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Oncology Section

Should the Urologist Demarcate the Surgical Specimen after Radical Prostatectomy

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ABSTRACT

Introduction: Although the literature about prostate cancer is vast in tracking discussion about diagnosis and treatment of prostate cancer, there are few publications about the best form of surgical specimen processing of radical prostatectomy. After the surgery, the urologist limits his responsibility to forward surgical specimen for analysis.

Aim: To evaluate if the urologist manipulation trying to locate and demarcate suspicious areas of a tumour can improve the microscopic examination.

Materials and Methods: Twenty surgical specimens of radical prostatectomy performed in patients with localised prostate cancer were macroscopically analysed by a single urologist and suspicious areas for cancer were marked with surgical thread. Later these areas were correlated with the findings in the microscopic study.

Results: It was observed that in 75.8% of cases, there was a positive correlation between the pit and the clinical pathology report on the cancer presence, and in 50% of cases, the demarcated areas corresponded to the area of most considerable extent of cancer throughout the prostate.

Conclusion: The demarcation of cancer suspected areas by Urologist, in surgical specimens from radical prostatectomy may provide additional information to the pathologist, directing the histopathological analysis of the prostate to the areas with more significant tumour extension compared to the other sections.

Keywords: Cancer, Pathology, Prostatic cancer

INTRODUCTION

The occurrence of cancer is increasing worldwide, and it is related to the populational growth and ageing, as well as an increasing prevalence of established risk factors related to lifestyle. There will be an estimated 17 million new cancer cases and 9.5 million cancer deaths (excluding non-melanoma skin cancer) in 2018. Almost 1.3 million new cases of Prostate Cancer (PC) and 359,000 associated deaths worldwide are expected in 2018, ranking as the second most frequent cancer and the fifth leading cause of cancer death in men [1].

Radical prostatectomy is the standard therapy for patients with localised prostate cancer and can be performed by open retropubic, laparoscopic techniques and robot-assisted surgeries [2].

The clinical importance of the anatomopathological report of radical prostatectomies surgical specimens has gained more importance in recent years. For patients with adverse histopathological findings, a variety of adjuvant therapies may be offered like radiation therapy, chemotherapy or hormone manipulation, isolated or combined. In this way, the pathologist report has become critical [3]. However, the histopathological analysis of these surgical specimens is a challenge, since the macroscopic recognition of areas affected by cancer is imprecise, compromising histopathology study. Thus, these surgical specimens must be carefully manipulated and analysed according to protocols that allow the correct diagnosis related to degree and stage of the disease [4].

Although the literature related to prostate cancer screening, diagnosis, and treatment is extensive, there are few publications about the best way to process radical prostatectomy surgical specimens, and more rarely studies correlating macroscopic to microscopic aspects of prostate cancer [5-10]. Without prejudice to the analysis of principal prognostic factors, such as the Gleason grade, the presence of compromised surgical margins and the presence of extraprostatic extension, Authors have sought greater efficacy in this processing, reducing the costs and time demanded in laboratories. Before the PSA era, PC cases were diagnosed in more advanced stages, usually ≥T2 stage, with palpable nodules and frequently identified macroscopically in the peripheral prostatic zone, allowing anatomic-pathological analysis to be directed at the tumour area and marginal areas [7].

This study aimed to evaluate the urologist's contribution to the histopathological study of radical prostatectomy surgical specimens.

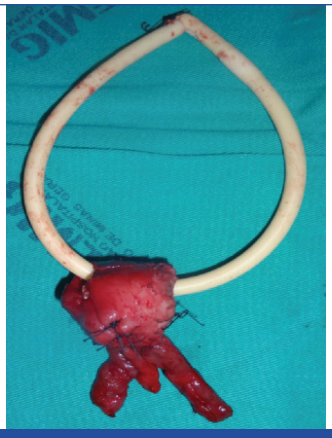
MATERIALS AND METHODS

In this pilot study, twenty radical prostatectomies were performed in patients diagnosed with localised prostate cancer (preoperative clinical stage ≤T2c), between September 2015 and June 2016. This study was done in a Public Hospital in the city of Belo Horizonte, Minas Gerais.

