

Metastatic Breast Cancer – a 10-Year Review

Introduction

The following report is an abridged version of the *Global analysis of advanced/metastatic breast cancer: Decade report (2005-2015)*, as published in the April 2018 edition of *The Breast* journal (*The Breast* 39 [2018] pp.131-138). This edited version also incorporates information relating to breast cancer statistics in the UAE, although it should be highlighted from the outset that there is a general paucity of available information relating to metastatic breast cancer in the country.

This report focuses on the issues around quality of life, communication and meeting the emotional needs of patients with metastatic breast cancer. It omits findings pertaining to the economic impact of metastatic breast cancer and issues around employment for those diagnosed with the disease. This additional information - along with the details of the various qualitative and quantitative surveys referred to throughout the report - can be found in the original article, which can be accessed through the link: <https://www.ncbi.nlm.nih.gov/pubmed/29679849>.

Metastatic Breast Cancer

Breast cancer is the most common cancer in women, with approximately 1.7 million new cases diagnosed globally in 2012. In 2015 there were an estimated 561,334 deaths from breast cancer worldwide, with the majority due to metastatic breast cancer.^{1,2,3} The projected death rate from breast cancer is predicted to rise to 805,116 deaths per year by 2030, representing a 43% increase in the absolute number of deaths from the disease.⁴ The UAE is ranked at 131 out of 172 countries for breast cancer mortality.⁵

Clinical studies have shown that in developed countries approximately 20-30% of patients who have early breast cancer will have a recurrence that is metastatic.^{6,7} Globally, 5-10% of newly diagnosed patients with breast cancer will present with metastatic disease, although there are notable regional variations.⁸ In high-income countries, fewer than 8% of patients with breast cancer are initially

¹ Lu J, Steeg PS, Price JE, Krishnamurthy S, Mani SA, Reuben J, et al. Breast cancer metastasis: challenges and opportunities. *Cancer Research* 2009;69: 4951-3.

² International Agency for Research on Cancer. Breast cancer: estimated incidence, mortality and prevalence worldwide in 2012. 2015. <http://globocan.iarc.fr/old/FactSheets/cancers/breast-new.asp> [Accessed 23 October 2017].

³ [3] DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO, Jemal A. International variation in female breast cancer incidence and mortality rates. *Cancer Epidemiol Biomark Prev* 2015; 24:1495-506.

⁴ World Health Organization. Projections of mortality and causes of death, 2015 and 2030. 2015. http://www.who.int/healthinfo/global_burden_disease/projections/en/ [Accessed 23 October 2017].

⁵ <http://www.worldlifeexpectancy.com/cause-of-death/breast-cancer/by-country/>

⁶ O'Shaughnessy J. Extending survival with chemotherapy in metastatic breast cancer. *Oncology* 2005;10 (Suppl 3):20e9.

⁷ Dowsett M, Forbes JF, Bradley R, Ingle J, Aihara T, Bliss J, et al. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. *The Lancet* 2015; 386:1341-52.

⁸ Cardoso F, Costa A, Norton L, Cameron D, Cufer T, Fallowfield L, et al. 1st International consensus guidelines for advanced breast cancer (ABC 1). *Breast* 2012; 21:242-52.

diagnosed with metastatic disease, but in the majority of low- and middle-income countries, approximately 20-30% of patients with breast cancer are initially diagnosed with metastatic disease.⁹

Factors influencing Metastatic Breast Cancer in the UAE

According to a 2010 report by the Centre for Arab Genomic Studies, Arab women are more likely to develop breast cancer at an earlier age, with research from the Weill Cornell Medical College in Qatar supporting the findings. In fact, the median age at diagnosis of breast cancer in the UAE is 10 to 15 years younger than in North America and Europe.¹⁰ This statistic is particularly concerning because breast cancer in younger women is generally more aggressive and less likely to have a sustained response to treatment than in older women.¹¹ In the UAE, around 15% of breast cancer cases are metastatic.¹²

Although there is evidence that increasing numbers of women in the UAE are taking up breast cancer screening,¹³ there is also information that despite having access to national screening programmes and the coverage of cancer screening by the health insurance, only around 75% of breast cancer patients in the UAE seek medical advice after experiencing a sign or symptom of the disease.¹⁴ There is also evidence that a lack of knowledge around methods and availability of screening may be leading to breast cancer going undetected. In one UAE study, almost half (44.8%) of women who never had a clinical breast exam and 44.1% of women who never had a mammography expressed a lack of knowledge about the existence of these screening techniques. Nearly one third of the participants interpreted the presence of a breast lump incorrectly and expressed fewer worries about the nature of the lump than would normally be expected.¹⁵

