Analysis of the Time to Initiate Oncological Treatment in Brazil: Demographic and Related-To-The-Tumor Factors

doi: https://doi.org/10.32635/2176-9745.RBC.2022v68n3.2354

Análise do Tempo para Início do Tratamento Oncológico no Brasil: Fatores Demográficos e Relacionados à Neoplasia

Análisis del Tiempo de Inicio del Tratamiento Oncológico en Brasil: Factores Demográficos y Relacionados con la Neoplasia

Glebson Santos Sobral; Yuri Barbosa Araújo; Simone Yuriko Kameo; Glebson Moura Silva; Dayane Ketlyn da Cunha Santos; Lêda Leonór Mendonça Carvalho

ABSTRACT

Introduction: According to the 60 Days Law, all Brazilians with cancer are entitled to start treatment within two months. However, previous studies point to the difficulty of patients in enforcing this regulation, by running into macro-structural problems in health systems. Objective: To assess the influence of demographic and cancer-related factors on the time elapsed to start cancer treatment in Brazil. Method: Cross-sectional study developed with data from PAINEL-Oncologia, a national public database, fed by different sources of information from the Sistema Único de Saúde [Brazilian public health system]. The following variables of interest were chosen: a) time of treatment; b) sex; c) age; d) diagnosis; e) staging; f) therapeutic modality. Then, the time elapsed between diagnosis and the start of cancer treatment was analyzed. Results: There was an exponential increase over the years in the proportion of cases treated in a timely manner, that is, within 60 days, as mandated by the Law. However, the prevalence of delays to start treatment is still considerable, especially among elderly, males, with cancers in less advanced stages and who needed radiotherapy as their first therapeutic modality. In addition, the waiting time was especially longer for male genitalia, head and neck, and breast cancers. Conclusion: Some demographic and neoplasia-related factors are involved in late beginning of oncological therapy.

Key words: neoplasms/epidemiology; time-to-treatment; epidemiologic measurements.

RESUMO

Introdução: É reservado a todo brasileiro com câncer, pela Lei dos 60 Dias, o direito de começar o tratamento em até dois meses. Todavia, estudos anteriores apontam a dificuldade dos pacientes em fazer valer essa normativa ao esbarrarem em problemáticas macroestruturais dos sistemas de saúde. Objetivo: Avaliar a influência de fatores demográficos e relacionados à neoplasia sobre o tempo para início do tratamento oncológico no Brasil. Método: Estudo seccional, desenvolvido com dados oriundos do PAINEL-Oncologia, uma base pública nacional, alimentada por diversas fontes de informação do Sistema Único de Saúde. Como variáveis de interesse, foram selecionadas: a) tempo de tratamento; b) sexo; c) idade; d) diagnóstico; e) estadiamento; f) modalidade terapêutica. Então, foi analisado o tempo transcorrido entre o diagnóstico e o início do tratamento oncológico. Resultados: Houve um aumento exponencial ao longo dos anos, da proporção de casos tratados oportunamente, isto é, em até 60 dias, como regulamenta a Lei. Entretanto, ainda há um considerável a prevalência de atrasos no início do tratamento, sobretudo entre indivíduos idosos, do sexo masculino, com cânceres em estádios menos avançados e que precisaram de radioterapia como primeira modalidade terapêutica. Além disso, o tempo de espera foi especialmente maior para os cânceres de órgãos genitais masculinos, de cabeça e pescoço e de mama. Conclusão: Alguns fatores demográficos e relacionados à neoplasia estão envolvidos no atraso do início da terapia oncológica.

Palavras-chave: neoplasias/epidemiologia; tempo para o tratamento; medidas em epidemiologia.
INTRODUCTION

Cancer is recognized as a preventable chronic disease\(^1\). Worldwide it is the second major cause of death second only to cardiovascular diseases\(^2\). For each year of the triennium 2020-2022, 625,000 new cases are estimated for Brazil, the most incident is non-melanoma skin cancer (177 thousand), followed by breast neoplasms (66 thousand), prostate (66 thousand), colon and rectum (41 thousand), lung (30 thousand) and stomach (21 thousand)\(^3\).

Although the developed countries account for more than half of the cases globally, they represent only 30% of deaths and 23% of potential years of life lost\(^2\). An epidemiological investigation conducted in Malaysia revealed that 50% to 88% of the deaths by breast cancer would be avoidable had they been diagnosed earlier with best access possible to treatment\(^4\). The most outstanding disparities occur in developing countries and favor worst outcomes in these settings.

