

# Intraductal Prostatic Carcinoma: Epidemiological and Anatomopathological Aspects in Dakar

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## Abstract

**Introduction:** Intraductal carcinoma is often associated with high-grade, high-stage adenocarcinoma. Its frequency is variable and it is considered a poor prognostic factor. In our context, when prostatic carcinoma is diagnosed, pathologists do not always report the presence of this anatomopathological entity. We therefore conducted a study to determine the epidemiological and anatomopathological profile of patients with this lesion in Dakar. **Materials and Methods:** This is a retrospective descriptive study covering a 1-year period from January to December 2022. It focused on cases of intraductal carcinoma diagnosed among prostatic carcinomas collected in the anatomopathology laboratories of Hôpital Général Idrissa Pouye (HOGIP) and Hôpital Militaire de Ouakam (HMO). It was based on archives of anatomopathological reports, blocks and slides. A total of 200 cases of prostatic carcinoma were collated and reviewed to identify those presenting with intraductal carcinoma according to the diagnostic criteria of Guo and Epstein. **Results:** 87 cases of intraductal carcinoma were found, representing 43.5% of prostatic carcinomas. The mean age was 71 years. Patients in their seventh decade were the most represented, *i.e.* 42.5%. The majority of samples examined were biopsies (72.4%). The mean PSA level was 965.91 ng/ml, with extremes ranging from 0.03 to 10,000 ng/ml. Histologically, 96.5% of cases (N = 84) were invasive prostatic carcinoma. Gleason score 8 (4 + 4) was the most common, accounting for 42.53% (N = 37). On average, the study found four (04) foci of intraductal carcinoma per specimen, with extremes ranging from 1 to 30. Dense cribriform architecture accounted for 78.16%, loose cribriform for 11.5%, solid for 8.04% and micropapillary for 2.3%. Six

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cases (6.9%) showed foci of comedonecrosis. The vast majority of radical prostatectomies (87.5%) were classified as pT3. Node invasion and perineural sheathing were observed in 12.5% and 52.32% of cases respectively. **Conclusion:** Intraductal carcinoma is a poor prognostic factor that must be systematically reported in the anatomopathological report. In Senegal, it is often associated with advanced stage, high-grade carcinoma and high PSA levels.

## Keywords

Intraductal Carcinoma, Prostate, Pathological Anatomy, Senegal

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## 1. Introduction

According to the WHO, intraductal prostatic carcinoma (IDC-P is defined as an intra-acinar and/or intraductal neoplastic proliferation presenting certain characteristics of high-grade intraepithelial neoplasia (PIN) but including cytological and architectural abnormalities much more marked. It is considered a poor prognostic factor often associated with adenocarcinoma of high grade, stage and Gleason score, increased prostate volume, extra-prostatic invasion and metastases [1] [2]. Similarly, several studies have reported lower cancer-specific and overall progression-free survival in affected patients [3] [4]. Current theories on the histogenesis of this pathology suggest that a large proportion of these lesions represent an adenocarcinoma with retrograde invasion into the prostate ducts [5]. The frequency of this pathology varies greatly (from 2% to 67%) depending on the studies and their own sampling [6] [7]. Prostate cancer remains a pathology diagnosed late, often at an advanced stage, with an increasing incidence in Senegal [8] [9]. In this same country, intraductal carcinoma is almost not reported in the pathological results of invasive prostate cancer, when it is present. Moreover, no study was found in black Africa, particularly in Senegal on intraductal carcinoma of the prostate. We therefore conducted a study aimed at evaluating the frequency of this entity in subjects presenting with prostate carcinoma in Dakar (Senegal), then to describe the epidemiological and anatomopathological characteristics.

## 2. Materials and Methods

This is a retrospective descriptive study over a period of one year, from January 1 to December 31, 2022. The study took place in the anatomopathology laboratories of the Idrissa Pouye General Hospital (HOGIP) and the Ouakam Military Hospital (HMO). The selection of patients was carried out from registers and reports of archived anatomopathological examinations of cases of prostate carcinoma. The archived histological slides of the selected cases were then reread, in order to look for the presence of foci of intraductal carcinoma.

