

Retrospective Analysis of Treatment Delay in Breast Cancer Radiotherapy

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Purpose: Breast cancer and the importance of early detection goes hand in hand, therefore one would assume similar emphasis to be placed on early treatment. Waiting lists for radiotherapy are a fact of life for many government hospitals in South Africa. The purpose of this study is to provide a detailed description of the magnitude of the problem at tertiary hospital in the Western Province [1].

Methods and Materials: The interval between surgery and start of radiotherapy for all female patients with diagnosed breast carcinoma (Stage I-IIIb) receiving post-operative radiotherapy was calculated. The data collected was exclusive to a specific tertiary hospital in the Western Province; the data was limited to 2013 and 2014. Separate bar graphs were made of 2013 and 2014 to display the variation between the current standard waiting period and the norm based on international guidelines.

Results: Median waiting periods for breast cancer patients from surgery to start of radiotherapy for 2013 and 2014 were 80 days and 68 days respectively. The recommended waiting period from surgery to start of radiotherapy is stated as 28 days according to the Joint Counsel for Clinical Oncology and 33 days by the National Cancer Plan, resulting in a median of 30.5 days. The median waiting period for 2013 and 2014 differs 55.14% and 61.87% from the standard. An increase of 17.6% in the median waiting period from 2013 to 2014 is observed, it is speculated that this increase is due to lack of resources and infrastructure [5,7].

Conclusion: The Joint Counsel for Clinical Oncology and the National Cancer Plan recommend that the interval from surgery to start of radiotherapy treatment should not exceed 28 - 33 days [5,7]. Although the majority of countries worldwide struggle to meet the recommended standards of waiting periods, South Africa (especially tertiary hospitals in the Western Province) has a significant deviation from the norm. If the standard waiting period cannot be achieved it is recommended that the waiting periods for radiotherapy be kept As Short As Reasonably Achievable (ASARA) [6].

Keywords: Retrospective Analysis; Breast Cancer Radiotherapy

Introduction

We live in times where great expectations are placed on the quality of care for patients with cancer. In first world countries it is often assumed that available treatments are timelessly implemented after diagnosis because of the abundant offer of diagnostic technology. However, delays in treatment onset have an adverse effect on patients [1].

In the Western world, as well as Northern Africa, breast cancer is the most common cancer among woman. Several international studies support the significance regarding cancer growth during the waiting period from diagnosis to start of radiotherapy, the waiting period should specifically be kept to a minimum [2].

In relation to breast cancer patients, extended waiting periods are one of the leading reasons for poorer therapeutic outcome. Treatment delay for patients being treated with radical intent should be kept to a minimum to avoid losing the advantage of adjuvant therapy. An exponential loss in adjuvant treatment advantage occurs when the period from surgery to adjuvant therapy is delayed by 3 months or more [2,3].

Over the last 20 years extended waiting lists for radiotherapy have become common in public funded health systems internationally. The principle cause for this is an imbalance between supply and demand of radiotherapy treatment [4]. An increase of breast

cancer awareness programs and the importance of early detection sparked a growing interest among women to go for regular check-ups and be attentive of the advantages of early detection [1].

This caused a ripple effect which resulted in an increased number of diagnosis of breast cancer which lead to extended waiting lists for patients in first world countries [3,4]. However in the developing world scenario a lack of resources are more commonly identified as the causes for delays [2].

Treatment delay has direct effect on the well-being of individuals, and the waiting lists for radiotherapy effect patients indirectly which may adversely affect the quality of care of cancer patients (Table 1). This article will primarily focus on the direct effects associated with treatment delay [4].

Direct effects of waiting lists for radiotherapy
Decreased effectiveness of curative radiotherapy (stochastic effects):
1) Decreased probability of local control
2) Increased probability of spread beyond the irradiated field
3) Decreased chance of cure because of 1 and 2
4) Increased chance of treatment complications
Decreased quality of life while waiting for treatment (non-stochastic effects):
1) Persistence or worsening of symptoms
2) Psychological distress
Indirect effects of waiting lists
Altered patterns of referral:
1) Adoption of inferior alternatives because radiotherapy is not readily available
2) Referral to distant locations
Altered patterns of practice of radiation oncology:
1) Decreased technical quality of radiotherapy
2) Narrowing scope of radiation oncology to technical practice
3) Decline in academic activity

Table 1: The effects of waiting lists for radiotherapy [4].

Treatment delay may affect the expected outcome of radiotherapy by allowing proliferation of clonogenic cells within the radiation field, thus leading to a decrease in the probability of local control. Radiobiological principles suggest that limiting waiting times for radiotherapy may have a clinically significant effect on local control. Local control of the tumour depends on eradication of every clonogenic cell and because of the nature of cell killing; the number of cells surviving a course of radiotherapy is directed by Poisson statistics [5]. Therefore the probability of achieving local control is inversely related to the number of clonogenic cells the tumour contains. Evidence supports that a relatively small increase in cell number may have a large effect on the probability of local tumour control [6].

