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The Role of Ultrasound as a Diagnostic Tool for Breast Cancer in the Screening of Younger Women (Age 25-38) in Guyana

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Abstract

Objective: Ultrasound is used in many ways, not only as an initial diagnostic tool for confirmation of pathology determined from biopsies of the breast but also staging of breast cancer. Ultrasound is inexpensive and readily available almost all over the country. In a recent publication from the UK, the incidence of breast cancer in women younger than 35 years was 1.4% and in those younger than 30 years it was 0.43%. Breast Cancer is the most commonly diagnosed cancer amongst women worldwide. There were approximately 1.38 million new cases of breast cancer in the year 2008 and by 2020 this figure is anticipated to escalate to 1.7 million.

Methodology: This research was a qualitative retrospective study which focused on charts from the Cancer Institute of Guyana that was acquired during the period of January 2010 to December 2016. Triple data entry was done to avoid errors. Data was entered into Microsoft excel 2007.

Results: A total of 80 charts were reviewed, with a 95% confidence level and a confidence interval of 9.42. The average age at which women were being screened is 33 from 2010-2016. Ultrasound showed sensitivity was 97% and the specificity 98%.

Discussion: Ultrasound was shown to be more sensitive than mammogram. Afro-Guyanese were the majority screened. Most persons had ultrasound done with both malignant and benign diseases being discovered with this modality. The malignant cases were more frequently diagnosed at stage II and the average of detection was 33.

Conclusion: Ultrasound is effective and sensitive in the diagnosis of breast cancer. It is also effective in diagnosing benign breast diseases in younger women with dense breast tissue. Ultrasound is cheaper and safer than other imaging modalities for screening and diagnosis.

Keywords: Screening; Ultrasound; Breast cancer; Sonomammogram; Lymph nodes; Ductal carcinoma *in situ*; Breast imaging-reporting and data system

Introduction

The efficacy of ultrasound as a diagnostic tool for the detection of breast cancer in younger women is becoming more evident. Ultrasound is used in many ways, not only as an initial diagnostic tool for confirmation of pathology determined from biopsies of the breast but also staging of breast cancer [1-9]. It is also combined with mammography, a procedure called sonomammography to aid in better detection of breast cancer. In a recent publication from the UK, the incidence of breast cancer in women younger than 35 years was 1.4% and in those younger than 30 years it was 0.43% [4]. Breast Cancer is the most commonly diagnosed cancer amongst women worldwide. There were approximately 1.38 million new cases of breast cancer in the year 2008 and by 2020 this figure is anticipated to escalate to 1.7 million [9]. Improvements in technology over the past 20 years have made real-time ultrasonography an important imaging modality for evaluation of breast lumps and detection of breast cancer [2]. The implication of mammography's unreliability for detecting cancers in dense-breasted women has been intensified by recent studies citing breast tissue density as an independent risk factor for cancer [10].

Many younger women believe that is not possible for them to have breast cancer. It was proven that this specific type of cancer is prevalent in women over 40, but it was noticed that in the past five (5) years more women between the ages 25-38 have developed breast cancer, for some a bit too late and about 5% to 6% of total breast cancer occurs in women younger than 40 years [4]. However, through awareness a regular screening programme can be developed for younger women [11,12].

As of February 2014, 14 states have enacted laws requiring that women be directly notified if they have dense breast tissue on a screening mammogram, and similar federal legislation has been proposed [1-3]. Proponents of breast density reporting legislation note that many women do not know their breast density or that dense breasts are associated with an increased risk of breast cancer, and that dense breast tissue can mask breast cancers resulting in false negative mammographic examinations [13]. Knowledge expands over a variety of topics such as etiology, early warning sign, treatment methods and early detection methods.

In some cases, a strong family history is a key factor in the person developing breast cancer. Other risk factors include stress, hormone imbalance and possibility of trauma to the area [14]. Women that have no children are also deemed at risk. Dense fibro glandular tissue per se is associated with an increased risk of breast cancer and also lowers the sensitivity of mammography to as low as 30%-48% [3].

Among women, Indo-Guyanese presented with the most cases of breast cancer (45%) while Afro-Guyanese had the majority of cervical cancer cases (39%) [15-18].

Hypothesis

Ultrasound is a very useful diagnostic tool in the screening of breast cancer for younger women.