The data were collected in the same way, by telephone interview, from the

histological examination reports and after rereading the slides, in an Excel collection file. The study parameters were: age, prostate specific antigen (PSA) level, type of sample, Gleason score, presence of nerve invasion, foci of intraductal carcinoma and comedonecrosis, predominant architecture, pT stage and metastases. After re-reading, all patients with histologically confirmed intraductal carcinoma were included (*i.e.* N = 87), whether they were associated with an infiltrating carcinoma or not.

### 3. Procedure

Firstly, a collection of 560 prostate sample identifiers was made.

Then an analysis of the corresponding histological examination protocols and reports made it possible to identify 200 prostate carcinomas. Finally, we carried out a double re-reading of the archive slides by senior pathologists.

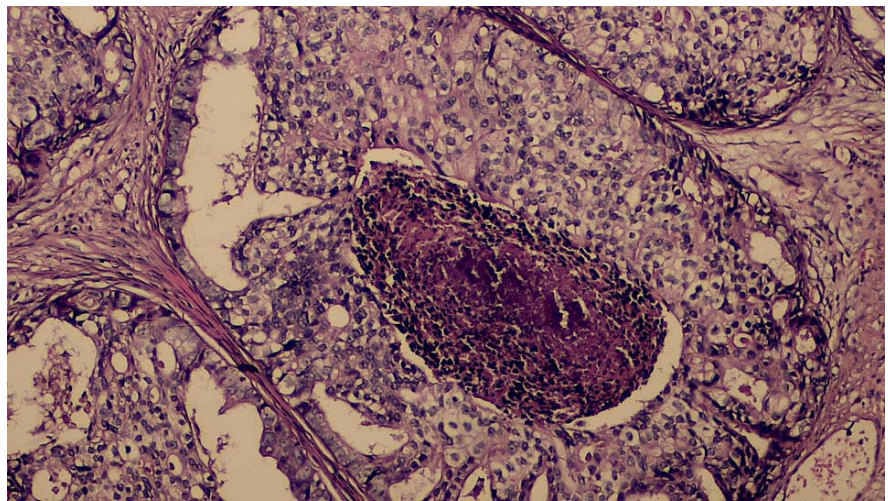
The identification of intraductal carcinoma was based on the criteria defined by Guo CC and Epstein JI [10]: intraductal proliferation with the presence of basal cells in the periphery with:

**Major criteria** (the presence of a single one makes the diagnosis)

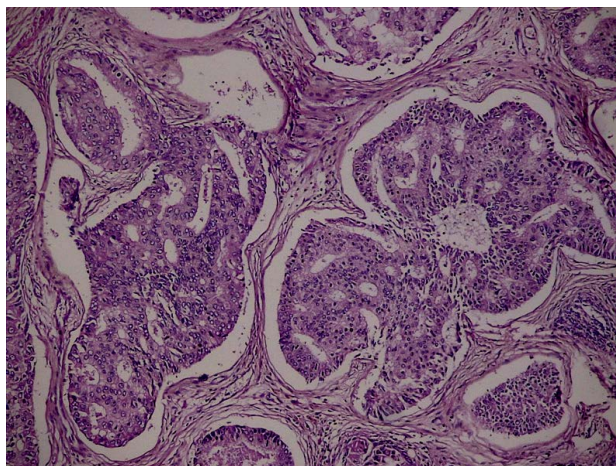
- Dense cribriform architecture (cells occupy at least 50% of the lumen) or solid (**Figure 1** and **Figure 2**);
- Loose cribriform architecture (cells occupy less than 50% of the lumen) or micropapillary architecture with markedly enlarged nuclei (6 times normal) (**Figure 3** and **Figure 4**);
- Non-focal comedonecrosis.

