Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(3):652-6

The role of atypical small acinar proliferation in prostate cancer diagnosis: A single center experience

Akgul Arici, Elif Akcay

Tokat Gaziosmanpaşa University, Faculty of Medicine, Department of Medical Pathology, Tokat, Türkiye

Received 28 May 2025; Accepted 23 June 2025
Available online 18 August 2025 with doi: 10.5455/medscience.2025.05.143

Abstract

Atypical small acinar proliferation (ASAP) is a condition that describes lesions that are suspicious for malignancy in prostate biopsies but do not contain sufficient histopathological findings to diagnose prostatic adenocarcinoma. This study aims to evaluate the relationship between the clinical and pathological features of cases diagnosed with ASAP between 2010 and 2023 and to evaluate the relationship between this diagnosis and the development of prostate cancer. As a result of the examination of prostate biopsies of 3215 cases in the Department of Pathology of Tokat Gaziosmanpaşa University, 127 (3.95%) cases diagnosed with ASAP were examined. 72 of these cases underwent repeat biopsy, and prostatic adenocarcinoma was detected in 34 (47.2%) of them. The prostate-spesific antigen (PSA) levels of the malignant cases were 30.3 ng/mL on average, which is significantly higher than the benign cases. In immunohistochemical analyses, positive staining patterns were observed with alpha methylacyl CoA racemase (AMACR) and negative staining patterns with high molecular weight cytokeratin (HMWCK) 34βE12 and p63. In patients diagnosed with prostatic adenocarcinoma, 79.4% had a Gleason score of 3+3=6, and 20.6% had a Gleason score of ≥7 (3 cases Gleason score 3+4=7, 1 case Gleason score 4+3=7, 1 case Gleason score 4+4=8, 2 cases Gleason score 4+5=9). Among the treatment options, radical prostatectomy was the most commonly used method. It has been demonstrated that ASAP diagnosis may be an important risk factor for the development of prostate cancer and that close clinical follow-up and repeat biopsy are necessary in these patients. ASAP diagnosis is a clinical condition that should not be neglected and requires careful pathological evaluation and a multidisciplinary approach.

Keywords: Atypical small acinar proliferation, prostate cancer, prostate biopsy

Introduction

Prostate cancer is one of the most prevalent malignancies among men and ranks second only to lung cancer in cancer-related mortality. It primarily affects individuals over the age of 50 and has shown a rising global incidence in recent years [1]. Although prostate-specific antigen (PSA) testing and digital rectal examination are commonly employed in the initial evaluation, a definitive diagnosis of prostate cancer can only be established through histopathological examination of prostate biopsy specimens [2].

Atypical small acinar proliferation (ASAP) is a diagnosis used by pathologists when the distinction between malignant and benign prostatic biopsy cannot be made with certainty. It is a lesion that is suspicious for malignancy, but histopathological findings are insufficient to diagnose prostatic adenocarcinoma. These lesions are small acinar proliferations that show some microscopic features of prostatic adenocarcinoma but do not meet the definitive diagnostic criteria [3,4]. ASAP is detected in 1-5% of prostate biopsies. It is emphasized that it is an important condition that requires clinical and pathological follow-up. It is recommended that these patients be followed up with a repeat biopsy. The rate of prostatic adenocarcinoma detection in repeated biopsies after ASAP diagnosis has been reported as 30-50% [5,6].

Histopathological features of ASAP include proliferation of acinar structures surrounded by small single-layer epithelial cells with nuclear atypia and small focal size (less than two dozen acini, focal size <1 mm). Immunohistochemical (IHC) analysis usually shows no staining with basal cell markers such as high molecular weight cytokeratin (HMWCK) 34βE12 and p63, while positive staining can be seen with alpha methylacyl CoA racemase (AMACR) [7].

CITATION
Arici A, Akcay E. The role of atypical small acinar proliferation in prostate cancer diagnosis: A single center experience. Med Science. 2025;14(3):652-6.

Corresponding Author: Akgul Arici, Tokat Gaziosmanpaşa University, Faculty of Medicine, Department of Medical Pathology, Tokat, Türkiye
Email: drakgularici@gmail.com

DOI: 10.5455/medscience.2025.05.143

This study aims to retrospectively examine the clinical and pathological features of cases diagnosed with ASAP between 2010 and 2023, to evaluate the relationship between this diagnosis and the development of prostate cancer and the repeat biopsy results in terms of diagnosis and follow-up.