Aim: To compare patient breast cancer screening methods and show the importance of ultrasound.

Objectives: Determine how effective is the use of ultrasound in the diagnosis of breast cancer in younger women. Show the stage of the breast cancer at which first diagnosis was made. Identify at what age these women were when first diagnosed.

Importance of the study: Younger women have a tendency to have denser breast. Dense breast tissue appears as a solid white area on a mammogram, which makes it difficult to see through. Ultrasound is a much better tool to "see" through the dense tissue [19]. This study will help to create awareness about the importance of early screening for younger women with the use of ultrasound. They must be aware that the risk for breast cancer is there and can be detected early for them too. Thus both the private and public health officials need to put systems in place to address this problem so that women's lives can be saved if diagnosis is made early. Awareness is being made for the use of mammography and ultrasound for breast cancer screening.

Literature Review

Most significantly, a 2004 study found that 90% (36 of 40) cancers detected by ultrasound alone were categorized as stage 0 or 1, suggesting that breast ultrasound screening can detect breast cancer in early stages there by having the potential to reduce morbidity and mortality [10].

Using ultrasound as a first line diagnostic tool was studied by S.R.C. Benson et al. There were 796 patients with confirmed breast cancer in this study. The specificity in this case was not significant as positives on ultrasound was 710 (89%) and on mammography 706 (89%). There was 537 symptomatic patients, ultrasound positives were 497 (93%) and mammography 465 (87%). They determined that ultrasound is significantly better than mammography for detecting invasive breast cancer (92% patients). There was a 9% increase of detection with the combination [13].

A study from India with a total of 166 patients complaining of breast mass in one or both breasts were examined and evaluated with USG and mammography. The lesions were confirmed on histopathology (FNAC/biopsy). The study showed that out of the 30 diagnosed malignancies two lesions were missed on mammography and four lesions were missed on ultrasonography, Overall specificity for USG in breast masses is 86.9% and for mammography it is 78.6%. Combining both the modalities the specificity is 97.6%. The "p" value is obtained which is highly significant for combination of ultrasonography and mammography in comparison with any individual modality (p=0.0059 and p=0.0001 respectively) [12].

A study in Ontario, Canada showed that for women with average risk of having breast cancer should only have one screening method performed, namely mammography and women with a high risk should have both mammography and ultrasound of the breast done as their screening methods. The results are as follows; they included 5 prospective, paired cohort studies in high-risk women, 4 of which were relevant to the Ontario context. Adjunct ultrasound identified between 2.3 and 5.9 additional breast cancers per 1,000 screens. The average pooled sensitivity of mammography and ultrasound was 53%, a statistically significant increase relative to mammography alone (absolute increase 13%; $P<0.05$). The average pooled specificity of the combined test was 96%, an absolute increase in the false-positive rate of 2% relative to mammography screening alone [11].

A systematic search and review of studies involving mammography and breast ultrasound for screening of breast cancer was conducted for the period 1/2002-8/2008. The relative percentage of carcinomas found in supplemental breast ultrasound examinations as a fraction of the total number of detected cancers was reported in 4 studies with a mean percentage of 22.5% (15%-34%). The study was mainly focused on ACR 2 to ACR 4 on the effectiveness of breast ultrasound. The majority of cancers were detected in breast tissue of ACR types 3 and 47.

A study done by Okello, et al. showed that ultrasonography detected 27% more mass lesions that would have been otherwise missed by mammography. In this study the missed malignant lesions were about 10 mm or less in size, the most likely reason for them being missed were due to dense breast tissues obscuring visualization on mammography. But they were detected using ultrasound as it's not limited by breast density. A total malignancy rate of 14.95% (22/148) is three fold higher compared to a previous study by Paulo et al. which showed a prevalence of 4.2% among symptomatic patients with dense mammogram [3]. The study concluded by saying that breast ultrasound scan resulted in significant incremental breast cancer detection rate (of 27%) among symptomatic women with mammographically dense breast tissue [3].

In this article a patient had both mammography and ultrasound done and the visualization of the axillary lymph node was only possible in the ultrasound due to the lack of abundant fat tissue. The specificity of ultrasound was 69.6% and mammography was 73.9% with histologically verified cases [1]. One patient had a mass in the subclavian region that could have only been detected using ultrasound because of its location. This particular study showed a 72.2% sensitivity of ultrasound and a 32.3% sensitivity of mammography. Palpation was 32.3%. The technique involved in mammography makes it difficult to isolate axillary lymph nodes [1].

