



PROSTATE CANCER: PICTURE OF A REALITY OF PATIENTS IN TREATMENT
CÂNCER DE PRÓSTATA: RETRATO DE UMA REALIDADE DE PACIENTES EM TRATAMENTO
CÁNCER DE PRÓSTATA: RETRATO DE UNA REALIDAD DE PACIENTES EN TRATAMIENTO

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ABSTRACT

Objective: to describe sociodemographic and clinical data and the possible doubts, difficulties and limitations faced by patients in the treatment of prostate cancer. **Method:** this is a descriptive, cross-sectional, quantitative approach, performed with 213 men in the treatment of prostate cancer. The data were obtained through an interview form and analyzed with the help of the SPSS program. **Results:** sample composed of men predominantly over 50 years old, white, married, retired, with complete elementary education. The initial diagnosis was through alterations in PSA and/or rectal touch, by SUS, with staging II. The manifestations of changes in sexual and urinary function were highlighted in the difficulties and limitations. **Conclusion:** the knowledge of the characteristics and opinions of the participants regarding the diagnosis and treatment may contribute to the planning of the care provided, aiming to establish preventive, therapeutic and other actions aimed at better care. **Descriptors:** Prostatic Neoplasms; Men's Health; Health Profile; Oncology Nursing.

RESUMO

Objetivo: descrever os dados sociodemográficos e clínicos e as possíveis dúvidas, dificuldades e limitações enfrentadas pelos pacientes em tratamento de câncer de próstata. **Método:** estudo descritivo, transversal, de abordagem quantitativa, realizado com 213 homens em tratamento de câncer de próstata. Os dados foram obtidos através de um formulário de entrevista e analisado com auxílio do programa SPSS. **Resultados:** amostra composta por homens predominantemente acima dos 50 anos, brancos, casados, aposentados, com ensino fundamental completo. O diagnóstico inicial foi através de alterações no PSA e/ou toque retal, pelo SUS, com estadiamento II. Das dificuldades e limitações sobressaíram as manifestações de alterações na função sexual e urinária. **Conclusão:** o conhecimento das características e opiniões dos participantes diante do diagnóstico e tratamento poderão contribuir para o planejamento da assistência prestada visando estabelecer medidas preventivas, terapêuticas e outras ações voltadas para melhor assistência. **Descritores:** Neoplasias da Próstata; Saúde do Homem; Perfil de Saúde; Enfermagem Oncológica.

RESUMEN

Objetivo: describir los datos sociodemográficos y clínicos y las posibles dudas, dificultades y limitaciones enfrentadas por los pacientes en tratamiento de cáncer de próstata. **Método:** estudio descriptivo, transversal, de enfoque cuantitativo, realizado con 213 hombres en tratamiento de cáncer de próstata. Los datos fueron obtenidos a través de un formulario de entrevista y analizado con auxilio del programa SPSS. **Resultados:** muestra compuesta por hombres predominantemente arriba de los 50 años, blancos, casados, jubilados, con enseñanza fundamental completa. El diagnóstico inicial fue a través de alteraciones en el PSA y/o toque retal, por el SUS, con etapa II. De las dificultades y limitaciones sobresalieron las manifestaciones de alteraciones en la función sexual y urinaria. **Conclusión:** el conocimiento de las características y opiniones de los participantes frente al diagnóstico y tratamiento podrá contribuir para el planeamiento de la asistencia prestada, visando establecer medidas preventivas, terapéuticas y otras acciones dirigidas para mejor asistencia. **Descriptores:** Neoplasias de la Próstata; Salud del Hombre; Perfil de Salud; Enfermería Oncológica.

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INTRODUÇÃO

Prostate cancer is considered the second most common type of cancer in men worldwide, with the highest frequency of diagnosis in 87 countries, including all countries in America and most of Europe, Australia and Africa. According to the latest worldwide estimate, about 1 million new cases were expected worldwide in 2012.¹⁻² Without considering non-melanoma skin tumors, prostate cancer in Brazil is the most incident in all regions of the country, estimated for 2016 about 61,200 cases per 100,000 inhabitants in every country and for the southeast region, about 62,36/100,000 new cases.²