Metastatic Breast Cancer Survival Rates

Data from between 1995 and 2013 indicate that median survival for metastatic breast cancer is approximately 2-3 years in developed countries.^{16,17} Over the past decade, substantial resources directed toward breast cancer education, research, and advocacy efforts have led to improvements in diagnosis, treatment and outcomes. However, these efforts have primarily benefited patients with early breast cancer. As a result of advances in understanding of the disease and treatment and increased use of mammography screening, high 5-year relative survival rates occur in early breast cancer patients. Yet

⁹ Unger-Saldana K. Challenges to the early diagnosis and treatment of breast cancer in developing countries. *World Journal of Clinical Oncology* 2014;5: 465-77.

¹⁰ <https://gulfnews.com/xpress/news/uae-s-median-age-of-breast-cancer-diagnosis-10-15-years-younger-than-in-west-1.2100559>

¹¹ <https://www.thenational.ae/uae/health/younger-women-need-breast-cancer-checks-health-experts-warn-1.448028>

¹² Globocan. Fact Sheets by Population. N.p., n.d. Web. 25 Nov. 2015.

¹³ <https://www.thenational.ae/uae/growing-numbers-of-uae-residents-attend-free-breast-screenings-1.663517V>

¹⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5757829/>

¹⁵ <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0105783>

¹⁶ National Cancer Institute. SEER stat fact sheets: female breast cancer. 2015. <http://seer.cancer.gov/statfacts/html/breast.html> [accessed 23 October 2017].

¹⁷ Weide R, Feiten S, Friesenhahn V, Heymanns J, Kleboth K, Thomalla J, et al. Metastatic breast cancer: prolongation of survival in routine care is restricted to hormone-receptor- and Her2-positive tumors. *SpringerPlus* 2014; 3:535.

despite some progress in the treatment of metastatic breast cancer over the past decade, only modest improvements in outcomes have been reported from real-world and clinical trial data and the 5-year survival rate for metastatic breast cancer remains poor at approximately 25%.¹⁸

Communication Needs for Patients with Metastatic Breast Cancer

Patients with metastatic breast cancer often report difficulty in obtaining the information they want and need about their type of metastatic disease and the goals of treatment for advanced disease. Indeed, patients with metastatic breast cancer report the support provided to them is often inadequate compared with the information and services available at the time of diagnosis of early breast cancer.¹⁹

Health care providers indicated that patients should be spoken to in realistic terms about their condition and be informed that although there may be multiple treatment options and emerging agents in clinical development that can help them to live well and live longer, metastatic breast cancer is incurable, progressive, and ultimately fatal in most cases. Although 83% of responding health care professionals in one survey identified 'learning about how to bring bad news to patients and families' as a key training topic, only 43% had received this form of training. Physician training and information on how to conduct conversations about disease progression and end-of-life care can be beneficial,²⁰ but evidence suggests that these are often unavailable.

One general population survey on breast cancer showed that approximately 28% of the public feel that patients with metastatic breast cancer should not talk about their illness with anyone other than their health care professional. Although this belief was most prominent in India and Taiwan, it was also reported in developed countries, including the United Kingdom, France, and Germany. The consequences of these public beliefs can be particularly damaging in developing countries where individuals are not encouraged to engage with health care professionals at an early stage of the disease, which is likely to contribute to poorer outcomes.²¹ It has also contributed to the sense that patients' voices are being lost within the public's discussion about breast cancer.

Quality of Life for Patients with Metastatic Breast Cancer

Maintaining quality of life is one of the most crucial goals for patients with breast cancer. The quality of life for patients with metastatic breast cancer has not improved, and in some cases, may have declined in the past decade. Patient support organisations report that compared with those with early disease, patients with metastatic breast cancer have greater needs in terms of psychological and financial support as well as access to services and information about how to deal with ongoing issues of anxiety, pain, and sleep disruption.

¹⁸ National Cancer Institute. SEER stat fact sheets: female breast cancer. 2015. <http://seer.cancer.gov/statfacts/html/breast.html> [accessed 23 October 2017].

¹⁹ Johnston SR. Living with secondary breast cancer: coping with an uncertain future with unmet needs. *European Journal of Cancer Care* 2010;19: 561-3.