**Minor criteria**

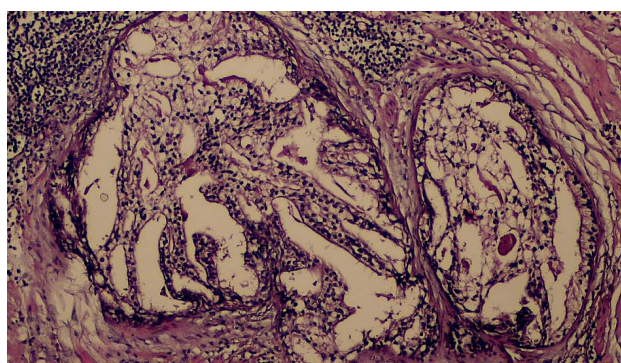
- At least 6 glands involved;
- Irregularly shaped glands with right-angled branching;
- Frequent/easily identifiable mitoses;
- Two (2) cell populations (mitotically active at the periphery and quiescent cells at the center).



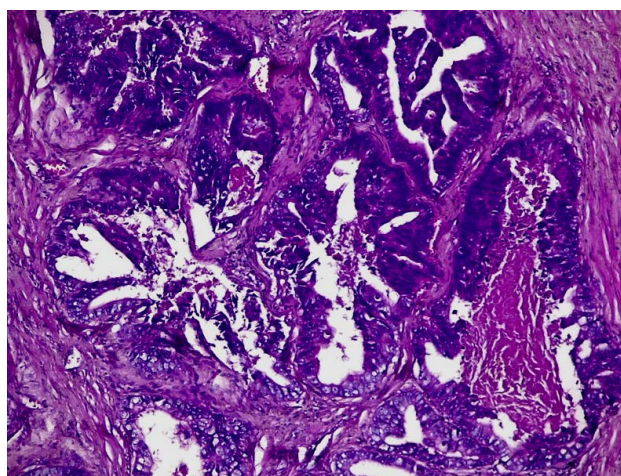
**Figure 1.** Solid architecture IDC-P with central comedonecrosis (HE  $\times 100$ ).



**Figure 2.** IDC-P dense cribriform architecture (HE ×100).



**Figure 3.** IDC-P loose cribriform architecture (HE ×100).



**Figure 4.** IDC-P micro-papillary architecture (HE ×100).

Data entry and analysis was carried out with EPI-INFO software version 7.2.6 and Microsoft Excel 2010. For the descriptive analysis, the qualitative variables were described by frequency tables. The quantitative variables were described by their position (average, median) and dispersion (standard deviation, extremes) parameters.

## 4. Results

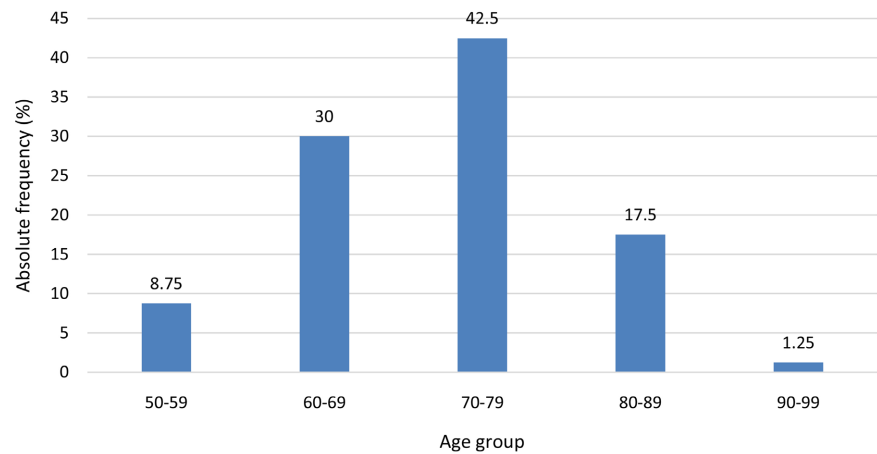
During the study period we identified 200 cases of prostate carcinoma. After re-reading, 87 cases of intraductal carcinoma were found, *i.e.* a frequency of 43.5%.

The average age was 71.5 years with a standard deviation of 8.83, a median of 72 years and extremes of 52 and 91 years. Patients in the seventh decade were the most represented, *i.e.* 42.5%, followed by those in the sixth decade aged 60 - 69 (30%) (**Figure 5**).