The risk factors identified for its development are related to age, heredity and ethnic origin.³ Most diagnoses of prostate cancer are associated with men over 65 years old and less than 1% with men under 50 years old. With the increase in the world's life expectancy, the number of new cases is expected to increase by about 60%. The hereditary factor should be considered, since approximately 25% of the cases have a family history. Men who had a diagnosed father or brother have a two to threefold increase in the risk of developing neoplasia. This risk increases by approximately 11 times if the diagnosis occurs in a parent or sibling before 40 years old. Ethnicity is also associated with prostate cancer, being approximately 1.6 times more common in blacks compared to whites, a difference that can be attributed to lifestyle or factors associated with the detection of the disease.²⁻⁴

Prostate cancer is considered a cancer of good prognosis, if diagnosed and treated in a timely manner. Although in Brazil, as in other countries such as Australia, Canada and the United Kingdom, it is not recommended to organize screening programs, evidence-supported positioning posing more risks than benefits. Disease control actions should focus on other strategies, such as primary prevention and early diagnosis.²

The initial diagnosis is usually based on findings from the rectal examination and/or prostate specific antigen (PSA) clinical examination. For the diagnosis of certainty, it is necessary to perform the histopathological study of the tissue obtained by prostatic biopsy. The assessment of tumor extension should be individualized, based on the results of the touch examination, PSA dosage, Gleason score and biopsy. These results define the prognosis and the best treatment option for the patient.³⁻⁴ Therapeutic modalities

include vigilant observation, surgery, radiotherapy and hormone therapy, which can be used alone or in combination.⁴

Prostate cancer is a public health concern, especially in developed countries, as it increases in concomitance with the life expectancy of the male population. Although the knowledge of the social and clinical characteristics of these patients can help health professionals in the planning of their actions, in the orientation of the intervention choices and in the improvement of the care provided, few studies are published in the world on these characteristics. Most focus their discussions on isolated or combined therapeutic techniques, male behaviors in preventive exams and preventive measures, and the profile of these patients has a limited literature.⁵

Considering these and considering that the diagnosis and treatment of the disease can cause significant changes in the lives of men and, consequently, generating possible doubts, difficulties and limitations, the approach of these questions may add data allowing to increase the knowledge of the patient and contributing to a better quality of life during treatment.

Based on the foregoing, the objective of the study was to describe sociodemographic and clinical data and the possible doubts, difficulties and limitations faced by patients in the treatment of prostate cancer.

METHOD

Article prepared from preliminary results of the thesis project << *Quality of life of individuals under treatment of prostate cancer: subsidies for planning health promotion actions* >> that will be presented to the Ph.D. Program in Health Promotion of the University Of Franca/SP, Brazil.

This is a descriptive, cross-sectional, quantitative study, conducted at the Hospital do Câncer de Franca, located in the interior of the state of São Paulo. The population consisted of 412 men diagnosed with prostate cancer in the treatment of hormone therapy and/or radiotherapy during the data collection period, from February to November, 2015. Of this total, a convenience sample of 213 men with cognitive conditions to understand and answer the questions of the instrument of data collection and who signed the Informed Consent Term-TCLE. Of the 199 excluded, 68 ended the treatment at the time of collection, 47 had no cognitive conditions, 44 did not agree to participate, 35 were not found and 5 died.

An interview form with closed and open questions was elaborated by the researchers to obtain the data, for socio-demographic and economic characterization of patients (age, skin color, marital status, education, current work situation, family income and dependents), clinical (year and place of diagnosis, what led to the diagnosis, beginning of treatment, family history and clinical staging) and questions related to possible doubts about the disease and treatment, difficulties faced, limitations of current status, social support received and satisfaction with care. This instrument was previously submitted to an evaluation by three professionals with recognized knowledge in the area to content, clarity, objectivity, comprehensiveness, pertinence and accuracy of information.

The interview to obtain the data was performed by the author, in the return scheduled by the hospital, individually and in a private place. If necessary, some data were later retrieved from the medical records. The collected information was organized, tabulated and submitted to descriptive statistical analysis with the statistical

software Statistical Package for the Social Sciences (SPSS), version 19.0. The variables are presented by means of absolute and relative frequencies.

The research project was approved by the Research Ethics Committee of the Santa Casa de Misericórdia Foundation of Franca, under CAEE n° 36664214.7.0000.5438.

