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ABSTRACT OF THE PhD THESIS ENTITLED:

CONSERVATIVE SURGICAL TREATMENT IN BREAST CANCER

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CONTENTS
PhD THESIS

CHAPTER I **6**

Anatomy and physiology of the mammary gland **6**

1.1 Development of the mammary gland……………………………………………6

1.1.1 Development of the mammary gland during puberty 6

1.2 The anatomy of the adult mammary gland…………………………………..7

1.3 The anatomy of the thoracic wall muscles……………………………………..10

1.4 Breast and thoracic wall fascia…………………………………………………12

1.5 The anatomy of breast and thoracic wall nerves…………………………...14

1.6 Vascular anatomy……………………………………………………………...16

1.7 Lymph node anatomy…………………………………………………….....16

1.8 The anatomy of the axilla……………………………………………………..18

1.9 Mammary gland physiology…………………………………………………..20

1.10 Hormones that influence the mammary gland…………………………..20

1.11 The mammary gland during the menstrual cycle……………………….....21

1.12 The postmenopausal mammary gland…………………………………..22

1.13 The mammary gland during pregnancy…………………………………...22

1.14 Lactation……………………………………………………………………23

CHAPTER II **25**

The diagnosis of breast cancer **25**

2.1 Screening………………………………………………………………………...25

2.2 Clinical exam……………………………………………………………………..26

2.2.1. History 26

2.2.2 Periodic self-examination of the breast (self-screening) 28

2.3 Para-clinical examination………………………………………………………29

2.3.1 Mammography 29

2.3.2 Ultrasound 31

2.3.3 Other investigation methods 32

2.4 Cytological examination…………………………………………………...33

2.5 Biopsy…………………………………………………………………………..33

2.6 Other clinical forms…………………………………………………………... 35

2.7 Differential diagnosis……………………………………………………...37

2.8 TNM staging…………………………………………………………………………...38
2.9 pTNM staging………………………………………………………………………..40
3.0 Grading – G…………………………………………………………………………41
CHAPTER III 42
Conservative surgical treatment of breast cancer 42
3.1 Selection of patients for conservative breast surgery……………………………..43
3.2 Conservative breast surgery………………………………………………………45
3.3 Wide local excision: surgical technique……………………………………………..46
3.4 Excision of impalpable tumours……………………………………………………...50
3.5 Factors that influence conservative surgery following intervention…………….51
3.6 Treatment dependent factors……………………………………………………......56
3.7 Adjuvant systemic therapy…………………………………………………………...58
3.8 Factors that influence the cosmetic result of conservative interventions………59
3.9 Patient related factors…………………………………………………………………59
3.10 Tumour related factors………………………………………………………………60
3.11 Surgical intervention related factors………………………………………………..62
3.12 Conservative breast surgery following neo-adjuvant therapy…………………...63
3.13 Radiotherapy…………………………………………………………………………64
3.14 Treatment of cosmetic defects resulted from conservative breast surgery……65
3.15 The meaning and treatment of local recurrences……………………………….…65
CHAPTER IV 68
Clinical study and conservative breast surgery 68
4.1 Clinical results…………………………………………………………………………73
4.2 Recurrences……………………………………………………………………………79
CHAPTER V 82
Histopathology 82
5.1 Introduction…………………………………………………………………………..82
5.2 Material and method………………………………………………………………...82
5.3 The results of studies on morphological parameters ……………………………...88
5.4 Results of the histopathological analyses of cases presenting local ipsilateral recurrences…………………………………………………………………………...108
CHAPTER VI 113
Immunohistochemical study (IHC) 113
6.1 Material and method…………………………………………………………………113

6.2 Results…………………………………………………………………………..122
6.2.1 Evaluation of hormonal receptors (ER, PR)…………………………..123
6.2.2 Evaluation of Her2/neu status………………………………………….127
6.3 Immunohistochemical analyses of recurrences…………………………………..144
CHAPTER VII 148
DISCUSSIONS 148
7.1 Discussions regarding clinical aspects……………………………………………..148
7.1.1 Problems related to the primary breast cancer surgery 148
7.1.2 The problem of axillar lymphadenectomy in breast conserving surgery 151
7.1.3 The aspect of local recurrences following conservative surgery 155
7.1.4 Discussion about the indications of conservative breast surgery 158
7.2 Discussions about the histopathological study (HP)……………………………..160
7.3 Discussions about the immunohistochemical study (IHC)…………………….168
CHAPTER VIII 178
CONCLUSIONS 178

ABSTRACT

Key words: breast cancer, conservative surgery, tumour size, breast-tumour relationship.

INTRODUCTION

Breast Cancer is an important public health problem, with an incidence and a very high prevalence worldwide, basically at present breast cancer represents 20-25% of women's cancers and about 15-20% of all cancer deaths.

This doctoral thesis is structured in two parts:

A: general part is structured in three chapters where the theoretical part is dealt with.

B: special part structured in five chapters.