The average total PSA level was 965.91 ng/ml with a standard deviation of 1785.8, a median of 200 ng/ml and extremes of 0.03 and 10,000 ng/ml. The cohort was mainly made up of biopsy samples, *i.e.* 72.41% (N = 63), followed by transurethral resections of the prostate (TURP) representing 17.24% (N = 15) (**Table 1**).

**Table 1.** Distribution of absolute and relative frequencies of Gleason score sampling types, predominant IDC-P architecture, T class.

	Workforce (N)	Frequency (%)
<b>Sampling (N = 87)</b>		
Biopsy	63	72.41
TURP	15	17.24
Radical prostatectomy	8	9.20
Adenectomy	1	1.15
<b>Gleason Score (N = 84)</b>		
6 (3 + 3)	4	4.76
7 (3 + 4)	19	22.62
7 (4 + 3)	18	21.43
8 (4 + 4)	37	44.05
≥9	6	7.14
<b>IDC-P architecture (N = 87)</b>		
Dense cribriform	68	78.16
Solid	7	8.04
Loose cribriform	10	11.5
Micro-papillary	2	2.3
<b>Class (N = 8)</b>		
T2	1	12.5
T3 a	5	62.5
T3 b	2	25



**Figure 5.** Distribution of patients according to age group (N = 87).

Histologically, 96.5% of cases (n = 84) corresponded to invasive prostatic carcinoma. The Gleason score 8 (4 + 4) was the most represented, *i.e.* 44.05% (n = 37) (**Table 1**). Only 3.45% (n = 3) of the samples showed an isolated intraductal adenocarcinoma without an invasive focus. An average of 4.3 foci of intraductal carcinoma were identified on the samples with a standard deviation of 4.9, a median of 3 and extremes of 1 to 30.

The dense cribriform architecture was largely predominant, *i.e.* 78.16% (n = 68 cases) (**Table 1**). Comedonecrosis was observed in six cases, *i.e.* 6.9%, all having Gleason scores 8 and 9, and dense or solid cribriform architecture. The vast majority of radical prostatectomies (87.5%) were classified as pT3 and lymph node invasion was observed in 12.5% of cases (n = 1) (**Table 1**). Perineural sheathing was observed in 56.32% of the cohort (n = 49 cases). No distant metastases have been documented.

## 5. Discussion

Intraductal carcinoma was described in prostate cancers in 1985 and was only recognized as a diagnostic entity in 2016 by the WHO, which included it in its classification [10]. Its frequency varies widely depending on patient cohorts. It is 2% to 3% in patients at low metastatic risk and 67% for those at high risk or with confirmed metastasis [7] [11] [12]. In our series, IDC-P represented 43.5%, associated in a large majority (49%) with high-grade invasive carcinoma (Gleason score 8 or 9). This frequency could be explained by the fact that prostate cancer in Senegal is often high grade, diagnosed at an advanced, metastatic stage [9]. These data support the relationship between the presence of this anatomopathological entity and the aggressiveness of prostate cancer [1] [7]. Isolated intraductal carcinoma, without an associated focus of invasive carcinoma, is rare. Its frequency varies widely in the literature. It is less than 1% in several large studies with large biopsy cohorts [6] [10], but 10% in the study by Brian. D *et al.* concerning radical prostatectomies [13]. Our series finds an IDC-P percentage of 3.4%. This result could be explained by the fact that our cohort is

made up of mixed samples, the vast majority biopsy (72.4%).

Conventional IDC-P (IDC-P with invasive carcinoma) would represent retrograde spread of high-grade invasive acinic carcinoma, into the prostatic ducts and acini. It is associated with poor prognosis criteria for radical prostatectomies [2]. While studies would suggest that isolated IDC-P or IDC-P with low-grade adenocarcinoma may represent a *de novo* precursor lesion associated with better prognosis [2]. These entities are currently pathologically indistinguishable [2].

Patients with classic adenocarcinoma of the prostate are generally over 50 years old with an average age close to 70 years, as found in our work and several studies [2] [7] [14]. This observation, found in several states in sub-Saharan Africa, could be due to the delay in consulting patients and the absence of systematic screening from the age of 45 - 50 [9].

