

Delays in breast cancer: Do they matter?



'...all women have the right to access to healthcare, but considerable challenges exist in implementing breast healthcare programmes when resources are limited.'^[1]

Breast cancer constitutes a significant burden of disease in South Africa. The latest available statistics of the National Cancer Registry published in 2009 reveal that breast cancer is the leading cause of cancer in South African women and accounts for 20.82% of all female cancers. The lifetime risk of developing breast cancer for all South African females is 1 in 33. The risk varies between the various racial groups and is 1:11 for white, 1:22 for coloured, 1:17 for Asian and 1:36 for black women.^[2]

In 2012, breast cancer resulted in 522 000 deaths worldwide. The majority of these deaths occurred in less developed regions (324 000), where breast cancer is the most frequent cause of cancer death in women.^[3] Reasons cited for this higher mortality include advanced stage at presentation and delays in treatment attributable to lack of public awareness, absence of organised breast cancer screening programmes, and lack of accessible and effective treatment for breast cancer.^[4]

Since primary prevention of breast cancer is still unavailable, breast cancer control efforts are currently directed at promoting early detection. Early detection has many benefits including decreased morbidity and mortality. Longer waiting times prior to the diagnosis of breast cancer and initiation of treatment are of prognostic concern: delays can lead to stage progression, worsening of disease or treatment complications.^[5] It is therefore intuitive that delays in the detection and diagnosis of breast cancer need to be minimised in order to improve outcomes.

Delays can be classified as either patient delay or system delay.^[5] Patient delay time (PDT) refers to the delay in seeking medical care after the self-discovery of a breast cancer symptom. System delay time (SDT) conceptually refers to the time between registering for the first medical visit and the actual commencement of therapy. This type of delay occurs within the healthcare system and includes delays getting appointments, scheduling diagnostic tests, receiving a definitive diagnosis and initiating therapy. The sum of the two is referred to as the total delay time (TDT). There is wide variability in delay times between developed and developing countries. The mean TDT in the USA has been reported as 4.9 weeks and the median TDT in Denmark as 9.3 weeks. Even within developed countries there is variability in TDTs. A multinational analysis of female breast cancer patients from 12 eastern European countries reported a TDT of 14.4 weeks.^[6]

Most developing countries report only PDT or SDT, making it difficult to compare standards and outcomes in the different resource settings. China is one of few developing countries where mean TDT has been reported: 21.7 weeks. In this issue, Dalwai *et al.*^[7] quantified SDT at a regional hospital in KwaZulu-Natal.^[7] The small retrospective study conducted over a 12-month period confirmed a mean SDT of 10 weeks, which is well over the international benchmark of 6 weeks. What makes this study

valuable beyond the quantification of the SDT is that each delay was further assessed and policy changes proposed to improve the diagnostic and staging pathways.

There are no national data quantifying TDT in South Africa. A survey of the breast centres revealed TDTs ranging from 2 weeks to 19 weeks, with a national average of 8.1 weeks (Table 1). The survey also confirmed a wide variation in access to breast imaging, staging investigations and initiation of treatment. Only one centre was able to quantify PDT.

It is unclear whether delays of any type are associated with adverse consequences. Caplan^[5] reviewed the results of earlier and more recent studies on the effects of delay on prognosis, especially survival, following a diagnosis of breast cancer. Earlier studies revealed that increased delay resulted in more advanced stages of disease and poorer survival. These earlier studies support the logical conclusion that advanced disease at diagnosis will lead to poorer prognosis and shorter survival; however, more recent studies report mixed results, particularly with respect to survival. A 2010 study reported that delays to treatment (surgical or systemic) both less than or more than 90 days were associated with similar survival outcomes.^[8] However, a later study concluded that a longer treatment delay (>6 weeks) was a statistically significant risk factor for shorter survival.^[9] There also seems to be a correlation between treatment delay and survival according to stage: intervals ≥ 60 days from a biopsy-confirmed breast cancer diagnosis and treatment initiation had no effect on survival in patients with early-stage disease, but were associated with significantly worse survival in those with advanced-stage disease.^[10] This confirmed the findings from an earlier study where the adverse effects of long delays on survival disappeared within individual stages of disease.^[10]

These mixed results of delays and survival outcomes have raised several questions. It seems illogical that longer delays should be associated with increased survival compared with shorter delays. Why then the conflicting data? A number of possible explanations have been put forward. One is the biological characteristics of the tumour which could be the driver of survival, rather than any form of delay. A rapidly growing lesion suggests a sinister process and some degree of urgency to both patients and clinicians. It seems reasonable to assume that such lesions will present much earlier than indolent tumours.^[12] A further reason for this paradox is statistical: insufficient patients presenting with long delays to adequately power the studies, or the arbitrary allocation of delay intervals that were not long enough to have a negative effect on survival.^[13]

The mixed results notwithstanding, it is advisable to minimise any delay to breast cancer treatment. Although studies specifically reporting on the quality of life associated with delays and advanced disease are lacking, there are data that suggest a significant increase in the cost of breast cancer treatment according to stage. In a recent Canadian study, the overall mean cost of breast cancer care for patients with stages III and IV disease was at least twice that for stage I disease. The increase in cost resulted from higher resource utilisation, including hospital visits, chemotherapy and radiotherapy.^[14]