Law number 12,732 dated November 22, 2012\(^5\) ensures all Brazilians with confirmed diagnosis of cancer the right to initiate treatment in until 60 days. Later, other legal dispositions complemented the so-called 60-days Law as it is known nowadays in addition to 30 days for proven diagnosis and obligation to report cancer cases across the national territory\(^6,7\).

Nevertheless, several studies developed in different country regions reveal that the time between the diagnosis and beginning of the treatment exceeds largely what the 60-days Law determined. Between 2012 and 2014, at the Federal District, women with breast cancer needed to wait in average 211.8 days to begin the therapy\(^8\). In Amazonas in 2016, the median of waiting time was 111 days for several groups of neoplasms\(^9\). According to recent integrative literature review, most of the patients are unable to begin the treatment before three months\(^10\).

Sacramento et al.\(^11\), while studying cases of prostate cancer consulted at a reference hospital in Espírito Santo, before and after the approval of this Law\(^5\), found no impact over the time between the diagnosis and beginning of the treatment.

Some sociodemographic factors are associated with the delay of beginning the treatment and appear to repeat for several types of cancer, reflecting problematics of health systems macrostructure. Black individuals with low socioeconomic and educational level living in non-metropolitan areas and health-uninsured tend to delay more to be diagnosed and initiate the treatment of several neoplasms\(^12-15\).

National-based studies are still scarce because there was no tool to facilitate this analysis in the past. To meet this demand, it was created “PAINEL-Oncologia”\(^16\) in May 2019 which replaced the former “module treatment”, connected to the Cancer Information System (Siscan) and gathers neoplasms cases of the entire country in a single base.

This information are originated from the Health Information Systems (SIS) adopted by the National Health System (SUS) and do not address cancer incidence in the country as a whole. “PAINEL-Oncologia” is an important management tool, allowing the expressive increase of cases captured and quality of the information in addition to gathering and reconciling conflicting and complementary data in a single system\(^17\).

This study aims to analyze the influence of demographic factors and related to the neoplasm over the time between the diagnosis until the beginning of the oncologic treatment.

METHOD

Some of the factors delaying the beginning of oncologic treatment in Brazil were tentatively identified through a sectional study with data from “PAINEL-Oncologia”, a public database with different SIS/SUS information that allows to detect the interval between the diagnosis date and the first cancer treatment\(^17\). These data are but a portion of the cases in the country, exclusively available from different SIS.

The definition of the case according to “PAINEL-Oncologia” is based on the combination of the National Health Card (CNS) with the International Classification of Diseases and Related Health Problems (ICD-10)\(^18\) reported, the same CNS with more than one ICD represents different cases\(^17\). All the data are referenced to February 2021 and initially tabulated in duplicate by two different investigators in the statistical package Epi Info 2000 of the Centers for Disease Control and Prevention which analyses the consistency. Cases with diagnosis information for the period 2013-2020 were gathered for all the Brazilian regions, the object of the study.

The following variables of interest were selected: a) time to the treatment; b) sex – male and female; c) age; d) diagnosis; e) therapeutic modality – surgery, chemotherapy, radiotherapy and both (chemo and radiotherapy); f) staging – 0, I, II, III, IV and “does not apply” for surgical cases given the nature of the database feeding “PAINEL-Oncologia”\(^17\). Later, the variable “time to the treatment” was subdivided to meet the goals of this study and compliance with the Law number 12,732/12\(^5\) – ≤ 60 days (timely) and > 60 days (off-time). In addition, the variable “diagnosis” which refers to the neoplasm reported at the anatomopathological exam (ICD-10: C00-D48) was categorized in: “malignant neoplasms”
Analysis of the Time to Initiate Oncological Treatment

(C00-C97, except C44 and C73, cited by the Law – other malignant neoplasms of the skin and malignant neoplasm of the thyroid gland, respectively); “neoplasms in situ” (D00-D09) and “neoplasms of uncertain or unknown behavior” (D37-D48)\(^{19}\).

The exclusion criteria were cases without information about the time to treatment, cases with time to treatment prior to diagnosis (negative time) and lack of information about variables of exposure.

Time series charts were prepared to evaluate the shift of the distribution of cases treated timely for the malignant neoplasms as they account for near all the cases included in the analysis and because other neoplasms (D00-D09 and D37-D48) had higher percentages of timely treatment during the entire period analyzed.

Subsequently, a descriptive analysis of the data through the distribution of the variables of the study population was carried out. Being categorical variables, proportions were calculated, and Pearson’s chi-square test was utilized to compare the groups. As the odds ratio (OR) may overestimate or underestimate the power of the association when the outcome analyzed is common, the prevalence ratio (PR) must be preferred in these situations\(^{20,21}\). Francisco et al.\(^{22}\) have also affirmed that PR appears to be more appropriate to analyze subgroups than OR.