Delay may also affect the outcome of radiotherapy by permitting spread of the cancer beyond the treatment volume. The cumulative probability that the tumour has acquired a metastatic clone increases as over time [6]. The risk of first metastasis while waiting for radiotherapy treatment may be relatively small because waiting times are short compared to the lifespan of the tumour prior to diagnosis, but the consequences of metastasis is weighted to the point that the risk cannot be ignored [5].

In 1993 the Joint Counsel for Clinical Oncology (JCCO) defined targets for waiting period in radiotherapy. Patients were defined in 1 of 4 categories: urgent cases, radical radiotherapy, palliative treatment and a specific sub-group for woman receiving adjuvant radiotherapy following surgery. Table 2 defines the standard for good practice and a maximum acceptable waiting time for the different categories [7].

Patient group	Waiting times for radiotherapy	
	Good practice	Maximum acceptable delay
A) Urgent	24 hours	2 days
B) Radical	14 days	28 days
C) Palliative	2 days	14 days
D) Post-operative	-	Within 28 days of surgery if radiotherapy is the only additional treatment

Table 2: A summary of the 1993 standards on waiting period according to the JCCO [7].

In 2005 the National Cancer Plan was concerned that the waiting times as set out by the JCCO in 1993 was not being adhered to. The Royal College of Radiologists funded a national re-audit in 2005; it revealed that in spite of the external funding used to reduce the waiting period, there was a persisting shortfall in provision [8]. This survey showed a 16% increase in the number of patients receiving radiotherapy between 1997 and 2002, indicating that treatment had become more complex [7]. There is some evidence that the known increase in cancer incidence in an ageing population and changes in disease management are also leading to increased demand [4].

The National Cancer Plan has been concerned about reducing waiting times internationally in the hope that, by 2008, the interval from diagnosis to treatment should not exceed 1 month. By 2012, there should only be 1 month from the general practitioner referral to treatment. Unfortunately in 2015 this has not been accomplished and according to a report of EUROCHIP-pilot where a study was conducted in various countries internationally, the average waiting period ranges from 54 - 80 days [7,8]. Delay of cancer treatment can be calculated as the difference between "date of first visit to general practitioner" and "date of first treatment". EUROCHIP- pilot concluded their own an average acceptable waiting period of 28 - 33 days, taking into account the ageing population and the increased complexity of radiotherapy plans [4,9,10].

Methods

A retrospective study will be done in a quantitative manner consisting of primary data from a tertiary Hospital in the Western Cape. Tygerberg Hospital was selected for this study as a government funded hospital have more contributing factors towards a longer waiting period than private practices [9].

All female patients with breast cancer (Stage I-IIIb) seen at the Tygerberg Hospital Department of Oncology, 2013 and 2014 were identified thus no sampling method is used. In total 270 patients and 281 patients were seen in 2013 and 2014 respectively. These patients were identified after a pathological confirmation of infiltrating breast cancer. Patients were only included in this study if they were older than 18 years and treated with radical intent, by means of surgery and radiotherapy.

If the patient meets the selection criteria the waiting period from surgery to start of radiotherapy treatment is counted and the total, written in days, recorded. Patient data is anonymized by allocating a code to replace each patient's information. Retrospective data is used and the information gathered is captured and organised on an excel spreadsheet. The tendencies regarding treatment delay will be evaluated based on international guidelines, the UICC (Union for International Cancer Control) as well as the EUROCHIP, European Cancer Health Indicator Project [7-9].

The number of patients for each month as well as their date of surgery and starting date of radiotherapy treatment is collected, a median waiting period is then calculated as representative for 2013 and 2014. The involvement of patient data is justified in order to conclude whether the treatment delay of a specific tertiary hospital in the Western Cape Province aligns with evidence based guidelines of international acceptable standards. A comparison is made between the median waiting period for the respective years, 2013 and 2014, and a median value of international standards on waiting periods. The results are displayed on a bar graph.

Results

A total of 551 patients were used in this study, 270 patients and 281 patients were seen in 2013 and 2014 respectively. Table 3 illustrates a comparison of waiting times between 2013 and 2014 for each of the categories of treatment intent (radical, palliative, adjuvant or postoperative). For the purpose of this study, patients who experienced an elective delay (because of patient preference or previous initial planned chemotherapy) are excluded from the analysis, as are male patients since the breast carcinoma is a rare occurrence among men [4,7-10].

The median waiting period for 2013 and 2014 are represented in figure 1 where a visual comparison can be made on the graph alongside the median value of international waiting period standard. The waiting period is presented in days, measured from the date of surgery and starting date of radiotherapy treatment. The median waiting period for 2013 and 2014 differs 55.14% and 61.87% from the international waiting period median. For radical treatments, a 17.6% increase in the median waiting period value between 2013 and 2014 was noted. The number of patients used in this study increased by 4%, although there was an increase in

	2013	2014
Radical	151	113
Palliative	11	16
Post-operative	119	168
Total	281	297

Table 3: Analysis of waiting list status with treatment intent for 2013 and 2014 at Tygerberg Hospital.