RESULTS

Based on the socio-demographic data presented in Table 1, it can be observed that the participants' ages ranged from 43 to 96 years old, with a mean age of 74.4 years old, with a higher frequency in the age groups of 70 to 79 years old and 80 to 89 years old, with 73 (34.3%) and 71 (33.3%), respectively. The dominant skin color was white with 135 (63.4%), the number of married people prevailed, 166 (77.9%). The total elementary education was informed by 164 (77.0%) participants, and in the current work situation, the number of retirees prevailed, with 167 (78.4%).

Table 1. Socio-demographic data of patients with prostate cancer under treatment at the Hospital do Câncer de Franca. Franca (SP), Brazil, 2016.

Sociodemographic characteristics	N	%
Age		
43 to 49 years old	2	0.9
50 to 59 years old	14	6.6
60 to 69 years old	47	22.1
70 to 79 years old	73	34.3
80 to 89 years old	71	33.3
> 90 years old	6	2.8
Skin color		
White	135	63.4
Brown	45	21.1
Black	33	15.5
Marital status		
Married	166	77.9
Widow	24	11.3
Single	15	7.0
Divorced/Separated	8	3.8
Education		
Illiterate	12	5.6
Incomplete elementary school	14	6.6
Complete elementary school	164	77.0
Incomplete high school	5	2.3
Complete high school	11	5.2
Incomplete higher education	2	0.9
Complete higher education	5	2.3
Occupation		
Retired	167	78.4
On leave	32	15.0
Active	14	6.6
Total	213	100

Regarding family income, mos of the participants reported living with two to three minimum wages or one salary, 125 (58.7%) and 70 (32.9%), respectively. The remaining 18 (8.5%) reported income of four to five minimum wages. Of the total number of participants, 171 (80.3%) had two to three

dependents and 21 (9.9%) had only one. Another 21 (9.9%) reported from three to six dependent people.

Regarding the clinical data, presented in Table 2, it is observed that the diagnoses of the disease were performed between 1999 to 2015. The beginning of treatment of 176

(82.9%) participants occurred within a year after the diagnosis. The most frequent reasons that led to the diagnosis of the disease were altered PSA examination and signs and symptoms of urinary function, with 77 (36.2%) and 62 (29.1%), respectively. Diagnostic tests were performed in most cases by SUS, in special medical outpatient clinics, for 70 (32.9%) participants, and in Basic Health Units, for 55 (25.8%).

By questioning the history of cancer in the family, most of them, 124 (58.2%) said no and did not know. The closest relationship was the first degree, with 55 (25.8%).

The initial clinical staging of the disease followed the American Joint Committee on Cancer (AJCC)⁶ classification and was categorized and grouped by stages (I, IIA, IIB, III, IV), based on the results of initial examinations available in the medical records. It was observed that staging II (A and B) was predominant in 124 (58.2%) participants. It is important to note that 38 (17.8%) and 37 (17.4%) participants were diagnosed at more advanced stages of the disease (III and IV, respectively).

Table 2. Clinical data of patients with prostate cancer being treated at the Hospital do Câncer de Franca. Franca (SP), Brazil, 2016.

Clinical features	N	%
Beginning of treatment after diagnosis		
Up to 1 year	176	82.7
Up to 2 years	14	6.6
Up to 3 years	23	10.8
Initial diagnosis		
AlteredPSA	77	36.2
Change in urinary function	62	29.1
Other exams	47	22.1
Altered PSA and rectal touch	22	10.3
Altered rectal touch	5	2.3
Location of diagnosis		
Medical Specialty Outpatient Clinic	70	32.9
Basic Health Unit	55	25.8
Health center - Health insurance	54	25.4
Other hospitals	34	16.0
Family history		
No or do not know	124	58.2
First degree relative	55	25.8
Relative of second degree	12	5.6
Relative to prostate cancer	11	5.2
Relatives of first and second degree	11	5.2
Clinical Staging		
I	14	6.6
II A	58	27.2
II B	66	31.0
III	38	17.8
IV	37	17.4
Total	213	100

Table 3 shows the results to the open questions related to possible doubts about the disease and the treatment, difficulties and limitations faced, social support received and satisfaction with care. According to the data, 109 (51.2%) participants reported having no doubts and among those who had, 91 (42.7%) questioned the treatment (if it will cure them and its duration). Although 74 (34.7%) reported not having difficulties with the disease, 83 (39.0%) presented difficulties related to the symptoms of urinary function (burning sensation, incontinence, weak urine flow, frequent urination and blood in the urine) and erectile dysfunction. A set of symptoms, such as weakness, heat waves and leg pain, totaled 40 (18.8%) manifestations. The limitations faced focused on the consequences of the disease and treatment on sexual life, with 167 (78.4%), manifested by

the inability to obtain and maintain erection for the sexual act and by the decrease or absence of libido.