Material and Methods

Our study was conducted retrospectively with the approval of Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee (Date: 29.02.2024 Decision No: 24-KAEK-062). Our study included 127 cases diagnosed with ASAP as a result of histopathological examination of 3215 prostate biopsy materials in Tokat Gaziosmanpaşa University Faculty of Medicine Pathology Department between January 2010 and December 2023. Pathology reports of the cases were scanned retrospectively from the pathology archive. The preparations of the cases with hematoxylin-eosin (HE) and HMWCK 34βE12, p63, and AMACR IHC staining were reviewed. The age of the cases, PSA values, the number of cores detected with ASAP, the number of cases that underwent repeat biopsy after ASAP diagnosis, repeat biopsy diagnoses, the time between ASAP diagnosis and repeat biopsies, the number of cases diagnosed with prostatic adenocarcinoma after ASAP diagnosis, and the histopathological features of the tumor in cases that underwent radical prostatectomy after ASAP diagnosis were recorded from the pathology reports and the automation system records. The obtained data were evaluated in light of the literature information. Statistical analyses were performed using SPSS 22.0 program. Categorical variables were presented as numbers and percentages, and continuous variables were presented as mean and standard deviation (median, minimum-maximum when necessary).

Results

As a result of the retrospective scanning of our Pathology laboratory archive between January 2010 and December 2023, 127 (3.95%) cases diagnosed with ASAP were identified as a result of histopathological examination of prostate biopsy material belonging to 3215 cases. Of the 127 cases diagnosed with ASAP, 72 (56.7%) underwent a repeat biopsy, while 55 (43.3%) did not. Of the 72 cases that underwent repeat biopsy, 34 (47.2%) were diagnosed with malignancy (prostatic adenocarcinoma), and 38 (52.8%) were diagnosed with benign. The average time between the first and second biopsies was 14.5 months (1-129).

The age range of the cases ranged from 46 to 83 years, and the mean age was 65.2±7.4. The mean PSA value was 16.1 ng/mL (0.59-550). The mean number of cores diagnosed with ASAP in prostate biopsy samples was determined as 1.3.

The mean age was 65.4 (46-77) years in malignant cases with repeat biopsy results, 63.7 (48-73) years in benign cases with repeat biopsy results, and 66.5 (53-83) years in cases without repeat biopsy.

The mean PSA values were 30.3 ng/mL (1.4-550) in malignant cases with repeat biopsy results, 8.3 ng/mL (2.9-30) in benign cases with repeat biopsy results, and 9.6 ng/mL (0.59-43) in cases without repeat biopsy.

The number of cores diagnosed with ASAP was; The mean re-biopsy result was 1.5 cores in malignant cases, 1.3 cores in benign cases, and 1 core in cases without re-biopsy.

In the histopathological evaluation of the cases diagnosed with ASAP, it was seen that IHC staining was performed in 120 cases (94.5%) and not in 7 cases (5.5%). In the histopathological examination of the cases, it was observed that the acinar structures in the fibromuscular stroma were slightly crowded together in HE stained sections, there was slight crowding in the nuclei, slight nuclear pleomorphism, nucleoli were prominent in some nuclei, and the luminal edges were partially prominent (Figure 1). In the atypical architecture of the acinar proliferation focus described in the IHC analysis, diffuse strong cytoplasmic expression was observed with AMACR (Figure 2), while basement membrane loss was observed with HMWCK 34βE12 (Figure 3) and p63.

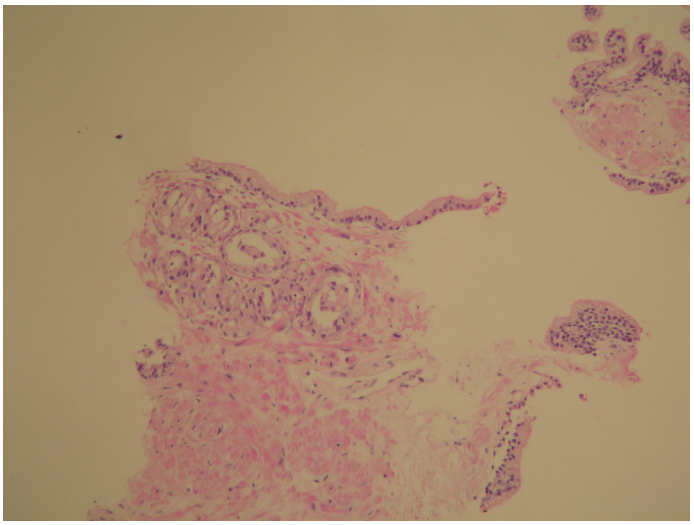

Figure 1. Atypical acinar proliferation with mild nuclear pleomorphism and nuclear crowding in the fibromuscular stroma (HE x 100)