²⁰ Danesh M, Belkora J, Volz S, Rugo HS. Informational needs of patients with metastatic breast cancer: what questions do they ask, and are physicians answering them? *Journal of Cancer Education* 2014; 29:175-80.

²¹ Shulman LN, Willett W, Sievers A, Knaul FM. Breast cancer in developing countries: opportunities for improved survival. *Journal of Oncology* 2010, 595167. 2010.

Research has revealed that 80% of patients report quality of life as the main area in need of improvement in metastatic breast cancer care. Patients reported that fatigue, insomnia, lack of concentration, neuropathy and pain have the most substantial impact on quality of life.¹⁹ However, patients with metastatic breast cancer represent a smaller proportion of patients in the breast cancer community and are perceived as ‘failures’ by the medical community due to the need for ongoing treatment and are often feared by patient support organisations.²² Consequently, patients with metastatic breast cancer often receive less support than those with early breast cancer. Over the past decade, there has been a notable lack of improvement in quality of life for patients with metastatic breast cancer who have multiple and unique unmet needs.

Emotional Support for Patients with Metastatic Breast Cancer

Following behind quality of life issues, patients with metastatic breast cancer indicated their greatest need was for emotional care. Distress, depression and anxiety, social isolation and stigmatisation, reduced self-worth, financial distress, and sexual dysfunction also have a great impact on patients with metastatic breast cancer.^{23,24,25} Patients with metastatic breast cancer experience considerable emotional distress,^{26,27} with approximately one-third of patients with the condition experiencing major depression and anxiety and one-quarter suffering mild depression.^{28,29,30} Surveys also indicate that access to mental health services is often either lacking or not pursued by patients, which has a negative impact on patients and caregivers.³¹ Despite the impact of metastatic breast cancer on emotional health, only one-third of patients with considerable anxiety or depression have access to mental health support services.³⁰ It has been found difficult to determine whether a patient's needs are being addressed or met as there is no harmonised approach for the definition and assessment of quality of life in clinical trials that translates into practice. Most tools to address quality of life were developed for patients with early breast cancer, so it is particularly challenging to evaluate the quality of life of patients with the metastatic form of the disease.¹⁹

²² Wardley A. The need for advanced breast cancer treatment guidelines: results of an internet-based survey. *Breast* 2008; 17:275-81.

²³ Luoma ML, Hakamies-Blomqvist L. The meaning of quality of life in patients being treated for advanced breast cancer: a qualitative study. *Psycho-oncology* 2004; 13:729-39.

²⁴ Banning M, Tanzeen T. Living with advanced breast cancer: perceptions of Pakistani women on life expectations and fears. *Cancer Nursing* 2014; 37: E12-8.

²⁵ Milbury K, Badr H. Sexual problems, communication patterns, and depressive symptoms in couples coping with metastatic breast cancer. *Psycho-oncology* 2013; 22:814-22.

²⁶ Caplette-Gingras A, Savard J. Depression in women with metastatic breast cancer: a review of the literature. *Palliative Support Care* 2008; 6:377-87.

²⁷ Turner J, Kelly B, Swanson C, Allison R, Wetzig N. Psychosocial impact of newly diagnosed advanced breast cancer. *Psycho-oncology* 2005; 14:396-407.

²⁸ Aranda S, Schofield P, Weih L, Yates P, Milne D, Faulkner R, et al. Mapping the quality of life and unmet needs of urban women with metastatic breast cancer. *European Journal of Cancer Care* 2005; 14:211-22.

²⁹ Grabsch B, Clarke DM, Love A, McKenzie DP, Snyder RD, Bloch S, et al. Psychological morbidity and quality of life in women with advanced breast cancer: a cross-sectional survey. *Palliative Support Care* 2006; 4:47-56.

³⁰ Kissane DW, Grabsch B, Love A, Clarke DM, Bloch S, Smith GC. Psychiatric disorder in women with early stage and advanced breast cancer: a comparative analysis. *The Australian and New Zealand Journal of Psychiatry* 2004; 38:320-6.

³¹ Mosher CE, Johnson C, Dickler M, Norton L, Massie MJ, DuHamel K. Living with metastatic breast cancer: a qualitative analysis of physical, psychological and social sequelae. *Breast* 2013; 19:285-92.

