunity to express my heartfelt gratitude and appreciation for the assistance and support which has been given me so unstintingly by my superiors and colleagues and all those with whom I have been in contact in connection with the present study.

Stockholm, March 1952

Arne Lindell

INTRODUCTION

The present investigation deals with two problems concerning carcinoma of the uterine cervix: (1) the influence of age on the prognosis and on various other factors, and (2) the morbidity rate in different age-groups of the population.

Numerous papers have already been published on several of the problems discussed here. The results have been widely divergent, however, and it therefore seemed worth-while to investigate these two problem complexes anew. As far as the first problem is concerned, it has been possible to base the study upon a large material in which the treatment was uniform and the follow-up was thorough. As regards the second problem, conditions in Sweden have proved exceptionally favorable for a total stock-taking.

The principal question in the first part of the present paper is whether the age of the patient is of any significance to the course and prognosis of the disease. Related questions, which will also be discussed, include the incidence of cervical carcinoma in different age-groups, the stage distribution and its changes at different ages and during different periods of time, the cancer death rate during the first five years after treatment, the duration of symptoms and its relation to age. Finally, the influence of intercurrent deaths will be considered.

The material in the first part consists of 5,258 cases of carcinoma of the uterine cervix. This is the total number of patients treated by irradiation at the Radiumhemmet in Stockholm during the period, 1914 to 1944, inclusive, the last year for which the five-year results were available for the present study. The computations involved have been performed with the aid of punch-cards.

The second part of the study is concerned with the morbidity rate of carcinoma of the uterine cervix and its changes during different periods of time and at different ages.

The investigation in the second part is based on the total female population of Sweden for the years, 1920 to 1949. Every case of cervical carcinoma that could be traced during the period concerned is included, or altogether 10,863 cases. The reason for the extension of the study to include the whole country was the impossibility to determine the population within the Radiumhemmet's area of activity, which varied slightly during the period under survey.

PART ONE

The Relation between Age and Various Factors in the Radiumhemmet's Material of Cervical Carcinoma

CHAPTER I

Statistical Requirements of a Material of Carcinoma of the Uterine Cervix

Certain requirements must be met in order to make a dependable statistical analysis of the incidence, course and prognosis of cervical carcinoma.

In the first place, the disease must be carefully defined.

Secondly, the material must be representative. The ideal material would consist of all cases of cervical carcinoma within a geographically defined area. However, such ideal material is scarcely within the bounds of possibility.

Most institutions do not cover a geographically defined area, which results in some degree of selection, intentional or unintentional. The selection may favor certain social categories, certain races or certain age-groups. The selection may also be determined by the prevailing attitude to radiological and to surgical treatment. Some institutions may receive mainly early cases, while the material in others will consist principally of advanced cases. As a rule, the extent of the selective process will increase in proportion to the degree of decentralization of treatment within the same area.

As a result of selection, a considerable variation in the distribution of early and advanced cases of cervical carcinoma is noticeable at different institutions. This is clearly illustrated by the following figures from the *Annual Report on the Results of Radiotherapy in Carcinoma of the Uterine Cervix* (Sixth Volume 1951).[3] The quoted figures represent the lowest and highest percentages of cases in the respective stages:

Stage	I	3.6	to	36.9	per cent
»	II	16.5	to	49.9	»
»	III	9.8	to	60.7	»
»	IV	2.3	to	30.8	»

The proportion of cases not accepted for treatment also varies from one institution to another. In the Sixth *Annual Report*, the number of cases "not treated" varies from 0 to 39.9 per cent.

The clinical picture in carcinoma of the uterine cervix is far from uniform, and the therapeutic results, like the prognosis, also vary widely from case to case. Consequently, it is essential that any investigation be based on a large material.

Finally, a regular follow-up is required in order to form an opinion on the course of the disease and the results of treatment.

In summary, conclusions concerning the incidence, course and prognosis of carcinoma of the uterine cervix, must, to be statistically valid, be based on an extensive material consisting of strictly defined cases. In addition, the material must represent a defined geographical area, and the follow-up must be thorough.

Most of the statistical works published hitherto on carcinoma of the uterine cervix do not fulfill the foregoing requirements. For this reason, a detailed survey of the literature on the problems concerned in the present study would seem to be of limited value. Only a few publications will be referred to as the various problems are brought up for discussion.

The statistical methods used will not be concentrated in a special chapter, but will be described in connection with their application.

CHAPTER II

Stage-Grouping in Carcinoma of the Uterine Cervix

For the purpose of comparing materials and therapeutic results from different periods of time and from different institutions, it is essential that cervical carcinoma be classified in as uniform groups as possible.

Numerous systems of classification have been suggested, and cervical carcinoma has been grouped on various grounds: surgical, morphological, histopathological and anatomical. Surgical classification on the basis of operability was satisfactory in the days when surgery was the sole form of treatment, though even then there was a certain margin of uncertainty depending on the attitude of the surgeon and on his skill, as well as on the general condition of the patient. Gross morphological classification into two types, everting and inverting, can be used at early stages, but is often worthless in more advanced cases in which it is not always possible to form an opinion of the appearance of the primary tumor. Histopathological classification is helpful under certain circumstances, but those who have seriously concerned themselves with the study and treatment of cervical carcinoma are now agreed that the anatomical extent of the growth at the first examination must form the basis of the primary classification.

HEYMAN[45] stated that, to be of value, stage-grouping requires:

"that the definitions of the different stage-groups should be as simple and precise as possible;

"that the rules for allocating cases to their appropriate stages should be easily interpreted and should offer ample opportunity for being applied in a uniform way by the examining clinicians;

"that one stage should be differentiated from the other by characteristics easily recognized on clinical examination even by a less experienced examiner;

"that the system of grouping should be sufficiently complete to include every possible type of case;

"that each stage-group should contain a number of cases sufficient for a statistical evaluation of the result within that particular group."

It has been difficult to reach universal agreement on stage-grouping in cervical carcinoma. Now, however, most of the leading therapeutic centers have adopted