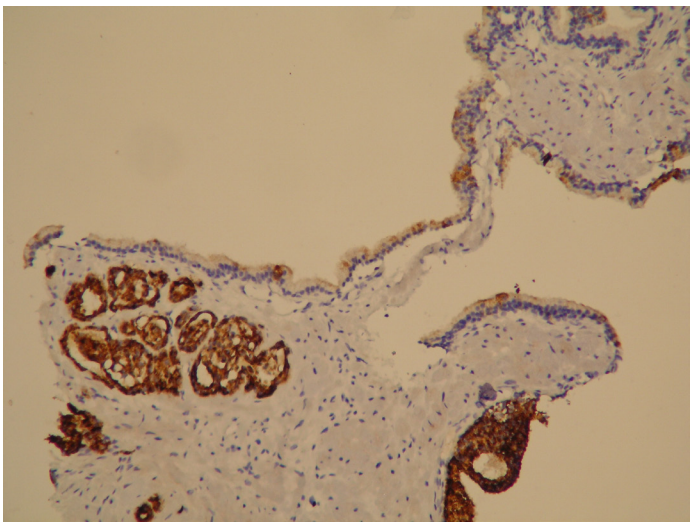

Figure 2. Diffuse strong cytoplasmic staining with AMACR in atypical acinar proliferation focus (AMACR x 100)

DOI: 10.5455/medscience.2025.05.143

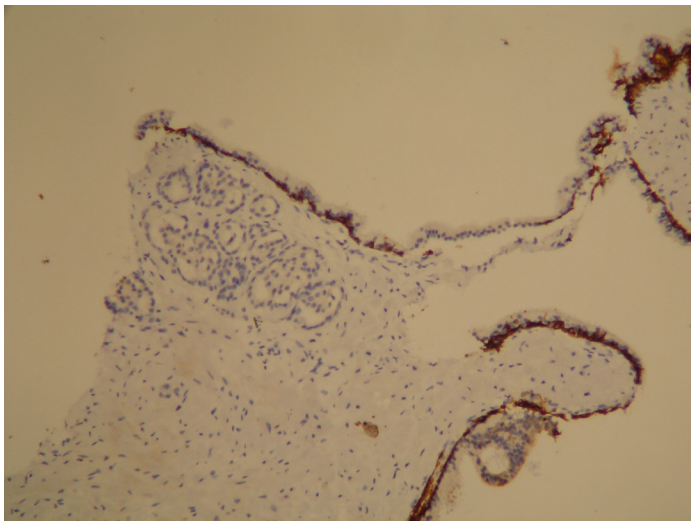

Figure 3. Positive staining in basal cells with HMWCK 34βE12 in benign prostatic glands, loss of basement membrane with HMWCK 34βE12 in atypical acinar proliferation focus (HMWCK 34βE12 x 100)

Of the 34 cases diagnosed as malignant on repeat biopsy, 28 (82.4%) were diagnosed with prostatic adenocarcinoma on the second biopsy, and 6 (17.6%) were diagnosed with prostatic adenocarcinoma on the third or subsequent biopsies. The mean time between the first biopsy and the biopsy in which the malignant diagnosis was made in these cases was 18.7 months (1-118). In 27 cases diagnosed with prostatic adenocarcinoma, Gleason score was 3+3=6 (79.4%), and 7 cases (20.6%) were diagnosed with Gleason score 7 and above (3 cases Gleason score 3+4=7, 1 case Gleason score 4+3=7, 1 case Gleason score 4+4=8, 2 cases Gleason score 4+5=9) (Table 1). Radical prostatectomy was performed in 26 cases (76.5%), radiotherapy in 7 cases (20.6%), and radiotherapy+chemotherapy in 1 case (2.9%).