Based in the study design, crude PR were estimated with their respective confidence intervals of 95% (CI\(_{95}\%\)) and considered statistically significant with \(p<0.05\) by the test \(\chi^2\) of Wald. All the analyzes were processed with the software Statistical Package for Social Sciences (SPSS), version 20.0.

Because only secondary public data were utilized, the study was not submitted for review by the Institutional Review Board, but it complied with Resolution. 466/2012\(^{23}\) of the National Health Council. The data are deidentified addressing Collective Health information only.

**RESULTS**

Of the total 1,921,267 cases extracted from “PAINEL-OncoLOGIA”\(^{16}\), 776,117 were excluded according to the motives presented in Figure 1 and 1,118,640 (96.8%) of the remaining cases were diagnoses ruled by Law 12,732/12\(^{12}\).

Until 2017, the proportional distribution of cases treated in until 60 days remained nearly stable and lower than untreated in the same period. Henceforward, this relation became gradually favorable, 3.85 times greater for timely against off-time treatment in 2020 (Graph 1).

The absolute drop of cases from PAINEL-OncoLOGIA\(^{16}\) for the biennium 2019-2020 suggests that the cases of the last year may not be consolidated yet at the database (Graph 2).

As shown in Table 1 with all the types of neoplasms (n=1,155,150), it was noticed lower prevalence of malignant neoplasms initiated timely against other neoplasms: neoplasms \textit{in situ} and neoplasms of uncertain or unknown behavior. For the population of interest – only malignant neoplasms – it was found a negative association between males and timely oncologic treatment.

Adults and mainly older adults had lower PR of timely beginning compared with younger population.

Higher prevalence of timely first treatment was found for referrals to surgery compared to chemotherapy. In counterpart, lower prevalence of timely treatment were detected for chemotherapy associated with radiotherapy and mainly radiotherapy alone.
Timely treatment was negatively associated with initial stages and the grade of association tends to be positive at later stages.

Since Law 12,732/12 entered into force and time-series were initiated, the biennia gradually presented more positive associations, particularly the most recent, 2019-2020.

For the types of malignant neoplasms analyzed by groups according to ICD-10 it was found negative association between timely treatment and the following malignant neoplasms: C60-C63, male genital organs; C00-C14, lip, oral cavity and pharynx; C50, breast and C51-C58, female genital organs. In counterpart, for another malignant neoplasms, positive association with timely treatment was detected.

**DISCUSSION**

Most likely, the expressive growth of cases since 2018 results from Directive 643 of the same year which determined that the anatomopathological procedures register should contain fields for CNS and ICD-10. Because of the legal pressure to monitor the time to treatment, there was an important advance of diagnostic information available at the databank in comparison with the former period since only breast and cervical cancers had SISCAN’s mandatory fields. Despite continuous efforts, much information before 2018 were unable to retrieve.

The excision of small and superficial masses of soft tissues especially those with less than 5 cm of diameter is common in unspecialized clinics due to the presumption of non-malignity of these injuries. Later, the diagnosis is determined with anatomopathological exam and these cases are registered at “PAINEL-Oncologia” within the time interval from 0 to 30 days with surgery as excision modality of the first treatment. This can partially explain why non-malignant neoplasms had more odds of receiving timely treatment.

In line with the 60-days Law and by extension with the objective of this article the findings discussed below address only malignant neoplasms.