The main inclusion criteria were an indication of surgical treatment for prostate cancer, stage ≤T2c and age <75 years. Patients that received previous treatment for prostate cancer, such as hormone therapy, radiation therapy or chemotherapy were not eligible.

After surgery, all specimens were analysed macroscopically in a warm ischaemia interval <30 minutes between removal of the prostate and its immersion in 10% formaldehyde solution. The macroscopic analysis was performed by a single urologist, who was responsible for the preoperative preparation of the patient and consisted of bimanual palpation of the entire prostate. The hardened or altered areas on the surface were demarcated with 2-0 (not absorbable) silk thread with a circular needle. All specimens were then photographed, and demarcated areas registered. The bladder catheter was held in the surgical specimen by suturing its extremities to better indicate the location of the apex and base of the prostate [Table/Fig-1].

The prostate was measured in three dimensions: (1) from the apex to the base; (2) from left to right; and (3) anteroposterior. The apex and base of the prostate were sectioned from the rest of the gland and analysed by the cone technique, with sagittal sections [11,12]. The surgical specimens were then sectioned into three thirds (distal, medial and proximal), each of these three segments being sectioned into sections of approximately 3 mm and sampled separately. Each slice of the prostate was



[Table/Fig-1]: Specimen showing dermacated area by the urologist using a 2-0 silk thread held with the bladder catheter.

then divided into sextants and received meticulous attention. The analysis of the samples of the demarcated areas with surgical thread occurred separately. From the preceding, the prostate was not examined in its entirety, but by sampling, as it occurs in the regular laboratory routine. After the microscopic exam, the non-identification of the neoplasia in the sampled material implied in processing the entire specimen.

The paraffin-embedded sections were stained with haematoxylin-eosin. A single pathologist examined the surgical slides for the anatomopathological report, and another pathologist participated as a reviewer of the examinations performed. Also, the pathologists, the examiner, and the reviewer answered four questions about the specimen: (1) Did the presence of the delayed bladder catheter better indicate the position of the apex and base of the prostate?; (2) Was the demarcated area with surgical thread affected by cancer?; (3) Did the demarcated area present a greater tumour extension about the other sections analysed?; (4) Did the demarcation with a surgical thread of suspected areas for cancer, in this case, provides additional information for the histopathological study or harm histopathological study or was indifferent? The questionnaires answers were sent to the urologist responsible for the demarcation, which then correlated the demarcated areas to the microscopic findings.

Ethical Declarance

The procedures followed were in accordance with the Ethical Standards of the Institutional Committee on Human Experimentation and with the Helsinki Declaration of 1975 that was revised in 2000. Institutional Ethics Committee previously approved this Project with CAAE 43110315.5.0000.5134 and written informed consent was obtained from all participants.

STATISTICAL ANALYSIS

The descriptive analysis was constructed using absolute and relative frequencies for qualitative variables and mean±Standard Deviation (SD) for quantitative variables. The analyses were developed in software R version 3.2.1, and a significance level of 5% was adopted.

RESULTS

In this study, suspicious areas were identified for the presence of prostatic adenocarcinoma on the surface of the prostate. The demarcation occurred in areas suspected at palpation of the surgical specimen in the period of warm ischaemia. All 20 surgical specimens had suspected areas, and all received at least one demarcation, with a total of 33 demarcations. It was observed that in 75.8% of the cases there was a positive correlation between the demarcated area and the microscopic finding of cancer in the anatomic pathological report, and for the right apex, there was a definite correlation in all cases. Considering all the demarcated areas the assertiveness was at least 60%. The overall sensitivity was 37.7%, with the lowest sensitivity for the left apex (16.7%) and the highest for the left middle third (63.6%). The general sensitivity was 84.9%, being >80% for all areas, except for the left middle third (66.7%) [Table/Fig-2].

Demarcated area	N	Correctness	Sensitivity	Specificity
Right apex	5	5 (100%)	5/14=35.7%	6/6=100%
Left apex	3	2 (66.7%)	2/12=16.7%	7/8=87.5%
Right middle third	6	5 (83.3%)	5/11=45.5%	8/9=88.9%
Left middle third	10	7 (70%)	7/11=63.6%	6/9=66.7%
Right base	4	3 (75%)	3/10=30%	9/10=90%
Left base	5	3 (60%)	3/9=33.3%	9/11=81.8%
Total	33	25 (75.8%)	25/67=37.3%	45/53=84.9%

[Table/Fig-2]: Evaluation of the correctness, sensitivity, and specificity of the demarcated areas.