Table 1. Distribution of cases diagnosed with ASAP in prostate biopsies

	n	(%)
Prostate biopsies cases	**3215**	
ASAP diagnosis	**127**	**(3.95)**
Repeat biopsy	**72**	**(56.7)**
Malignant diagnosis	34	(47.2)
Benign diagnosis	38	(52.8)
No repeat biopsy	**55**	**(43.3)**
Prostatic adenocarcinoma	**34**	
Gleason score 6	27	(79.4)
Gleason score ≥7	7	(20.6)

ASAP: atypical small acinar proliferation

Discussion

ASAP describes small foci of acinar proliferation frequently encountered in prostate biopsies, morphologically suggestive of malignancy but lacking sufficient histopathological findings. The term ASAP was first reported by Icdzkowski et al. in their studies published in 1997 [3,8]. ASAP diagnosis is seen in approximately 5% of prostate biopsies. However, different rates have been reported in various studies. In the study by Totaro et al., the ASAP rate in prostate biopsy of 4,567 patients was found to be 2.6% [9]. In another study, this rate was found to be 12%. These different rates reported were attributed to the experience of pathologists and the fact that the studies were conducted in different centers and with different patient populations [10,11]. In our study, the rate of patients diagnosed with ASAP was 3.95%, which is consistent with the literature.

To detect suspicious lesions in prostate tissue, pathologists assess architectural and cytological features, along with the presence or absence of the basal cell layer. IHC serves as a valuable ancillary technique when a conclusive diagnosis cannot be reached with routine HE staining. The most commonly used basal cell markers in IHC are HMWCK 34βE12 and p63. These markers exhibit positive staining in the basal cells of benign prostate glands. In contrast, malignant lesions, which lack a basal cell layer, do not exhibit such staining. Additionally, AMACR has emerged as a significant marker in recent years, showing positive staining in malignant prostate glands. Evaluating IHC results in conjunction with findings from HE-stained sections enhances diagnostic accuracy in ambiguous cases [6,12,13].

Since ASAP diagnosis carries a risk of prostate cancer, a second prostate biopsy is routinely recommended by the guidelines. It is stated in the literature that the rate of repeat biopsy after ASAP diagnosis is between 47% and 63% [14]. Similarly, in our study, it was seen that 56.7% of our ASAP diagnosed cases underwent a repeat (second) biopsy. It is stated that cases that did not undergo repeat biopsy for different reasons were lost to follow-up, and the diagnosis of malignancy may be missed. O'Connor et al. stated that the risk of developing prostate cancer within 5 years in patients diagnosed with ASAP is 20%, emphasizing the importance of repeat biopsy [15].

Prostatic adenocarcinoma detection rates in repeat biopsies performed after ASAP diagnosis vary between studies, but range from 30% to 60%. This rate is 42% in the study conducted by Mallen et al. and 47.1% in the series of Imanaka et al. [5,16]. In our study, the rate of prostatic cancer in repeat biopsies performed after ASAP diagnosis is 47.2%, which is consistent with the literature. It also reveals the importance of close follow-up and the necessity of repeat biopsy in individuals diagnosed with ASAP. Prostate cancer diagnosis was given in the second biopsy in the majority of our cases (82.4%) and in the third and subsequent biopsies in 17.6%. This situation shows that malignancy cannot be excluded even in cases with a benign diagnosis in a repeat biopsy, and that clinical follow-up and further biopsies are necessary. In the literature, it is recommended to perform a repeat biopsy within 3-6 months after an ASAP diagnosis [8,16]. This period was 14.5 months on average in our series. This situation explains the high rate of prostate cancer diagnosis in the second biopsy. The fact that the period between the first and second biopsies

DOI: 10.5455/medscience.2025.05.143

in our study was longer than the recommended period may be due to patients losing follow-up or differences in interpretation between clinics. Again, in our series, the period between the ASAP diagnosis and the biopsy with a malignant diagnosis was 18.7 months on average.

In the evaluation of prostate biopsy pathology results, it is recommended to interpret the patient's age, PSA value, lesion size, Gleason score, and clinical general condition of the patient [17]. The ages of our ASAP diagnosed cases ranged from 46 to 83. As a result of repeat biopsy, the mean age in the malignant diagnosed group was 65.4 years, which was higher than the benign diagnosed group, and this is consistent with the literature. It is known that advanced age is a risk factor for prostate cancer [1,10].