**Table 1. Variables related to the patients treatment with malignant neoplasm. PAINEL-Oncologia, 2013-2020, Brasil**

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>Prevalence of timely treatments (%)</th>
<th>PR (CI95%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis (n=1,155,150)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other neoplasms³²</td>
<td>36,510 (3.2%)</td>
<td>99.0%</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td>1,118,640 (96.8%)</td>
<td>52.9%</td>
<td>0.535 (0.533-0.536)</td>
<td></td>
</tr>
<tr>
<td><strong>Year of diagnosis (n=1,118,640)⁴⁵</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013-2014</td>
<td>257,010 (23.0%)</td>
<td>43.6%</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>2015-2016</td>
<td>263,372 (23.5%)</td>
<td>43.9%</td>
<td>1.007 (1.002-1.012)</td>
<td></td>
</tr>
<tr>
<td>2017-2018</td>
<td>305,266 (27.3%)</td>
<td>52.8%</td>
<td>1.212 (1.205-1.219)</td>
<td></td>
</tr>
<tr>
<td>2019-2020</td>
<td>292,992 (26.2%)</td>
<td>69.2%</td>
<td>1.587 (1.579-1.595)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex (n=1,118,640)⁴⁵</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>584,130 (52.2%)</td>
<td>56.1%</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>534,510 (47.8%)</td>
<td>52.4%</td>
<td>0.934 (0.931-0.937)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (n=1,118,640)⁴⁵</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20 years</td>
<td>20,025 (1.8%)</td>
<td>84.0%</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>20-59 years</td>
<td>503,861 (45.0%)</td>
<td>57.7%</td>
<td>0.687 (0.683-0.691)</td>
<td></td>
</tr>
<tr>
<td>≥ 60 years</td>
<td>594,754 (53.2%)</td>
<td>50.8%</td>
<td>0.605 (0.601-0.609)</td>
<td></td>
</tr>
<tr>
<td><strong>First therapeutic modality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=1,118,640)⁴⁵</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>616,084 (55.1%)</td>
<td>49.3%</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>223,745 (20.0%)</td>
<td>30.8%</td>
<td>0.625 (0.620-0.629)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy + radiotherapy</td>
<td>14,083 (1.3%)</td>
<td>37.8%</td>
<td>0.768 (0.752-0.785)</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>264,728 (23.7%)</td>
<td>80.8%</td>
<td>1.640 (1.635-1.646)</td>
<td></td>
</tr>
</tbody>
</table>
Timely treatment was more prevalent in females as the results of the present study have concluded. Although corroborated by former studies, tim differences between genders are greater prior to the diagnosis, males tend to neglect the symptoms and postpone seeking medical help because of an alleged model of masculinity where men would be more resilient to diseases and less self-caring.

Patients older than 60 years of age have lowest prevalence of timely treatment, partially because of older adults diminished perception of the severity of their health conditions and fear of cancer diagnosis. In addition, comorbidities are more frequent in this population requiring a careful and long evaluation before oncologic therapy. As mentioned earlier, other sociodemographics are involved in the delay of beginning the treatment.
as Black race, lower educational and socioeconomic level, uninsured health care and non-metropolitan areas residence11-15. As PAINEL-Oncologia does not offer these variables, the analysis was waived in this study.

Independent multiple locations and staging IV tumors were less likely of receiving timely treatment. Because the health system is unable to absorb all the patients, most advanced and symptomatic neoplasms are prioritized to begin timely treatment43. Hypothetically, the system overload, a characteristic of Latin American countries can be lessened with well-planned early diagnosis and screening programs which reduce mortality while allow early detection of initial stages tumors15,32.

It was found that the surgery as modality of first treatment had more odds of occurring timely, because of better access to this type of therapy as some general hospitals are able to offer oncologic surgeries with less waiting time in comparison with high complexity centers1,15,33. Some diagnoses are confirmed later than the first intervention because specimens are collected during surgery followed by anatomopathological test to confirm the malignancy2,6,17 which most likely contributes to this finding.

On the other hand, radiotherapy either associated with chemotherapy or alone was the less prevalent modality of timely treatments. These therapies rely on referrals to reference centers which usually have to deal with large volume of consultations and procedures causing delays in the beginning of the treatment15,33.

Neoplasms of male genital organs had the worst performance of time between diagnosis and beginning of the treatment, influenced by heterogeneity of conducts for prostate cancer. In view of the natural history usually indolent, extensive literature advocates active surveillance with monitoring of low-risk prostate tumors with periodical evaluation for potential definitive treatment16-36. Thus, the time to begin treatment may be prolonged in many cases although it does not necessarily mean worsening of patients’ survival37. Furthermore, specifically for this group of neoplasms, the pre-treatment apprehension should be a matter of attention for fearing painful therapies and possible changes of body image. Individually, it may also delay the treatment28,38.

The second group with more time to begin the treatment as the present study concluded was head and neck cancers, consistent with former epidemiological analyzes which found mean waiting time of 12 weeks, regardless of the therapeutic modality adopted39. Because of difficult location and advanced stage usually found in these types of tumor it is advisable that the treatment is decided as early as possible but not compromising the quality of the care40. However, the aspects related to the quality of the care are precisely the main factors of delay of beginning the treatment of head and neck cancer. Ordering and analysis of additional diagnosis, increase of interdisciplinary referrals, expansion of therapeutic options and refinement of techniques utilized, demanding skilled teams are hurdles that damage the timely beginning of the treatment notwithstanding the advances achieved39,41-43.

