

# Evaluation of PSA requests in men under 40 years of age

## *Avaliação das solicitações de PSA em homens com menos de 40 anos de idade*

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### ABSTRACT

**Objectives:** To evaluate the frequency of PSA requests in men under age 40 years; and to observe the possible influence of medical specialty of the requesting physician. **Material and method:** This is an observational, cross-sectional study using the database of a national clinical laboratory on PSA requests from October 1, 1997 until December 31, 2016. Descriptive statistics were used. The work was approved by the Ethics Committee of our institution. **Results:** 2,514,375 PSA requests were evaluated, 158,399 (6.3%) in men younger than 40 years old. These percentages did not vary significantly when observed over time (1998-2016). The prevalence of requests for patients under 40 years of age, was 18.2% among general practitioners; 16.5% among cardiologists, 8.4% among geriatricians and 6.8% among urologists. **Conclusion:** There is a very high frequency of PSA requests in men with low probability of benefiting from the test. It is necessary to invest in the dissemination of best practices related to prostate cancer screening, especially among clinicians and cardiologists.

**Key words:** prostate-specific antigen; mass screening; prostatic neoplasms; medical overuse.

### RESUMO

**Objetivos:** Avaliar a frequência das solicitações de antígeno prostático específico (PSA) para homens com menos de 40 anos, bem como observar a possível influência da especialidade do médico solicitante. **Material e método:** Estudo observacional, de corte transversal, que utilizou o banco de dados de um laboratório clínico brasileiro de grande porte com as solicitações de PSA no período de 1º de outubro de 1997 a 31 de dezembro de 2016. Os dados foram analisados por estatística descritiva. O trabalho foi aprovado pelo Comitê de Ética de nossa instituição. **Resultados:** Foram avaliadas 2.514.375 solicitações de PSA, 158.399 (6,3%) em homens com menos de 40 anos. Esses percentuais não variaram significativamente quando observados no tempo (1998-2016). Entre as solicitações com identificação da especialidade do médico para pacientes com menos de 40 anos de idade, 18,2% foram de clínicos, 16,5% de cardiologistas, 8,4% de geriatras e 6,8% de urologistas. **Conclusão:** Há uma frequência muito elevada de solicitações de PSA em homens com baixa probabilidade de se beneficiarem com a realização do exame. Faz-se necessário investimento na divulgação das melhores práticas em relação ao rastreamento do câncer de próstata, especialmente entre os clínicos e cardiologistas.

**Unitermos:** antígeno prostático específico; programas de rastreamento; neoplasias da próstata; uso excessivo de produtos e serviços de saúde.

### RESUMEN

**Objetivos:** Evaluar la cantidad de solicitudes del antígeno prostático específico (PSA) para hombres menores de 40 años, así como observar la posible influencia de la especialidad del médico solicitante. **Material y método:** Estudio observacional, de corte transversal, que utilizó la base de datos de un gran laboratorio clínico brasileño con las solicitudes de PSA desde el 1 de octubre de 1997 hasta el 31 de Diciembre de 2016. Se analizaron los datos mediante estadística descriptiva. El estudio fue aprobado

por el comité ético de nuestra institución. **Resultados:** Se evaluaron 2.514.375 solicitudes de PSA, 158.399 (6,3%) en hombres menores de 40 años. Los porcentajes no variaron significativamente con el tiempo (1998-2016). La prevalencia de solicitudes para pacientes menores de 40 años, fue de 18,2% entre los clínicos, 16,5% entre cardiólogos, 8,4% geriatras y 6,8% entre los urólogos. **Conclusión:** Hay una cantidad muy grande de solicitudes de PSA en hombres con baja probabilidad de sacar provecho de la realización del test. Es necesario invertir en la divulgación de mejores prácticas de tamizaje del cáncer de próstata, especialmente entre los clínicos y cardiólogos.

**Palabras clave:** antígeno prostático específico; tamizaje masivo; neoplasias de la próstata; uso excesivo de los servicios de salud.

## INTRODUCTION

Prostate cancer (PCa) is the most prevalent cancer among men, if we do not consider non-melanoma skin cancer; it ranks second as a cause of male death by cancer in the United States<sup>(1)</sup> and fourth in Brazil<sup>(2)</sup>.