Figure 1: A comparison between the median international waiting period and the median waiting period of Tygerberg Hospital in 2013 and 2014.

the number of palliative patients from 2013 to 2014. This indicates that, although all waiting periods for patients treated with radical intent exceeds the standard waiting period, patients requiring palliative treatments are prioritised within a shorter time frame as recommended in the JCCO document [7-9].

Discussion

A national re-audit of radiotherapy waiting times was carried out in Great Britain in 2003. An exploratory hypothesis was set up to establish the reasons for increasing delays in treatment, and these are discussed below. We know that new equipment does not always make it possible to shorten individual treatment times [1,3]. The 2003 report Equipment, workload and staffing for radiotherapy showed an increase in exposures per course of treatment from 27.5 in 1997 to 31.95 in 2002. This reflects the increased complexity leading to improved accuracy and quality that has become possible with newer machines [6]. There may be an increase

in the time taken to treat each patient and reduction in the total number who can be treated in a given time. There may, however, be improved outcomes for patients that do receive treatment. Studies showed no obvious correlation between staffing levels, equipment provision and waiting times [9].

A study published in 2013 revealed that treatment delays up to 16 weeks (112 days) have no negative impact on the loco regional outcome. In comparison with other studies it was trivial as this study consisted of a small cohort, 48 patients. This study consisted of retrospective data and ran over a 10 year period [11].

Studies done on a larger scale reported conflicting outcomes on the spectrum form. Results varied from improvement in the therapeutic outcome with therapy less than 4 weeks after surgery to no difference in outcome when radiotherapy was delayed up to 6 months [12-14].

In a systemic review representing Level 1 evidence reported a relative risk of local failure of 1.16% for curative intent adjuvant breast radiation therapy. Although no impact on distant metastatic or overall survival was demonstrated. This translated into a linearly increasing risk of local recurrence associating to 1.0% per month delay for breast cancer [4].

Possibly the study with the greatest statistical significance is the breast conservation study reported by Punglia and colleagues in 2008. This study involved approximately 18,000 patients with Stage I-II breast cancer, treated from 1991 to 2002. A strong correlation between treatment delays with the risk of local recurrence with delays greater than 6 weeks from surgery was reported [15]. Additional factors that correlated with loco regional failure were age < 40 years, positive nodal status, high tumour grade and negative hormonal receptor status [3].

The extent of the data for this study could not be independently checked, but as treatments are documented automatically as they are given, potential for error and bias is very unlikely [3]. For radical and adjuvant treatments, there has been a modest increase in waiting times, from 2013 to 2014, over the already long treatment delay. The percentage of patients that are failing to be treated within the JCCO targets increased from 2013 to 2014 [7,8].

Waiting period in this study was recorded from surgery to start of radiotherapy treatment. Many patients will already have experienced delays in treatment before this time, and these results will therefore be an under-estimate of total waiting times. This treatment delay problem has become much more evident when the new National Cancer Plan targets come into force in 2005, and the target waiting period from diagnosis to treatment is 1 month [16].

Several studies support that the 1 month waiting period from diagnosis to treatment implemented by the National Cancer Plan is impracticable [16]. Numerous European countries such as Netherlands, France, Germany and the UK as well as the United States and Canada still lag behind suggested waiting period. In comparison with the waiting periods of these first world countries, South Africa's (including the tertiary hospital in the Western Cape) treatment delay can be seen as acceptable [5,6,9].

Conclusion

The main finding of this study is that the treatment delay that is currently experienced at Tygerberg Hospital is far from the international waiting period standard. It has been identified that an extended treatment waiting period is associated with an increase in the risk of local recurrence [3]. This association has been shown to be statistically significant in breast cancer and in head and neck cancer. In contrast, studies found no significant association between delay in radiotherapy and the risk of distant metastasis in any site [3,5].

Although the waiting period is similar to other practices worldwide, this delay is still significant when compared to international waiting period standards. This treatment delay may have a detrimental effect on the overall value of a radiotherapy program because it potentially affects every patient in need of radiotherapy. Unfortunately, one of the sad ironies of modern radiotherapy, in some publicly funded health systems, is that the negative effects of the prevailing delays in radiotherapy are probably sufficient to cancel out the positive effects of the many advances in radiotherapy over the last twenty years [6,9,16].

How long, then, is it reasonable for patients to wait for radiotherapy? Given that there is no theoretical reason to believe that there is a threshold below which delay is safe, studies believe that it is prudent to apply the principle that delays in radiotherapy should be As Short As Reasonably Achievable (ASARA), modelled on the ALARA principle which guides risk management in the field of radiation protection [4,9,11].

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