Studies find that patients with prostate carcinoma with IDC-P have higher PSA levels than their counterparts without IDC-P, although there is no statistically significant correlation [4] [15].

The PSA level is correlated with the clinical stage [16], it increases with the extension of the disease. Prostate cancer in black Africa is frequently associated with a significant elevation in PSA, often greater than 10 times normal, as corroborated by our work (median PSA = 200 ng/ml) as well as several West African studies [17] [18] [19]. This result confirms the diagnostic delay (a long evolution of the disease before diagnosis).

An average of four (04) foci of intraductal carcinoma were identified on the samples. Most of our cases fulfilled the major criteria (architecture, cytonuclear atypia) and to a lesser extent comedonecrosis.

Dense cribriform architecture was largely predominant, accounting for 78.16%, followed by loose (11.5%) and solid (8.04%) cribriform architecture. These results are similar to those of Guo CC [10] who found 68% cribriform. According to several authors, “dense cribriform” and solid patterns as well as the presence of comedonecrosis have a poorer prognosis [2] [7] [20]. The six cases in our series who presented with comedonecrosis had a dense or solid cribriform architecture and a Gleason score 8 or 9, indicating a poor prognosis.

Perineural invasion is a major prognostic factor and especially predictive of metastasis [21]. It varies considerably depending on the types of patients and samples, but especially depending on the Gleason grade. It is higher in radical prostatectomy cohorts than in biopsy cohorts, as well as among high-grade carcinomas [7].

Its prevalence is increased in invasive carcinomas with IDC-P, as evidenced by the study by Saeter T [4] which found a twice as high proportion of perineural invasion, in patients with invasive carcinoma associated with IDC-P (72%) compared to their counterpart without IDC-P (39%), this difference being statistically significant. This same author highlighted a close relationship between IDC-P and the stromal reaction which will play a determining role in the promotion of tumor invasion facilitating perineural sheathing [4]. Invasive carcinomas associated with IDC-P are often high grade [22] and of advanced clinical

stage cT3-4 (particularly following radical prostatectomy) [13] [23]. Thus the type of sample, the invasive nature, the high grade and stage could explain the proportion of perineural invasion in our study (56.3%). This proportion is higher than that of biopsy series, notably Cohn [24] (8.5%) and Ahmad [25] (29.14%) and is closer to that of Zereba P. [26] (44%), Lee JT. [27] (52.1%), being series relating to prostatectomies.

Lymph node invasion is a poor prognostic factor and several authors maintain that the presence of an intraductal carcinoma associates a greater risk of lymph node metastasis [21]. Among our patients, 12.5% had lymph node involvement, this low proportion being explained by the low proportion of surgical specimens in our cohort.

Among patients with invasive prostate carcinoma, those associated with IDC-P have an increased risk of metastases [2] [3]. The bones, particularly the vertebrae, are the predilection sites for metastatic prostate carcinoma [10].

## 6. Limitations of the Study

This work could present limits which we were able to identify as follows.

- This was a retrospective study.
- Our study was limited to determining the epidemiological and anatomopathological profile of intraductal carcinoma in Senegal.
- We were unable to carry out the immunohistochemistry and molecular biology techniques which would have allowed respectively better diagnostic accuracy, and molecular typing.
- We were unable to have the necessary hindsight to assess the prognosis and precisely the survival of our patients given the duration of the study and missing information. Nevertheless, our study presents positive points.
- This is a multicenter study and the first focusing on intraductal prostatic carcinomas to our knowledge in Senegal, hence its originality.
- It was carried out in the cosmopolitan city of Dakar where we find the populations of all origins, with the contribution of the Pathological Anatomy and Cytology laboratories of a university hospital and the Ouakam Military Hospital, all of which polarizes a large part of the urological samples.

## 7. Conclusion

In Senegal, intraductal carcinoma is often associated with invasive carcinoma of the prostate as well as poor prognostic factors, such as high grade, advanced stage, and high PSA level. It is necessary to mention its presence in all pathological reports. In perspective, a prospective study with study of molecular alterations and an evaluation of patient survival according to therapeutic regimens, will allow a good assessment of its prognostic impact and better management.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.



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