Another study showing the effectiveness of ultrasound over mammography was conducted by Gordon and Goldenburg in 1995. The age range was 27-72 with an average of 51 years old. The records of breast ultrasound examinations of 12,706 women were retrospectively reviewed [20]. Results: There were 1575 solid masses detected sonographically that were nonpalpable and nonvisible by mammography; percutaneous biopsies (FNABs) were performed on 279 of these. As the study concluded, Ultrasound can detect unsuspected, mammographically occult cancers in radiographically dense breasts and can alter treatment planning when a second cancer is found in a breast that otherwise was considered appropriate for conservative surgery [4].

A retrospective study from January 2012-June 2012, a total of 40 patients was observed; the patients had mammography and ultrasound of the breast. The statistical measures of accuracy, sensitivity and specificity were calculated using the SPSS program. The results we obtained suggest that age and the physical density of breast potentially affect mammogram images of women with 41 years or smaller with sensitivity 66% and specificity 68% [5].

A particular study showed the importance of ultrasonography of the breast as it relates to ductal carcinoma *in situ*. High resolution ultrasound is detecting more of this specific type of cancer [21]. The study concluded that cystic or solid lesions accounted for approximately 80% of US findings of DCISs detected by US alone, and most were similar to benign forms. The smaller lesions are hard to detect on mammography so they may be missed completely if ultrasound of the breast is not advised. Results: Ultrasound findings, DCIS was classified into cystic or solid mass (56 cases), ill-defined hypo echoic mass (34 cases), micro lobulated mass (22 cases), duct dilatation (7 cases), and calcification (7 cases) [6].

More than half of the women younger than 50 years have heterogeneously dense (50%-75%) or very dense (>75%) glandular breast tissue. One-third of women older than 50 years have also dense breasts and the sensitivity of mammography in women with dense breasts is as low as 30%-48%. The interval cancer rate is highly increased in this group and, furthermore, dense breast tissue is itself a marker of increased risk of breast cancer in the order of 4-6 folds [8].

The addition of screening breast ultrasound in 8,647 women with mammographically normal, but dense breasts led to the detection of 28 additional cancers. Screening mammography detects 4 to 5 cancers per 1,000 women screened per year [22]. The high NPV in this study further indicates that patients whose supplemental screening ultrasound is negative are 99.9% likely to be free of a breast malignancy. These results provide reassurance for women whose dense breasts limit the reliability of mammograms for ruling out breast cancer [10].

A study that compared mammography only and a combination of mammography and breast ultrasound showed that in their sample size of 2712 women that were eligible from the period April 2004 to February 2006, forty participants (41 breasts) were diagnosed with cancer: 8 suspicious on both ultrasound and mammography, 12 on ultrasound alone, 12 on mammography alone, and 8 participants (9 breasts) on neither.

Sonographically detected cancers are small, invasive cancers, which are nearly all node negative. Ultrasound increases breast cancer detection in asymptomatic women with normal mammograms and dense breasts. The Breast Journal, Weigert and colleagues report the experience of using screening breast ultrasound in women with dense breasts and normal mammograms in Connecticut. They found that 3.2 additional cancers are detected per 1,000 screening ultrasound examinations.

Justification

In Guyana most patients have their screening and treatment done at the Cancer Institute of Guyana. According to "A profile of Cancer in Guyana" journal statistics from 2003-2012 for breast cancer showed that of a total of 1090 persons; 46% of all cases were from region. An observation on the routine breast cancer screening in Guyana suggested that a lot of the younger population of women do not perform routine screening because they think they are not a risk. Mammography is not really an option for these women as they are of child bearing age and in most situations they have either small breast, dense breast tissue or small dense breast. As such ultrasound is the recommended screening technique and it has been proven to be very effective. With this information being shared, more cases can be detected earlier thus increasing the chances of survival.

Methodology

This research was a qualitative retrospective study which focused on charts from the Cancer Institute of Guyana that was acquired during the period of January 2010 to December 2016. This institution provides an affordable option for most patients and as advocates in the fight against cancer, they receive sponsorship which they use to provide free screening, not only for breast cancer but for other types of cancers, primarily cervical and prostate. I have chosen this particular institute as the data is easily accessible, it's a central location and various patient types can be encountered.