Public awareness and understanding of metastatic breast cancer appears to be limited, with misconceptions and lack of awareness about metastatic breast cancer prevalent around the world. A recent US survey found that approximately 60% of the general public have little or no knowledge regarding metastatic breast cancer.³²

Patient and Caregiver Qualitative Research responses suggested there are two contradictory views of patients and caregivers about metastatic breast cancer: Some believe the condition is a curable disease similar to early breast cancer, whereas others believe it is a hopeless condition for which treatment is futile. There is also a misconception by the general public that numerous treatment options are available for metastatic breast cancer, although the majority agree that more options are needed. Moreover, there is also a misunderstanding among the general public that all patients with metastatic breast cancer can have a long life. One global general population survey revealed that 74-87% of respondents in 14 countries incorrectly believed that early detection and treatment prevent disease progression, while 48-76% said that metastatic breast cancer is curable. Furthermore, some members of the public view patients with metastatic breast cancer as less worthy of treatment than patients with early breast cancer – a trend that is most pronounced in Asia. These findings are consistent with the limited information from reliable sources that are available to the public about metastatic breast cancer and with the finding that fewer than 50% of the public worldwide believes reliable information on metastatic breast cancer is easy to access.

Misconceptions and lack of understanding can cause patients to feel they are perceived badly by others, which can result in increased feelings of isolation. Approximately half of patients with metastatic breast cancer report feelings of isolation and shame, even within the breast cancer community. Public misunderstanding of metastatic breast cancer and the resulting stigmatisation and isolation can have a devastating impact on patients. Patient and Caregiver Qualitative Research revealed that family and friends may choose to refrain from contact as they are concerned about exposing patients to infection while their immune system is suppressed. These findings were supported by a study of the value of support groups in metastatic breast cancer and the shared experiences of patients.³³

Interpersonal Relationships and Metastatic Breast Cancer

Studies have shown that that interpersonal relationships between patients and their caregivers, and with others close to them, are crucial to the patient's wellbeing. However, along with the common concerns over a loved one's well-being, caregivers can themselves face economic and psychological problems as well as marital and family anxieties.³⁴ Caregiver worries focus on their loved one's well-being, disease status, and ability to maintain life activities.³⁵ A diagnosis of metastatic breast cancer affects both members of a couple, wherein the patient and their partner often act as a primary source of

³² Pfizer Inc. Breast cancer: a story half told [website]. 2014.

<https://www.storyhalftold.com/index.php%3fsource%3dbing%26HBX%5fPK%3ds%5fa%2Bstory%2bhalf%2btold%26o%3d124870541%a6297732250%a60%26skwid%3d43700016924842940> [Accessed 20 October 2017].

³³ Leadbeater M. Evaluating use of a support group in secondary breast cancer care. *Nursing Times* 2004; 100:34-6.

³⁴ Grunfeld EA, Maher EJ, Browne S, Ward P, Young T, Vivat B, et al. Advanced breast cancer patients' perceptions of decision making for palliative chemotherapy. *Journal of Clinical Oncology* 2006; 24:1090-8.

³⁵ Mayer M. The experience of caregivers of women with metastatic breast cancer: insights from the Make Your Dialogue Count survey. *Cancer Research* 2016;76. P1-11-06.

support for each other.³⁶ The demands of providing care for a loved one extend beyond personal relationships; caregivers experience psychological and economic strain resulting in decreased well-being and symptoms of stress.³⁷ In turn, stress can lead caregivers to overlook their own needs.^{33,38}

At times, it is the spouses or children who often become caregivers to patients with metastatic breast cancer. Responses to patient and caregiver qualitative research revealed that in some countries, mostly in the developing world, caregivers and health care professionals 'shield' patients from their diagnosis, reflecting a family-centred approach to decision-making. In contrast, in other countries, usually in the developed world, decision-making is focused on the patient's informed consent and empowerment.^{39,40} The report also found that in some cultures, patients with metastatic breast cancer try to protect members of their support network, including caregivers, who may find the situation difficult to understand, which can lead to difficulties in relationships. Strategies are needed to identify and meet the psychological, occupational, and other needs of caregivers surrounding balancing work, commitments at home and caregiving.