Table 1. Survey results of breast centre TDTs

Hospital	Patient delay*	System delay					Total delay**
		Imaging†	Histology‡	Staging§	MDT clinic¶	Treatment	
Groote Schuur	Breast clinic appointment 1 - 2 wk	MMG 50% same day, rest <1 wk	<1 wk	Most within 1 wk, CT scan or bone scan needed: up to 6 wk	<1 wk	Surgery 1 - 6 wk Chemo: 2 - 3 wk RT: 12 wk	Best case: 2 wk Average: 3 - 4 wk
Tygerberg	Breast clinic appointment 3 - 4 wk	MMG same day	4 wk	CT scan, bone scan 4 - 6 wks	<1 wk	Surgery: 8 wk Chemo: same day RT: 12 wk	11 - 19 wk
Chris Hani Baragwanath	3 - 12 wk (only unit to quantify PDT)	Nil – same day and core biopsy	2 wk	Not available	1 day	Surgery: 1 wk Chemo: 3 wk RT: 12 wk	3 - 5 wk
Helen Joseph	Open access	1 wk	2 wk	2 - 3 wk	Nil	Surgery: 2 wk Chemo: 3 - 4 wk RT: 12 wk	8 - 9 wk
Charlotte Maxeke Academic	-	Nil – same day	2 - 3 wk	Staged while awaiting histology (1 - 2 wk)	4 days	Surgery: <1 wk Chemo: 1 - 2 wk	3 - 6 wk
Grey's	-	Biopsy same day, MMG 2 - 3 wk	2 - 3 wk	Staged while awaiting histology (2 - 3 wk)	1 - 2 wk	Surgery: 6 - 8 wk Chemo: 3 wk	7 - 10 wk
Addington/ Inkosi Albert Luthuli	-	Nil – same day and core biopsy	2 wk	Staged while awaiting histology (2 wk)	3 days	Surgery: 5 wk Chemo: 2 wk	4 - 8 wk
Bloemfontein	-						

*Patient delay: Time from patient noticing lump to being seen at breast clinic.

†Imaging delay: Time from breast clinic visit to breast imaging.

‡Histology delay: Time from biopsy to histology result.

§Staging delay: Time from diagnosis of breast cancer to metastatic screening, where indicated.

¶MDT delay: Time from full work-up to discussion at multidisciplinary team meeting (MDT).

||Treatment delay: Time from MDT discussion to initiation of treatment either primary chemotherapy (CT) or surgery.

**Total delay: Sum of all the above.

MMG = mammogram; RT = radiotherapy.

Any attempt to reduce TDT in breast cancer must begin with addressing PDT. Data from a recent Turkish study suggest that promoting breast awareness and education on breast healthcare have the ability to decrease PDT independently of an existing screening programme; the mean PDT was 4.8 weeks.^[15] Mean PDT in South Africa is not known, but in a recent study 52.4% of patients presented with PDT >6 months.^[16]

Diagnosis of breast cancer and initiation of treatment are often delayed due to healthcare system-related factors. A Danish survey revealed that patients who consulted their general practitioner before the diagnosis of breast cancer experienced significantly longer SDT within secondary healthcare than those who were admitted directly to hospital.^[17] A similar finding of longer SDT was reported in a Turkish study, where the SDT was more than twice the PDT due to the majority of patients presenting to a general practitioner/family physician as opposed to a specialist (surgeon, gynaecologist, oncologist or physician).^[15] Taken

together, these studies suggest that the provision of comprehensive cancer centres may significantly decrease SDT. The study by Dalwai *et al.*^[7] underscores this point: the mean SDT of 10 weeks at a regional hospital did not include further investigations required by the centralised breast clinic team or delays to initiation of treatment.

Delay in the diagnosis and treatment of breast cancer does matter and remains a serious problem in most developing countries. Despite conflicting data regarding outcomes, it remains important to minimise delays to give the best chance of increased survival, maintain quality of life and curtail costs. Several papers have attempted to quantify psychological and behavioural patient attributes leading to patient- and system-related delay times;^[15] others, such as the paper by Dalwai *et al.*^[7] have focused exclusively on system-related delays. In most cases, the SDT far exceeded PDT, suggesting the need for comprehensive breast care centres to fast-track assessment of patients with breast cancer-related symptoms.

Clinical practice guidelines for breast cancer management should incorporate time guidelines for diagnosis and treatment.

Unlike in resource-enhanced settings, there are no guidelines regarding acceptable delays in resource-poor settings and no legislation addressing these breast cancer delays. There is an urgent need in South Africa to establish national norms to streamline the management of all breast cancer patients. Table 1 attests to wide variation in delay times at breast centres in South Africa. These delays need to be accurately quantified and discussed among various stakeholders: clinicians, politicians and patient advocates, in order to bring them in line with universally accepted delays. It is incumbent on the healthcare providers to invest in these regional breast centres. At present they are the only institutions with expertise and resources to provide comprehensive breast cancer care.

I Buccimazza

Breast Unit, Department of Surgery, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa
ines.buccimazza@gmail.com

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