The data was stored initially in log books, it was extracted by selecting data matching the criteria; then cross-referenced with a computerized version. The charts were then taken from the designated filing cabinets to verify all data was correct.

A total of 80 charts were reviewed which met the inclusion criteria listed below. Data extracted is reflected on a data collection sheet in Figure 2. Triple data entry was done to avoid errors. Data was entered into Microsoft excel 2007. Analysis was done for trends, frequencies, sensitivities and specificities using Microsoft excel 2007. The confidence intervals, positive predictive and negative predictive values are also calculated (Figure 3).

Inclusion criteria: Women already diagnosed with breast cancer, women with benign breast diseases.

Ethical consideration: IRB approval sought. No names were disclosed and unique IDs' used. Database is password protected and no other person has access. Database will be deleted upon completion of project.

Results

The aim of this project was to compare screening methods and show the importance of ultrasound. Mammography was the main modality chosen for the comparison as it is mostly chosen by physicians for breast screening. Ultrasound does not use radiation; therefore, it safer to have the procedure done. Mammogram is normally the gold standard for detection of breast cancer, however it is limited when younger patients need to be diagnosed. The dense appearance of the breast makes it hard to identify any mass and therefore an ultrasound is advised for further investigation [5]. The population of Georgetown is approximately 134,450; assuming half of them are women that will be 67,226 and approximately 1/3 of the women are adults between 25-38 years old, using 22,184 as my target population size and 5,546 as my study population for this study. Using the Sample Size calculator, a sample size of 80 was used, with a 95% confidence level, confidence interval of 9.42; 75% ± 9.42 persons agreeing with my hypothesis (Table 1).

Year	Age	Method of screening (n)			(T=80)	Disease diagnosis (n) (T=80)			
	(Mean)	*USG	*Mammo	*Sona	Total	*Malignant	Benign	*Neg	Total
2010	34	6 (67%)	1 (11%)	2 (22%)	9	8 (89%)	0	1 (11%)	9
2011	33	3 (60%)	1 (20%)	1 (20%)	5	4 (80%)	0	1 (20%)	5
2012	32	12 (60%)	5 (25%)	3 (15%)	20	13 (65%)	6 (30%)	1 (5%)	20
2013	34	9 (69%)	1 (8%)	3 (23%)	13	11 (85%)	0	2 (15%)	13
2014	36	3 (43%)	4 (57%)	0	7	6 (85%)	0	1 (15%)	7
2015	31	4 (80%)	1 (20%)	0	5	4 (80%)	0	1 (20%)	5
2016	34	12 (57%)	6 (29%)	3 (14%)	21	8 (38%)	11 (52%)	2 (10%)	21
	Total	49	19	12	80	54	17	9	80
*US-Ultrasound; Mammo-Mammogram; Sono-Sonomammogram; Mal-Malignancy; *Neg-Negative									

Table 1: Frequency table.

Figure 1 shows the average age at which women were being screened at as 33, the mode is 38 and the median is 36. The younger patients (25-32) accounted for 35% of the total sample taken. It is a frequency table showing the data collected in a more concise form.

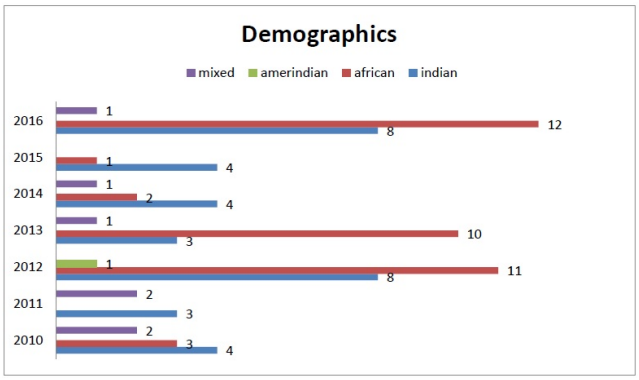


Figure 1: Chart showing the number of patients with dense breast screened from the various ethnicity against the period of 2010-2016. The primary location was region 4; Afro-Guyanese were being screened more regularly for the entire period; however Indo-Guyanese closely followed.

This may be so because this region is heavily populated with both these ethnicities however the Afro-Guyanese population is higher [22]. It was noted that the Amerindian population only had one patient, lack of awareness, their remote location and resources may be responsible for this (Table 2).