End of Life Planning for Patients with Metastatic Breast Cancer

Considerable effort is needed to ensure that the wishes of the patient and family are met in the terminal stages of metastatic breast cancer, when treatment can no longer control the disease. Although discussions regarding end of life are extremely difficult for patients and their families, it is critical that health care providers understand their needs for care options, where patients want to die, and other preferences.⁴¹ Timely end-of-life planning and communication can contribute to patient engagement and empowerment; however, approximately 65% of health care professionals who responded to the a breast cancer centre survey reported that end-of-life discussions are held too late, often after multiple changes in treatment. Many patients are referred to palliative care in the last week or two of life when they are too unwell to benefit from these services.^{40,42} Delays in end-of-life discussions can also limit the amount of time for patients to carry out desired activities in the final months and weeks before death.⁴³ Additionally, current practice tends to focus on institutional and hospice care;⁴⁴ although this varies

³⁶ Badr H, Carmack CL, Kashy DA, Cristofanilli M, Revenson TA. Dyadic coping in metastatic breast cancer. *Health Psychology* 2010; 29:169-80.

³⁷ Grunfeld E, Coyle D, Whelan T, Clinch J, Reyno L, Earle CC, et al. Family caregiver burden: results of a longitudinal study of breast cancer patients and their principal caregivers. *Canadian Medical Association Journal* 2004; 170:1795-801.

³⁸ Blum K, Sherman DW. Understanding the experience of caregivers: a focus on transitions. *Seminars in Oncology Nursing* 2010; 26:243-58.

³⁹ Aljubran AH. The attitude towards disclosure of bad news to cancer patients in Saudi Arabia. *Annals of Saudi Medicine* 2010; 30:141-4.

⁴⁰ Chittem M, Butow P. Responding to family requests for nondisclosure: the impact of oncologists' cultural background. *Journal of Cancer Research and Therapeutics* 2015;11: 174-80.

⁴¹ Irvin Jr W, Muss HB, Mayer DK. Symptom management in metastatic breast cancer. *Oncol* 2011; 16:1203-14.

⁴² Casarett DJ, Quill TE. "I'm not ready for hospice": strategies for timely and effective hospice discussions. *Annals of Internal Medicine* 2007; 146:443-9.

⁴³ Chunlestskul K, Carlson LE, Koopmans JP, Angen M. Lived experiences of Canadian women with metastatic breast cancer in preparation for their death: a qualitative study. Part II-enabling and inhibiting factors; the paradox of death preparation. *Journal of Palliative Care* 2008; 24:16-25.

⁴⁴ Cleary J, Ddungu H, Distelhorst SR, Ripamonti C, Rodin GM, Bushnaq MA, et al. Supportive and palliative care for metastatic breast cancer: resource allocations in low- and middle-income countries. A Breast Health Global Initiative 2013 consensus statement. *Breast* 2013; 22:616-27.

widely among patients, the majority prefer to be at home at their end of life.⁴⁵ This is important, not only in high-income countries with greater resources, but also in low- and middle-income countries.⁴⁶

Conclusions

The findings from this abridged version of the *Global analysis of advanced/metastatic breast cancer: Decade report (2005-2015)* report can be summarised as follows:

- Approximately 0.5 million people worldwide die from metastatic breast cancer (metastatic breast cancer) every year.
- There have been modest improvements in metastatic breast cancer outcomes over the past decade.
- Patients are not provided with adequate information about metastatic breast cancer
- There is a need for open discussion with patients and caregivers about realistic goals
- Physicians are not trained in communicating with patients about their disease
- Maintaining patients' quality of life is a crucial goal; however, this has not improved, and in some cases, may have declined in the past decade
- Public awareness and understanding of metastatic breast cancer is limited, with damaging consequences for patients and caregivers
- Relationships with caregivers are crucial to patients with metastatic breast cancer, and caregiver support needs are often overlooked
- A strong and united global effort among healthcare professionals, including clinicians, oncologists, pharmaceutical manufacturers, payers and policy makers and with advocates, families, and patients, is necessary to improve the outcome and quality of life for patients with metastatic breast cancer

The key takeaway from the report is that a strong and united global effort of all involved partners, health care professionals, including clinicians, and oncologists, pharmaceutical manufacturers, payers, policy makers, along with advocates, families, and patients is necessary to improve the outcome and quality of life of patients with metastatic breast cancer.

⁴⁵ Gomes B, Calanzani N, Curiale V, McCrone P, Higginson IJ. Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers. *Cochrane Database Syst Rev* 2013. CD007760.

⁴⁶ Gukas ID, Mbah N. Terminal events in women dying of advanced breast cancer: improving the care for terminal breast cancer patients in Africa. *International Journal of Surgery* 2005; 3:117-9.