Finally, breast cancer stands out since the absolute number of untreated cases before 60-days overcomes the first two groups of neoplasms referenced above. As it happens with head and neck cancers, more complexes procedures as needed require thorough preoperative appraisal and coordination of different teams as mastologist, plastic surgeon and nuclear medicine43,44. Typically, genetic tests are run for breast cancer as predictive and prognostic tool to evaluate the benefits of chemotherapy because of possible recurrence45. Depending on the histopathological type found, more sensitive imaging and secondary lesions biopsies are required to guide the surgical plan46, which impact the global time since diagnosis up to the beginning of the treatment.

Still, a study conducted at a reference institution of the State of Espírito Santo found time of timely treatment for women diagnosed with breast cancer with a median of 44 days until the first therapy, further to important increase of the number of patients who initiated the treatment in until 60 days47. Actually, there are Brazilian health services which are managing to meet the deadlines of Law number 12,732/12, although not the majority as the literature showed.

The study’s limitations are data loss by SIS/SUS which are interconnected and cause impact on the databases these systems provide information to as PAINEL-Oncologia17. The lack of publications based on PAINEL-Oncologia hampers the comparison of results even if the current findings are consistent with the literature’s epidemiology. However, the high heterogeneity of the population investigated is positive which allows good comparability with populations with similar profile of Brazil’s.

Because of high frequency of statistically significant associations with narrow CI48, even when PR between exposure and outcomes were weak because of the robust casuistry, it was decided to not use the adjusted analysis by Poisson regression with strong variance since all the variables would be included in the analysis and would remain in the final model as a bias.

CONCLUSION

It was found an exponential increase throughout the years of the proportion of cases treated timely in until 60
Analysis of the Time to Initiate Oncological Treatment

Analysis of the Time to Initiate Oncological Treatment

Analysis of the Time to Initiate Oncological Treatment

Analysis of the Time to Initiate Oncological Treatment

Analysis of the Time to Initiate Oncological Treatment

days as determined by Law number 12,732/12 after the analysis of the time between the diagnosis and beginning of oncological treatment in Brazil. It is still considerable the prevalence of delays to begin the treatment mostly for older male adults with less advanced cancers. It was also detected lower prevalence of timely treatment of patients who needed radiotherapy as first therapeutic modality. In addition, male genital organs, head and neck and breast cancers were more associated with delays to begin oncologic treatment.

Because of the continuous monitoring of time from the diagnosis and first treatment, it is probable that the utilization of PAINEL-Oncologia stimulates the qualification of data from SIS/SUS that feed it resulting in steady improvement of the information for the tool itself. The managers could rely on the present analysis to guide health policies to ameliorate the reality of oncologic treatment and reduce waiting time.

CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

ACKNOWLEDGMENTS

To “Coordenação de Pesquisa (Copes)” of UFS for the approval of the Project of Scientific Initiation which is the baseline of the present article.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

None.

REFERENCES


Analysis of the Time to Initiate Oncological Treatment


33. Ministério da Saúde (BR), Secretaria de Atenção Especializada à Saúde. Portaria nº 1.399, de 17 de dezembro de 2019. Redefine os critérios e parâmetros referenciais para a habilitação de estabelecimentos de saúde na alta complexidade em oncologia no âmbito do SUS [Internet]. Diário Oficial da União, Brasília, DF. 2018 dez 19 [acesso 2021 ago 20];Seção 1:173. Disponível em: https://www.in.gov.br/web/dou/-/portaria-n-1.399-de-17-de-dezembro-de-2019-23438206


38. Moraes V. Análise de fatores que levaram ao encaminhamento tardio em casos novos de câncer de próstata recebidos no Hospital Amaral Carvalho nos anos de 2015 e 2016 [dissertação na Internet]. Botucatu (SP): Universidade Estadual Paulista; 2018 [acesso 2021 nov 12]. Disponível em: http://hdl.handle.net/11449/154516


43. Hanna TP, King WD, Thibodeau S, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020;371:m4087. doi: https://doi.org/10.1136/bmj.m4087


47. Simião LJ. Estudo dos tempos entre o diagnóstico e tratamento do câncer de mama em uma instituição de referência no Espírito Santo [dissertação na Internet]. Vitória (ES): Universidade Federal do Espírito Santo; 2016 [acesso 2020 dez 30]. Disponível em: http://repositorio.ufes.br/handle/10/10100

Associate-Editor: Jeane Tomazelli. Orcid iD: https://orcid.org/0000-0002-2472-3444
Scientific-Editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777

Revista Brasileira de Cancerologia 2022;68(3): e-122354