PSA is one of the most important markers used in prostate cancer screening. A serum PSA value above 4 ng/mL is accepted as a criterion for prostate biopsy. It is known that the probability of prostate cancer increases with increasing PSA levels. However, an increase in PSA levels can also be seen in some benign lesions of the prostate (such as prostatitis, atrophy) [17,18]. In our study, while the PSA value was 16.1 ng/mL in cases diagnosed with ASAP, PSA levels were found to be significantly higher in cases diagnosed with malignancy (average 30.3 ng/mL). It shows that the PSA value is an important biomarker in the follow-up process in patients diagnosed with ASAP.

Yazdani et al. reported in their study that the number of cores diagnosed ASAP in the first biopsy was not significant in determining the probability of prostate cancer [19]. Another study reported that biopsies containing fewer cores had less sensitivity in detecting prostate cancer [20].

Gleason score is an important parameter in terms of the biological behavior and prognosis of the tumor in prostate cancer [17]. Prostate cancers detected in repeat biopsy after ASAP diagnosis are mostly low-grade (Gleason score 6), but can be seen in clinically significant higher-grade (Gleason score ≥7) tumors. In different studies, clinically significant (Gleason score ≥7) prostate cancer detection rates after ASAP were found to be between 4.8% and 22.5% [2,7,21]. In the study by Dorin et al., the Gleason score 6 prostate cancer rate in repeat biopsies after ASAP diagnosis was 81% [22]. Warlick et al. reported the Gleason score ≥7 prostate cancer rate as 17.3% [23]. Similarly, in our study, 79.4% had Gleason score 6 and 20.6% had Gleason score ≥7.

After the diagnosis of ASAP, treatment options are considered after the presence of malignancy and its clinical significance are determined as a result of a repeat biopsy [9]. In a study including 64 patients diagnosed with ASAP, it was reported that 71% of the 28 patients diagnosed with prostate cancer in the repeat biopsy underwent radical prostatectomy [5]. It was determined that 76.5% of our patients diagnosed with prostate cancer underwent radical prostatectomy, and the remaining cases underwent radiotherapy and chemotherapy.

Our study has limitations. It is retrospective in design and limited to data from a single center, and possible data losses. The ASAP diagnosis has inherent difficulties because it is not a definitive diagnosis, but rather identifies suspicious lesions that are not sufficient for the diagnosis of adenocarcinoma. Variability in pathologists' experience and interpretation, as well as limitations in biopsy technique and tissue sampling, may also influence diagnostic accuracy and outcomes.

Conclusion

ASAP refers to suspicious foci that are difficult to distinguish between malignant and benign in prostate biopsy. In our study, cases diagnosed with ASAP were evaluated retrospectively, and it was shown that this diagnosis may be an important risk factor for the development of prostate cancer. Approximately half of the cases diagnosed with ASAP were diagnosed with prostate cancer with a repeat biopsy, which reveals the necessity of clinical follow-up and repeat biopsy. Evaluating clinical, biochemical (PSA level), and pathological findings together, and performing a repeat biopsy in a timely and appropriate manner are important in the early diagnosis and treatment of prostate cancer. Therefore, ASAP is a histopathological diagnosis that should not be neglected and requires a careful and multidisciplinary approach.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The study was carried out with the approval of Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee (Date:29.02.2024 Decision No:24-KAEK-062).

References

1. Şimşek A, Özgör F, Küçüktopçu O, et.al. Yüksek dereceli intraepitelyal neoplazi ve atipik küçük asiner proliferasyonun prostat biyopsisinde öneminin değerlendirilmesi. The New Journal of Urology. 2014;9:48-52.
2. Schwartzmann I, Celma A, Regis L, et. al. The current value of histological findings in negative prostate biopsies to predict the future risk of clinically significant prostate cancer. Actas Urol Esp (Engl Ed). 2021;45:447-54.
3. Bostwick DG, Meiers I. Atypical small acinar proliferation in the prostate: clinical significance in 2006. Arch Pathol Lab Med. 2006;130:952-7.
4. Ji WT, Jin XF, Wang Y. The rate of clinically significant prostate cancer on repeat biopsy after a diagnosis of atypical small acinar proliferation: a systematic review and meta-analysis. Oncology. 2024;102:631-40.
5. Mallen E, Gil P, Sancho C, et. al. Atypical small acinar proliferation Review of a series of 64 patients. Scand J Urol Nephrol. 2006;40:272-5.
6. Oderda M, Rosazza M, Agnello M, et. al. Natural history of widespread high grade prostatic intraepithelial neoplasia and atypical small acinar proliferation: should we rebiopsy them all?. Scand J Urol. 2025;5:129-34.
7. Tsampoukas G, Manolas V, Brown D, et. al. Atypical small acinar proliferation and its significance in pathological reports in modern urological times. Asian J Urol. 2022;9:12-7.