It was also observed that in half of the 20 surgical specimens examined, the areas demarcated with surgical thread corresponded to the area of greater extent of cancer compared to the other investigated sections of the prostate. In the other half of the cases, in eight surgical specimens (40% of cases), the demarcated area was affected by neoplasia, although there was no description in the report regarding tumour extension. In two cases (10%), the demarcated areas corresponded in fact to the histopathological finding of post-atrophic prostatic hyperplasia in one patient, and fibromyomatous nodular formation in the other case.

Regarding the questionnaire, answered by pathologists, the examiner and the reviewer have 100% of concordance. According to their analyses, the bladder catheter maintenance was useful for correct orientation of the apex and base of the prostate in 100% of the cases. In the cases which the demarcated area corresponded to the area of higher tumour extension compared to the other sections analysed (50%), the pathologist stated that the demarcation was useful, providing additional information to the histopathological study. In the cases without the description of tumour extension predominance (40%) and in those cases where the demarcated area did not correspond to the cancer finding (10%), the demarcation was considered as indifferent to the histopathological study. In none of the cases investigated the pathologist reported that the demarcation with surgical thread, performed by the urologist, was detrimental to the histopathological analysis [Table/Fig-3].

	Yes	No
Did the presence of the delayed bladder catheter indicated the apex and base position of the prostate?	20 (100%)	-
Was the demarcated area with surgical thread affected by cancer?	18 (90%)	2 (10%)
Did the demarcated area present a greater tumour extension about the other sections analysed?	10 (50%)	10 (50%)
Did the demarcation with a surgical thread of suspected areas for cancer, in this case, provides additional information for the histopathological study?	10 (50%)	-
Did the demarcation with a surgical thread of suspected areas for cancer, in this case, was indifferent?	10 (50%)	-
Did the demarcation with a surgical thread of suspected areas for cancer, in this case, harm histopathological study?	-	20 (100%)

[Table/Fig-3]: Pathologist questionnaire.
The examiner and the reviewer have 100% of concordan/ce

DISCUSSION

The correlation between visible changes and microscopic findings in prostate cancer, the specific objective of this study, was controversial and imprecise. The tumour focus visible at macroscopy is at least 5 mm in its largest dimension, yellowish-white, and firm consistency, due to the local desmoplastic reaction. Some tumours look like

yellowish granulations in contrast to adjacent spongy or cystic prostatic tissue. The differential diagnosis includes tuberculosis, granulomatous prostatitis and both acute and chronic prostatitis. Also, there is a high variability in the reporting of the pT stage in radical prostatectomy specimens even by specialist uropathologists [13,14]. However, there are descriptions that its identification is often difficult or impossible, especially considering that the recent screening based on the serum PSA level has implicated in reducing the size of tumours in surgical specimens, making it even more difficult to identify them macroscopically. Exceptionally, the tumour may not be identified in the surgical specimens of radical prostatectomy between 0.07% and 4.2% of the cases [15-17]. Despite this, a more direct and efficient histopathological analysis of the prostate has been sought, with a reduction in the costs and time involved. While the submission of the whole prostate provides essential prognostic parameters, this procedure demands time and cost, since it involves the use of between 26 and 42 paraffin-embedded sections for the complete microscopic analysis. Therefore, several methods of partial analysis of surgical specimens have been discussed. According to data from the College of American Pathologists, only 12% of pathologists use total prostate compliance, while most adopt one of several partial methods already described [18]. Cohen MB et al., used alternating sections of the prostate along sections of the bladder, apical and junction borders with the seminal vesicles and did not observe differences in the type of cancer, tumour grade and Gleason score in 75% of cases, besides detecting the presence of compromised surgical margins in 85% of cases [19].