Parameters	Ultrasound	Mammography
Sensitivity	98%	94%
Specificity	100%	100%
NPV	89%	94%
PPV	100%	100%

Table 2: Sensitivity and specificity of Ultrasound versus Mammogram.

The sensitivity, the specificity, the negative predictive values and the positive values was calculated using the sensitivity and specificity calculator [17]. Ultrasound had one (1) false negative, eight (8) true negative, forty two (42) true positive and mammography had one (1) false negative and seventeen (17) true positive.

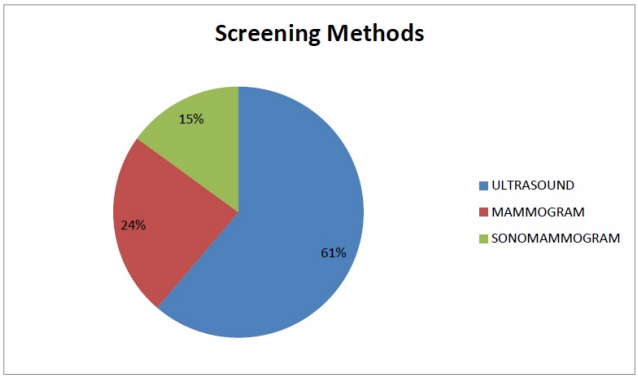


Figure 2: Pie Chart showing the various diagnostics methods.

Of the 80 cases analysed, 54 cases were screened using ultrasound only and 17 cases using mammogram only. Ultrasounds accounted for 61% of the method of screening. 2016 had the highest rate of screening; this can be attributed to increased public awareness on breast cancer. Sensitivity of Ultrasound was proven as: 97% and specificity was 98%. The combination of mammogram and ultrasound (sonomamorgam) had an overall sensitivity of 99% and specificity-100%. Sensitivity of mammogram was 94% and specificity-100%. The results of this research showed similarity too many of the studies that were reviewed where ultrasound is more sensitive than mammography. In some cases, where mammogram

shows no findings, ultrasound could have detected the lesion and therefore can be recommended in certain cases [4] (Figure 3,4 and 5).

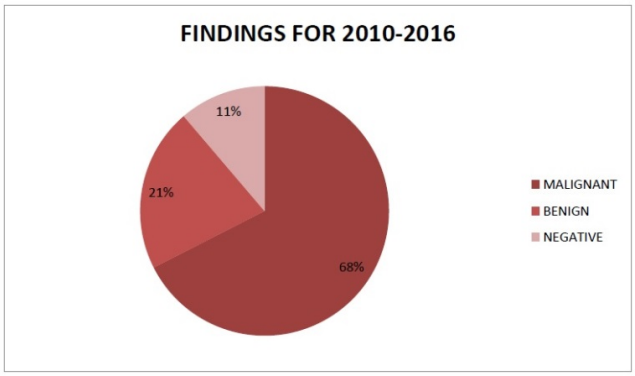


Figure 3: Pie Chart showing the percentage of the types of diseases detected in the time frame.

Method of diagnosis

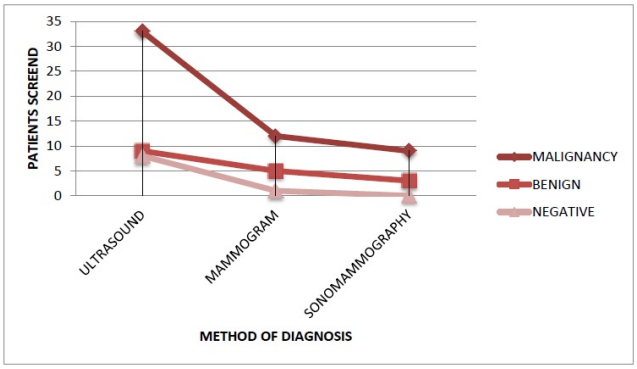


Figure 4: Method of diagnosis versus type of diagnosis. This shows what modality was used to detect both breast diseases. Most of the cases were diagnosed as malignancy 68%, while 21% were benign and 11% were negative for any disorders of the breast.