In the **first chapter** of the general part we address in detail, the anatomy and physiology of the breast throughout breast development stages of intrauterine period up to old age. We also dealt with, in detail, the anatomy of the muscular fascia of thorax, breast and chest wall, vascular anatomy and anatomy of the lymphatic, all of them having particular significance in surgical treatment. Physiologically the breast is presented in certain stages: during the premenstrual, menstrual cycle and in postmenopausal women, all these steps are strictly related with hormones namely oestrogen, progesterone, prolactin, ocytocine, human mammary placental lactogen.

Chapter II -breast cancer diagnosis - tackles in detail the stages to be completed in order to establish a correct and complete diagnosis. It is known that screening is a good way to discover breast neoplasm and proposed for this method is mammography with its advantages: simple with a sensitivity close to 100%.The clinical examination with a correct and detailed medical history plus examinations and laboratory tests help us to establish the diagnosis of mammary tumour. The diagnosis of certainty is put as you know based on the biopsy of the tumour, followed by the HP exam.

Chapter III aims to bring into balance the results of cosmetic and local control of the disease versus mastectomy.

Conservative surgery has the following advantages:

- aesthetic result acceptable
- low morbidity

- equivalent in terms of long-term results between conservative surgery and the crippling radical breast surgery.

In order to obtain good results, it is important to select patients who are appropriate for conservative surgery:

- T1 T2 tumours (<4 cm), N0, N1, M0
- T2 > 4cm in patients with large breasts
- single injury perceptible either clinically or on mammography.

Surgical procedures that were studied in detail so far, were quadrantectomy and wide local excision. The goal of wide local excision is to repel all invaded tissue and any trace of in situ carcinoma, ensuring a healthy edge to the macroscopic scale of 1 cm.

The special part devoted to personal study starts with the clinical study and details about the conservative surgical treatment, a study that was done by retrospective analysis of the observation sheets and sheets of oncological patients who underwent surgery for breast cancer, conservative interventions carried out in Surgery IV Clinic (C.F. Hospital) Craiova. The study was conducted on a sample of patients admitted and operated in the period 1995-2010.

The distribution by area of origin was 32% in rural areas and 68% in urban areas. There was a peak of incidence between 40-50 years and another between 60-70 years. With regard to the topography of the tumour we found 160 cases (52.8%) in the S-E quadrant, 49 cases in the S-I quadrant, 47 cases in the I-E quadrant, 26 cases in the I-I quadrant and 21 cases in the central one.

Of the 673 cases of breast cancer during the period studied, 303 cases have been operated conservatively. Starting from the year 2000 we practice extemporaneous HP exam and resection of margins from the edges of the remaining cavity after sectorectomy or quadrantectomy. Due to this attitude were discovered 40 patients who were eligible for conservative surgery, neoplastic cells at the edges of the resection piece which led to the transformation of the sectorectomy into the Madden type mastectomy.

In the cases we studied, postoperative treatment was recommended in 137 cases, 65 patients undergoing chemotherapy and 72 were recommended radiotherapy.

Of the total of 673 patients, 45,03% (303) have benefited from the conservative surgical treatment, 41,90% (282 cases) from radical surgery, both with curative purpose while 88 cases (13,07%) were treated with palliative intention only.

It is known that a greater number of relapses is attributed to conservative surgery compared with crippling radical surgery.

Thus in the study lot having a percentage of 4,52%, all cases were patients did not undergo radiotherapy, double the percentage of patients treated radically (2,16%). The relapses were deal with by sectorectomy (re-excision) in 3 cases and by radical mastectomy on request in all the other patients.

In the current HP study we analysed all the 303 cases of mammary tumours operated conservatively in terms of type, degree of histological differentiation of tumour size, lymph node status, invasive tumours association with carcinoma in situ component, surgical margin status, the age of patients and also watched the pairings between these morphological and clinical parameters and ipsilateral local recurrences.

The material we studied was represented by fragments of breast tissue that have been harvested from all 303 cases diagnosed with breast carcinoma and conservative operated over a period of 16 years, in the 1995-2010 period.

In the histological studies we used a classic histological technique of inclusion in paraffin. It has been observed that invasive tumours were more common than tumours in situ. Of invasive carcinomas most common histopathological form was NOS (63,37%) type, followed by Invasive lobular carcinoma (10,56%) and invasive mixt ductal-lobular carcinoma (6,27%).

Depending on the degree of differentiation of breast carcinoma it was found that the vast majority of cases (63,04%) were grade III tumours, the fewest (7,26%) were grade I and grade II was met in 249 cases representing 70%.

Analysing the status of the lymph nodes we found as recurrences happened in 7 cases of patients who all presented positive lymph nodes at the time of diagnosis of the primary tumour and 5 relapses in patients who presented negative lymph nodes. The study was done by Immunohistochemistry on a total of 82 patients with invasive breast carcinoma, operate conservatively during the period 1995-2010.

Of the 303 cases of breast carcinoma operated conservatively, 82 cases with invasive carcinoma were processed by Immunohistochemistry to determine tumour receptors and Her receptor 2, necessary for the correct and complete treatment. In

this lot studied IHC were included and those 11 cases of invasive mammary carcinoma who had ipsilateral recurrences.