In another partial method described for stage T2 tumours, partial analysis of visible tumour along marginal sections, base of the seminal vesicles and apex resulted in the presence of extraprostatic extension in 91% and detection of compromised surgical margins in 96%, reducing the number of paraffin blocks analysed in 31%, from 42 to 13. In the same study was reported that 92% of T2-stage tumours are visible at the macro analysis [6]. Few published studies have evaluated the correlation between visible changes and the microscopic finding of cancer in radical prostatectomy surgical specimens [5-10,20]. In one of the studies, after analysing 211 specimens within a 30-minute period of warm ischaemia, the author found a positive correlation in 63% of the cases, associating visible tumours with increasing tumour grade and stage [20]. The processing of the prostate as a surgical specimen is even more challenging considering the presence of proteolytic enzymes in the prostatic secretions, causing this gland to evolve to autolysis more quickly, making the fixation process essential. However, in the fixed gland, there are no differences in palpation between the tumour area and the benign prostatic tissue. Also, although there is a growing interest in obtaining prostatic cancer fragments for research purposes, there are recommendations for the surgeon to do not cross-section the prostate gland without consulting the pathologist. Especially, considering the difficulty in identifying the tumour areas and the potential damage of the fixation process and analysis regarding the presence of compromised surgical margins [5,21,22].

To identify tumour areas in surgical specimen and to better guide the histopathological study, palpation is a direct and straight forward method, without the interference of the rectum as it occurs in the digital rectal examination that is performed before fixation process that changes the usual consistency of the prostatic parenchyma. Palpation may detect tumour areas, considering that prostate cancer mainly arises in the peripheral prostate area in between 68% and 80% of the cases [23,24]. A study from Kowalik CG et al., evaluated if tissue elasticity was indicative of carcinomatous changes and employed urological surgeons to evaluate a prostate simulator indicating that the relationship of the nodule with the background prostate elasticity constitutes a critical tactile feedback [25].

Besides that, tumours of the peripheral zone are generally of a higher degree and are more frequently associated with the presence of extraprostatic extension, invasion of seminal vesicles and aggressive behaviour when compared to tumours that arise in the transition zone. However, for patients on active surveillance, there are limited data on transition zone sampling upon follow-up biopsy [26,27].

In the present study, the results indicated that in 75.8% of the total surgical specimens, there was a definite correlation between the palpated and demarcated areas and the microscopic finding of cancer in the histopathological study, and for the right apex, there was a definite correlation in all cases. Considering all demarcated areas, the hit was at least 60%. These findings may be justified because prostate cancer is multicentre in up to 80% of cases. However, among the 20 surgical specimens analysed, in a group of 10 specimens (50% of cases), the areas marked with surgical thread corresponded to the area of greater extension of cancer, compared to other sections of prostatic tissue. This finding is relevant because the tumour extension in surgical specimen has been correlated with the histological grade, stage, tumour progression, and patient survival, in addition to predicting the development of metastases, invasion of seminal vesicles and presence of extraprostatic tissue. Also, there are complex patterns of metastatic spread [28-34].

It is relevant to mention that when analysed in laboratories, the correct location of the apex and base of the prostate are essential for its processing. Also, there is the recommendation that in case of doubt, the pathologist should contact the surgical urologist and ask him about this guidance [35].

For this reason, despite being sectioned during the surgical procedure, as usual, the bladder catheter was maintained in the surgical specimen, and its extremities were sutured with not absorbable wire.

LIMITATION

It is critical to appoint that the small study sample can be a limitation, but it can support the outcome for future studies in large samples.

CONCLUSION

The leading role in the treatment of localised prostate cancer is the urologist who is responsible for detecting the disease, indicates and performs surgery, universally accepted as the gold standard. However, his work does not end with the surgical procedure. The results of this study suggest that palpation and demarcation with a surgical thread of suspected areas for cancer is a feasible procedure, does not affect surgical specimen processing and may provide additional information to the pathologist, directing the histopathological analysis of the prostate to the areas with more significant tumour extension compared to the other sections. Also, to be a quick and straightforward procedure, demarcation with the surgical thread may assist the pathologist in the processing of the surgical specimen, possibly with better cost-effectiveness. The exchange of information between urologists and pathologists should always exist in a clear, precise and unique way to benefit patients.

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