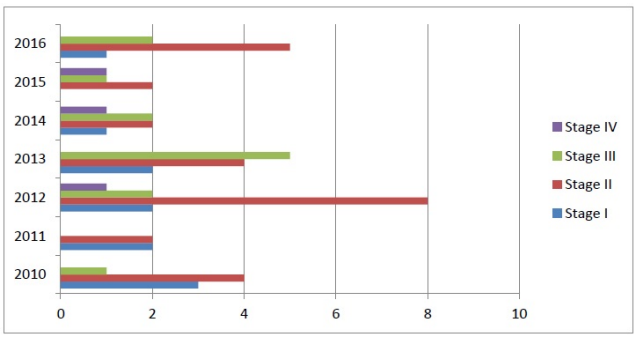


Figure 5: Graph showing the stages of breast cancer detected from the period of 2010-2016.

Most of the breast cancers were discovered in the early stages, particularly Stage II, with regular screening breast diseases can be detected early and may avoid any serious surgery such as mastectomy; a lumpectomy or FNA (Fine Needle Aspiration) may be requested instead. A palpable mass was the main reason for the patient to initiate a doctor's visit. In some cases the patients did not understand what was happening and neglected the doctor's request for further testing and returned at a later date. This is the main reason for the stage IV diagnosis.

The main disadvantage is that ultrasound is unable to screen for many types of breast cancer and it cannot replace a mammogram. It is also difficult to detect calcification in the ultrasound of the breast, and this is an early sign of breast cancer [23].

Computed tomography is a great option because of the detail that can be attained, however the radiation dose is higher than a mammogram, making this more dangerous. It is mostly used after initial diagnosing and treatment to see if any further spreading has occurred [16]. MRI has superior sensitivity to mammography and ultrasound in the detection of invasive cancer in high-risk groups. With the use of a high powered MRI machine, even the smallest lesion may be detected. Thus this modality is great for early detection. However, it is not available in all countries as yet and where it is; only a one machine in a central location may be found. It is very useful in women with very dense, non-fatty tissue [16].

Persons were very reluctant to fill out the data collection sheet, the information gathered from this showed that many persons earn between low and middle income. They learnt about mammogram and ultrasound due to outreaches that have been happening around the country in the past few years and also through television programmes about breast cancer awareness. They were not aware that dense breasts are common and that an ultrasound was a better option for them.

Limitation

In Guyana, access to data is very difficult; it is either the lack of records or the institution inability to assist students. Missing charts and duplication of names in some record books played a major role in data gathering. This placed a serious constraint on data collection.

Conclusion

Ultrasonography is effective and sensitive in the diagnosis of breast cancer. It is also effective in diagnosing benign breast diseases in younger women with dense breast tissue. Ultrasound is cheaper and safer than other imaging modality for screening and diagnosis. Mammography does have similar sensitivity as ultrasound but it was found to be more specific.

The researcher is actively promoting the use of ultrasound in screening for breast diseases in younger women and will present this data to increase awareness and advocacy among health care professionals on the importance and availability of ultrasound so that this tool can be more actively utilized especially among younger patients.

Recommendations

Radiologists are advising women to have a combined mammogram and breast ultrasound for better results. More awareness is required in order to stop breast diseases from progressing.

Glossary

Ultrasound: A type of imaging technique. It uses high-frequency sound waves to look at organs and structures inside the body.

Breast Cancer: Cancer arising in the mammary gland (usually in a woman or other female mammal, but occasionally in the rudimentary tissue of a male)

Screening: The testing of a person or group of people within the normal population for the presence of a disease or other condition. Breast tissue is composed of milk glands, milk ducts and supportive tissue (dense breast tissue), and fatty tissue (non-dense breast tissue).

DCIS: Ductal Carcinoma *in situ*.

BIRADS: Breast Imaging-Reporting and Data System which is a widely accepted risk assessment and quality assurance tool in mammography, ultrasound or MRI. Part of the initial implementation was to make the reporting of mammograms more standardized and comprehensible to the non-radiologist reading the report.

Sonomammograms: A combination of a breast ultrasound and a mammogram.

Breast Cancer Stages: The stages of breast cancer range from 0 to IV (0 to 4). Stage depends on the combination of tumor size (T), lymph node status (N) and metastases (M). For example, a cancer with a T1 tumor (less than 2 cm), no lymph nodes with cancer (N0) and no metastases (M0) is classified as stage I (T1N0M0). The highest stage (stage IV) is any cancer with metastases (M1), no matter the size of the tumor or the lymph node status [21].

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