Up to the end of the 1980's, PCa screening was carried out just with digital rectal examination (DRE). This procedure, however, just identified cancers in very advanced stages, having no impact upon reduction of mortality by PCa<sup>(3)</sup>.

The introduction of prostate-specific antigen (PSA) test as a screening test increased significantly the chance of diagnosing a PCa, but most of them localized and of low lethality potential<sup>(4)</sup>.

Regarding mortality reduction, two of the main long-term studies showed conflicting results<sup>(5, 6)</sup>, with different recommendations by several scientific specialty societies and governmental entities. At a recent publication, we reviewed conduct guides of the main national and international entities<sup>(7)</sup>. As for screening, all entities recommended PSA blood test alone or associated with DRE. The age suggested to start screening ranged from 40 years – for patients with increased risk, according to the American Cancer Society<sup>(8)</sup>, the American Urological Association<sup>(9)</sup>, and the Canadian Urological Association<sup>(10)</sup> –, and 55 years – for patients of average risk, according to the American Urological Association<sup>(9)</sup> and the US Preventive Service Task Force<sup>(11)</sup>. It is important to highlight that no entity recommends screening in men younger than 40 years.

The youngest patients presented low probability to benefit from screening, and great possibility of overdiagnosis and complications caused by the investigation or unnecessary treatment (overtreatment)<sup>(12)</sup>.

## OBJECTIVES

This work verified the frequency of PSA test ordering in men younger than 40 years, intended to screen for PCa. It also observed

the possible influence of physician specialty when ordering PSA measurement for those patients. The study was carried out using the databank of a large national Brazilian laboratory, since 1997, when it began measuring PSA levels.

## MATERIAL AND METHOD

The following data were surveyed from October 1, 1997 (beginning of PSA measurements) to December 31, 2016: exam date, town where specimen was drawn, patient age, specialty of the ordering physician (when available), and PSA test result. Besides those variables, the number of tests taken by male subjects and the total number of PSA tests were considered, monthly and by age group.

For analysis of the possible influence of medical specialty, just requests with this information from the databank were included, the specialties of interest being limited, that is, general practice, or (general) internal medicine, cardiology, geriatrics, and urology. Cardiologists and geriatricians were included because in Brazil they are frequently visited to do checkups in patients with no complains directly linked to their areas of acting, just like general practitioners.

The results from subjects with more than one test performed in the same year were excluded to minimize the possibility of the test being done with a diagnostic intent, not for screening.

Descriptive statistics was used, with analysis of measures of central tendency, dispersion, and association. For temporal analysis, the trend line was observed. There was no need to establish the sample size or to calculate the *p* value, because the work involved the whole universe of the databank.

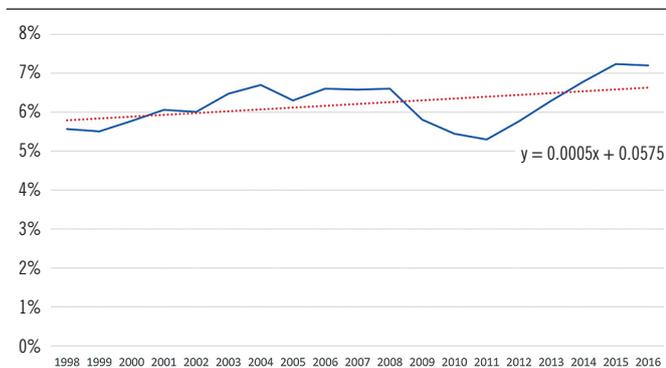
The study was conducted according to the resolution 466/12 of the National Health Council and approved by the Research Ethics Committee of the proposing institution (report no. 1.550.766 – CAAE 55705116.6.0000.5544).

## RESULTS

During the observed period, 2,514,375 PSA tests were performed for PCa screening. Among them, 158,399 (6.3%) were conducted in subjects younger than 40 years.

The curve equation demonstrated a slight increase trend of PSA test requests over the years, at an average rate of 0.05% per year (**Figure**).

The **Table** shows that 222,591 tests were requested with specialty identification of the ordering physician. General practice and cardiology were the specialties with the highest percentage of requests for patients under 40 years of age: 18.2% and 16.5%, respectively. Urologists presented the lowest percentage (6.8%).



**FIGURE** – Temporal evolution of the percentage of PSA requests for patients under 40 years old  
Blue full line: percentage of patients under 40 years old per year; red dotted line: trend curve (with trend graph equation).