Of the total number of participants, 22 (10.3%) reported not receiving social support, although 184 (86.4%) reported receiving it from their relatives, health professionals and volunteers. Finally, the opinion of the majority (96.2%) was satisfactory in the assistance offered by the institution.

Table 3. Data on doubts, difficulties and limitations faced, social support received and satisfaction with the care of patients with prostate cancer under treatment at the Hospital do Câncer de Franca. Franca (SP), Brazil, 2016.

Therapeutic characteristics	N	%
Doubts about disease and treatment		
None	109	51.2
If the treatment will cure it	59	27.7
Duration of treatment	32	15.0
If the sex life will be changed	4	1.9
If after the treatment the sexual activity returns	3	1.4
If you can use sexual stimulant	3	1.4
Changes in urinary function	3	1.4
Difficulties faced		
No	74	34.7
Symptoms of urinary function	46	21.6
Erectile dysfunction	37	17.4
Weakness	17	8.0
Leg pain	12	5.6
Heat waves	11	5.2
Diarrhea	4	1.9
Depression	4	1.9
Fear of dying	3	1.4
Weight gain	3	1.4
Weight loss	2	0.9
Limitations faced		
Sexual function	167	78.4
None	27	12.7
Urinary incontinence	16	7.5
Leaving home	1	0.5
Depression	1	0.5
Pain	1	0.5
Social support received		
Family, professionals and volunteers	129	60.6
Volunteers	55	25.8
Not received	22	10.3
Professionals and volunteers	5	2.3
Professionals and family	2	0.9
Satisfaction with care provided		
Good	205	96.2
Great	6	2.8
Bad	1	0.5
Not answered	1	0.5
Total	213	100

DISCUSSÃO

The age is an important risk factor for prostate cancer since both incidence and mortality increase significantly after 50 years old.⁷ The mean age of study participants was 74.4 years old and 99.1% were older than 50 years old, corroborating with the observation that age was an important risk factor for the sample studied.

Some authors consider that skin color is also a risk factor for the disease, being approximately 1.6 times more common in blacks than whites, a difference that can be attributed to lifestyle or factors associated with disease detection.² In the studied sample, the predominance was with white participants (63.4%). A study carried out in the city of Rio de Janeiro, with 258 men with prostate cancer, 75.2% were white, the

survival in five years was 84.6% and for blacks and brown, 96.1%. Black or brown individuals had a 60% lower risk of dying from prostate cancer than whites for each year of follow-up.⁸

The highest prevalence of married participants (77.9%) was also found in a study conducted in Pelotas-RS, where 78.98% of the participants were married.⁹ The results of a study conducted with 163,697 patients treated with radical prostatectomy in the United States, showed that single, divorced and widowed subjects had a higher rate of locally advanced tumor and mortality compared to married men.¹⁰ Another study, conducted in China with 248 men, married participants demonstrated a greater mastery of physical health in social and In sexual satisfaction, concluding that marital status is an important determinant in the quality of life

of patients with prostate cancer.¹¹

The identification that most participants had complete primary education and retired corroborates with the results of a study conducted in the city of Ribeirão Preto, SP, Brazil, with 2620 men, in which there was a predominance of 54.5% with complete elementary education and 61.6% of retirees.⁵

The socioeconomic situation of the study participants showed that most of them had low income (from one to three minimum wages). This result refers to the considerations contained in the booklet Social Rights of the Person with Cancer: guidelines for patients, INCA¹², which considers that, regardless of the economic situation of the cancer patient, everyone has special rights. The rights include sickness, treatment outside the home, withdrawal from FGTS, PIS/PASEP, disability retirement, social security, retirement income tax exemption, among others. However, these rights are almost always not known to the patients, even considering that they are of great value to alleviate some difficulties, especially the financial ones, that can affect the family budget.