In **chapter VI** (Discussion), I merged the discussions relating to the clinical, histological point of view and IHC.

In the present paper I raised a number of issues related to the surgical intervention on the primary breast tumour, axillary lymphadenectomy issue in conservative surgery, the problem of local relapses after conservative surgery.

Histological study was carried out on the current batch of 297 patients with breast cancer stages 0-IIIB, with T1-T2 tumours and T4b with dimensions less than 5 cm. From this lot included in the study we analysed a number of morphological parameters (age, stages of the tumour on presentation, the size of tumours, histological type, the degree of differentiation, the surgical margin status, tumour, lymph node status, the presence of an in situ "component and extensive intraductal component) and relapses as well as establishing the existence of associations between local recurrences and the studied parameters.

The study's findings are:

1. Conservative treatment of breast cancer in the early stages I and II is a viable option that offers women the same chances of postoperative survival as mutilating surgery.
2. An essential element of that must into account in the application of conservative surgery in breast cancer, besides the patient option is represented by the ratio between the volume and size of the breast tumour; in this way we eliminate the arbitrary established maximum size of tumour for which you can opt for conservative surgery; regardless of the size of the tumour is important to obtain a good aesthetic result and complete oncological safety, otherwise, if this is impossible we prefer radical mastectomy followed by reconstruction.
3. Postoperative radiotherapy on san is required to obtain a satisfactory rate of local recurrence.
4. Complex preoperative oncological treatment can allow conversion of some cases towards the "conservative operation", as in the early cases can enhance surgical outcomes.

5. Conservative surgery in stages I and II must become the "gold standard" in the treatment of breast cancer, the results obtained by prospective analyses supporting this statement;
6. The term conservative palliative mastectomy is an original idea, that we think deserve reflection upon.
7. The age of patients at the time of diagnosis of primary breast tumour is a very important factor in terms of local recurrences. Thus, emergence of recurrences is more commonly seen in patients aged ≤ 40 years compared to the patients older than 40 years, the difference being highly statistically significant (p 0,01 <, HS).
8. The emergence of local relapses after conservative surgery for early breast cancer are correlated with primary tumours often poorly differentiated (G3) compared to moderate and well differentiated tumours (G1-G2) the difference being statistically significant (p 0.05, S <).
9. The emergence of local relapses after conservative surgery for early breast cancer does not correlate significantly with histologic type, presence of extensive carcinomatous intra-ductal component, dimensions of primary mammary tumours and lymph node status in case (p>0,05). However, invasive ductal carcinomas, in situ comedocarcinoma type determines more frequent local recurrences consecutive to conservative surgery, also, invasive tumours associated with an extensive in situ component will have recurrences over five times more often than those without the combination.
10. According to this study, the parameter that seems to be the most important in terms of the risk of ipsilateral relapses is the status of surgical resection margins. Thus, patients with positive surgical margins have a very high risk to develop statistically significant recurrences after conservative surgery compared to those with negative margins (p 0.001<,VHS)
11. Using conservative surgery as treatment for patients with positive margins is a controversial method, especially when to the positive margins we add another risk factor for local recurrences.
12. The rate of hormone receptor expression for ER and PR, as well as the rate of Her2-neu oncoprotein in cases of invasive breast carcinoma operated conservatively falls within the limits of the values observed in cases in which surgery is mastectomy.

13. Status of Her2/neu detected through IHC correlates statistically significant (p=0,034) with the absence of receptors for PR and we can not identify an insignificant correlation (p 0,539) between Her2/neu status detected by IHC and the absence of receptor ER.
14. The method of in situ hybridization with chromogen (CISH) is absolutely necessary for correct classification of Her2 cases with IHC equivocal exam.
15. Status of Her2 detected by CISH correlates highly statistically significant (p =0,00074, VHS) with hormonal phenotypes, Her2 negative tumours being characteristic of the classic imuno-phenotype ER + PR +, while Her2 positive tumours are characteristic of ER + PR-phenotype.
16. Between particular hormonal phenotypes and classic hormonal phenotype ER + PR + there isn't a highly significant statistical differences regarding the stage presentation of invasive breast carcinomas operated conservatively.
17. Compared to the classic phenotype ER + PR +, tumours lacking receptors for progesterone ER + PR- are associated statistically significant (p = 0,004) with poorly differentiated tumors-G3.
18. The IHC Her2 status after in situ hybridization correlates statistically significant with the degree of differentiation of studied carcinomas (p=0,028), Her2 positive tumours were poorly differentiated G3, and did not correlate with tumour stage at presentation.
19. Local ipsilateral recurrences after conservative surgery results are three times more common in carcinomas with initially positive Her2 status compared to those with Her2 negative status, but without any statistically significant differences.
20. Recurrences after breast conservative surgery and radiotherapy are associated, statistically significant, with the absence of oestrogen receptor (p =0,013), with absence of progesterone receptor (p = 0.037) and the phenotype lacking both hormone receptors ER-PR-(p = 0,028).