PSA: prostate-specific antigen.

**TABLE** – General frequency of PSA test orders according to patient age group and specialty of the requesting physician

	General practitioners		Cardiologists		Geriatricians		Urologists		Total	
	n	%	n	%	n	%	n	%	n	%
< 40	12,912	18.2	12,768	16.5	244	8.4	4,831	6.8	30,755	13.8
≥ 40	57,975	81.8	64,570	83.5	2,675	91.6	66,616	93.2	191,836	86.2
Total	70,887		77,338		2,919	1.3	71,447		222,591	

PSA: prostate-specific antigen.

## DISCUSSION

The introduction of PSA test as a screening test resulted in a considerable increase in PCa diagnoses<sup>(13)</sup>.

Tumors detected by screening tend to be slow growing and less prone to give rise to symptoms and cause patients' death. This occurs because the slower the growth is, that is, the longer

the patient has the cancer, although not manifesting it, the longer this tumor will be exposed to be discovered<sup>(14)</sup>. Tumors in very young patients are usually more aggressive, with fewer possibilities, therefore, of being detected by screening<sup>(15)</sup>. Besides, because they have a longer life expectancy, the diagnosis of indolent tumors in this age group leaves subjects more susceptible to morbidities secondary to treatment<sup>(15)</sup> for a longer time.

Although having low probability of benefiting from screening, a significant number of patients aged less than 40 years undergoes the test. Around 6.3% of the requests analyzed in this study were ordered for men in this age group, an average of more than 8 thousand requests per year. Actually, in 2016, the last analyzed year, almost 22 thousand patients younger than 40 years underwent the PSA test.

The analysis of requests with physician specialty identification proved that general practitioners and cardiologists order more tests for young patients than urologists and geriatricians. Such a scenario probably indicates the practice of these latter according to consensus and recommendations from their specialties.

Habitually, abnormal PSA levels demand result confirmation by means of prostate biopsy, an invasive procedure with frequent complications, such as bleeding, pain, infection<sup>(16)</sup>, urinary difficulties, anxiety crises because of the disease, and a large number of false-positive results<sup>(8, 17)</sup>. In three major randomized clinical studies [The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO)<sup>(16)</sup>, European Randomized Study of Screening for Prostate Cancer (ERSPC)<sup>(18)</sup> and Comparison Arm for ProtecT (CAP)<sup>(19)</sup>], the percentages of negative biopsies were, respectively, 67.7%, 75.8%, and 60.6%. Moreover, overdiagnosed cancers are overtreated, with the possibility of complications, such as urinary incontinence, erectile dysfunction, and bowel complications, besides long-lasting anxiety, with great impact on patients' quality of life<sup>(20)</sup>.

As far as we have observed, this is the first work studying the frequency of PSA use for PCa screening in patients aged less than 40 years, in a population-based sample.

Allard *et al.* (2012)<sup>(21)</sup>, at a survey with 969 Canadian family physicians, found just one (0.1%) professional who recommended that screening should begin before age 40. At a similar investigation, with 354 Brazilian doctors, three (0.8%) ordered PSA testing for subjects under 40 years of age with average risk, and 54 (15.2%), for subjects of higher risk (family history of PCa and black race)<sup>(22)</sup>.

Our study presents some limitations. Firstly, we are not certain that all exam orders have been aimed at screening. In an effort to minimize the possibility of a test being ordered to monitor a patient with established diagnosis, we excluded from the work all the patients with more than one test ordered in a 12-month period.

Another problem is the difference in the percentage of test orders for men younger than 40 years, when we consider the total requests (2,514,375 PSA tests) or just those tests with specialty identification and the specialties of interest (222,591). The percentage of orders was significantly lower in the first (6.3%) than in the second (15%) case. A possible explanation is that our laboratory suffered a brand expansion process, consequently, the number of medical orders without identification of the requesting doctor in tests from other cities and brands later

incorporated to our laboratory increased, once they could have a different screening pattern.

## CONCLUSION

The study showed a significantly high frequency of PSA orders for a population with low potential benefits from the test and high potential harm resulting from false-positive results.

Similar studies should be conducted in other populations, as well as a more detailed assessment of the consequences of PCa screening in this age group. Our study also indicates the necessity of educational programs aimed at the rational use of PSA testing.

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