DOI: 10.5455/medscience.2025.05.143

8. Leone A, Rotker K, Butler C, et. al. Atypical small acinar proliferation: repeat biopsy and detection of high grade prostate cancer. Prostate Cancer. 2015;2015:810159.

9. Totaro A, Di Gianfrancesco L, Pinto F, et. al. Rate of clinically significant prostate cancer on repeat saturation biopsy after a diagnosis of atypical small acinar proliferation. Urologia. 2021;88:194-9.

10. Sade AG, Sarıkaya Ş, Barışık NÖ, et. al. Histomorphological features of Atypical Small Acinar Proliferations (ASAP) that favor malignancy. South Clin Ist Euras. 2020;31:382-7.

11. Anbarasan T, Raslan M, Ghosh K, et. al. MP55-09 natural hıstory of atypıcal small acınar prolıferatıon (asap): a 10-year contemporary serıes. Journal of Urology. 2023;209:766-7.

12. Aydın H. Prostat biyopsilerinin histopatolojik değerlendirmesi. Üroonkoloji Bülteni. 2005;3:3-8.

13. Hasan IA, Gaidan HA, Al-Kaabi MM. Diagnostic value of cytokeratin 34 beta E12 (Ck34βE12) and α-Methylacyl-CoA racemase (AMACR) immunohistochemical expression in prostatic lesions. Iran J Pathol. 2020;15:232-8.

14. Caner E, Serkan A, Neslihan K, et. al. A new ASAP scoring system and risk table to predict second prostate biopsy outcomes. Arch Med Sci. 2024;20:1894-901.

15. O'Connor E, Dowling C, Casey M, et. al. Implications of a diagnosis of atypical small acinar proliferation (ASAP) and high-grade prostatic intraepithelial neoplasia (HGPIN) on prostate biopsy: a 5-year follow-up study. Ir J Med Sci. 2022;191:2035-40.

16. Imanaka T, Yoshida T, Taniguchi A,et. al. Implementation of repeat biopsy and detection of cancer after a diagnosis of atypical small acinar proliferation of the prostate. Mol Clin Oncol. 2020;13:67.

17. Bozlu M. Prostat biyopsilerinin klinik yorumu. Üroonkoloji Bülteni. 2007;2:8-11.

18. Öztürk U, Aydın M, İrkılata L, et. al. Predictive factors for detection of clinically significant cancer in repeat prostate biopsy. Somalia Turkiye Medical Journal. 2023;2:1-7.

19. Yazdani M, Samani PR, Mazdak H, et. al. Rate of clinically significant prostate cancer on repeated biopsy after a diagnosis of atypical small acinar proliferation. Immunopathologia Persa. 2023;9:e94

20. Leone L, Lacetera V, Montironi R, et. al. Biopsy follow-up in patients with isolated atypical small acinar proliferation (ASAP) in prostate biopsy. Arch Ital Urol Androl. 2014;86:332-5.

21. Norman RD, Garg H, Rickborn L, et. al. Clinically significant prostate cancer in men with high-grade intraepithelial prostatic intraepithelial neoplasia or atypical small acinar proliferation. JU Open Plus. 2023;1:e00049.

22. Dorin R, Wiener S, Harris C, et. al. Prostate atypia: does repeat biopsy detect clinically significant prostate cancer?. The Journal of Urology. 2015;193(4S): 708-9. Prostate. 2015;75:673-8.

23. Warlick C, Feia K, Tomasini J, et. al. Rate of Gleason 7 or higher prostate cancer on repeat biopsy after a diagnosis of atypical small acinar proliferation. Prostate cancer and prostatic diseases. 2015;18:255-9.