A study carried out to identify the knowledge of cancer patients in their legal rights, identified that sickness and disability pension rights were known to more than half of the interviewees, considering that the lack of knowledge was prevalent in the most of the rights that cover the social area.¹³

Confirmation that most participants only began treatment for the disease within one year after diagnosis or two to three years after can be justified by many factors, including the possible lack of vacancies in specialized hospitals, although the Law N° 12.732/14 establishing the right of the patient to start treatment by the SUS, within a period of up to 60 days from the diagnosis in a pathological report, or in a shorter term, according to the therapeutic need of the case.

A study conducted in Florida with 11,284 men found that for 50% of the population analyzed the average time to start treatment was 47 days after diagnosis and only 10% sought initial treatment soon after diagnosis. It pointed out that African-American men waited longer to start treatment, a fact that may be justified because of the place of residence, because they lived in neighborhoods with precarious health facilities, with less technology and specialized doctors.¹⁵

In this sense, information contained in the Atlas of Cancer¹ considers that with the

increased cost of treatment, as a result of the development of imaging techniques, radiotherapy equipment and high-cost anticancer agents, the availability and reception of treatment have been limited in many parts of the world, aggravating the lack of access to modern diagnostic services, oncological surgery and radiotherapy and chemotherapy equipment. It also considers that the drastic shortage of trained health professionals constitutes a major barrier to access to quality and equal health services for cancer diagnosis and treatment, drawing attention to the need for global scientific approaches and innovation to ensure Greater accessibility of patients to therapies.

The initial diagnosis of the disease for 48.8% of the participants was defined by routine exams, either by alteration in the individual PSA and rectal examination results or by the association of both of them. Also, 29.1% of the participants only sought the medical service with the presence of symptoms and 22.1% by medical indication when other tests were performed. Authors of a review article on prostate cancer have pointed out that patients with the disease in their initial stage, curable, do not develop any signs or symptoms related to the neoplasia. Symptoms will usually appear in locally advanced or metastatic disease. With this, they consider that prevention is the best option for the diagnosis of the disease in the early stages, allowing better results in the treatment of the disease.¹⁶

The National Cancer Institute recommends that in Brazil, as well as in Australia, Canada and the United Kingdom, not performing screening programs for prostate cancer, positioning backed by scientific evidence that point to more risks than screening benefits. Men who spontaneously require screening should be informed by their doctors about the risks and benefits associated with this practice.¹⁷

It is recommended the professional training; organization of care ensuring access to men with signs and symptoms in primary care and secondary care for confirmation of diagnosis; clarification to the population that spontaneously demand PSA and/or rectal examination on the possible benefits and risks and agility in confirming the diagnosis and treatment.¹⁸ The Brazilian Society of Urology also maintains the recommendation that men from 50 years old should look for a specialized professional for individualized evaluation. Blacks or first-degree relatives with prostate cancer should begin at age 45.⁴

The examination for the initial diagnosis of

the disease of the study participants was performed predominantly in the SUS. Law N° 13.04519, in its Article 4-A, obliges the units of the SUS to perform tests for the early detection of prostate cancer whenever this procedure is considered necessary by the doctor. However, the authors consider the need for a broader intervention in the health care of men in the basic network, aiming at the promotion, prevention, cure and rehabilitation of health conditions.²⁰

Although the number of participants (5.2%) with cases of prostate cancer in the family (parents and siblings) was small, a study² shows the fact that the hereditary factor should be considered, since men who had father or brother diagnosed, present a two to three fold increase in the risk of developing neoplasia. This risk increases by approximately 11-fold if the diagnosis occurs in a parent or sibling before 40 years old.

A study of 635,443 men with a history of cancer in the family found that 68% had prostate cancer cases in the family, either in first, second or third degree relatives.²¹ Another study was conducted with 16,472 men, 32.3% of whom were men. Family history of prostate cancer identified that men with this history were more likely to have low-risk disease at the time of diagnosis and less likely to have pathological adverse characteristics at the time of surgery, concluding that these findings may be due to stratification of risk and counseling of the patient and his family to the hereditary factor.²²

The results of the study demonstrated that 58.2% of the participants were initially diagnosed with clinical staging II, ratifying the study results²³ performed with 1,320 men, which found in 70% of the sample, classifying them as early staging. When prostate cancer is diagnosed, the patient is staged, comorbidities are evaluated and treatment options should aim not only at cancer control but also at maintaining quality of life.¹⁶

Treatment options for localized disease may be radical prostatectomy, radiation therapy, and even vigilant observation. For locally advanced disease, radiation therapy or combined surgery with hormonal treatment are indicated. For metastatic, the treatment of choice has been hormone therapy. The most appropriate treatment should be individualized and defined after considering the risks and benefits to the patient.⁷

Based on the question related to the possible doubts of the participants regarding the diagnosis and treatment, it was observed that among the 48.8% who reported doubts, most questioned about the treatment and its

duration, the others about the consequences on sexual function. In a study²⁴ conducted in Belo Horizonte, Minas Gerais, Brazil, with men undergoing oncological treatment, the interviewees' discourse showed that cancer represents a serious, complex, incurable disease associated with death. The moment of diagnosis is an impacting moment, marked by feelings of anguish, fear, sadness and despair. There is the need to leave their work activities and the effects of treatment on sexuality contribute to the sensation of reduction and loss of masculinity.

Of the difficulties faced, 39.0% of the participants reported those related to urinary function and erectile dysfunction. At lower frequencies they reported weakness, leg pains, heat waves, diarrhea, depression, fear of dying, increase and weight loss. Some manifestations support the findings in a study²⁵, conducted with prostate cancer patients undergoing radiotherapy, who exhibited obstructive and irritative urinary symptoms, pain, lack of energy, diarrhea, and changes in sex life.

Regarding the limitations faced, 78.4% reported inability to obtain and maintain erection for the sexual act and decrease or absence of libido. A study of 213 patients²⁶ of whom 143 received an association of two treatments (hormonal therapy and radiotherapy) and 70 with radiotherapy, showed that those who received an association of the two treatments had a greater negative impact on sexual function, weight gain and depression in relation treated with radiotherapy alone. Another study²⁷ of current review on male sexual health after radical prostatectomy or hormone therapy, considered that each treatment modality significantly affects sexual function and that younger patients and patients with nerve sparing surgery present better results.²⁷

When questioned about receiving social support and the quality of care provided, 89.7% of the participants mentioned receiving support from their relatives, health professionals or hospital volunteers, and 96.2% reported satisfaction with the care provided. In a review of the literature on adult cancer illness and repercussion in the family,²⁸ the authors concluded that having a family member with cancer generates positive or negative feelings for both the patient and the family, influencing how the family members organize and function before the process of illness and treatment. Among the positive points were the consolidation of the family relationship, the support of wives, children, relatives and the reconfiguration of intimate

life and sexuality. Negative points related to the denial of the family regarding the acceptance of the disease and the physical, emotional and financial burden.²⁸

Studies conclude that the presence of a disease such as cancer can be a difficult experience, generating fear and insecurity, highlighting the need for social support centered in the family. For this reason, social support needs to be centered also in the family, aiming to improve the difficulties inherent to the disease.²⁹ Support groups for patients with prostate cancer represent a possibility of maintenance and/or creation of a psychosocial support network considered essential for good coping with the disease.³⁰

The patient with prostate cancer, goes through limitations imposed by the disease and by changes in their family, social and themselves. The treatment routine and its consequences cause significant changes in their lives, so when entering health services it is essential that they receive humanized assistance.

CONCLUSÃO

Based on the proposed objective, the results showed that the sample consisted of men in treatment for prostate cancer, predominantly over 50 years old, white, married, retired, with complete primary education and low income. The initial diagnosis was made through alterations in the PSA and/or rectal touch, by the SUS, with staging II. In the report of the difficulties and limitations the manifestations of alterations in the sexual and urinary function stood out.

Given these results, it is worth considering that the study faced some weaknesses regarding the location of medical records and participants, resulting in the loss of some subjects able to participate. The study used a descriptive and transversal research design, hindering the generalizations for other populations with prostate cancer.

In spite of these difficulties, the results helped to define the knowledge of the social characteristics, clinics and opinions of the participants regarding the diagnosis and treatment of prostate cancer, and can contribute to the planning of the care provided, aiming to establish preventive, therapeutic and other actions aimed at better assistance.

It is recommended to carry out new research with larger samples that offer subsidies for the planning, execution and evaluation of the treatments, allowing the identification of the effects of the different

therapeutic modalities, their consequences in the life of the patients and the choice of therapeutic measures less impacting.

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Submission: 2016/04/30

Accepted: 2017/05/08

Publishing: 2017/06/15

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