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Molecular classification of breast cancer in Egyptian cohort: 10 years follow-up and survival

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Abstract: ***Background****:Molecular classification of breast cancer has been used recently beyond the conventional pathologic grade and histology. This resulting in classifying breast cancer into different molecular subtypes, understanding that clarify different risks of relapse and response to adjuvant therapies in patients. This also demonstrates that breast cancer subtypes are associated with unique patterns of metastatic spread with differences in relapse and survival.* ***Patients and Methods****: a retrospective cohort study of all non-metastatic breast cancer patients diagnosed and/or treated at National Cancer Institute, Cairo University from January to December 2003.* ***Results****: The most common molecular class was Luminal A (34%), and least was Luminal B HER2 enriched (10.7%). TN and HER2 enriched being more aggressive tumours were significantly associated with higher recurrence rate than other luminal classes (p = 0.003). The median DFS was 47.4 months. The median TLR of all patients was 88.4 months. The 5-year TLR was significantly longer in luminal class A (83.7%) than HER2 enriched (40.6%), p=0.001.* ***Conclusion****: TN and HER2 enriched being more aggressive tumours were significantly associated with higher recurrence rate than other luminal classes. The median DFS was 47.4 months. The median TLR of all patients was 88.4 months. The 5-year TLR was significantly longer in luminal classes than HER2 enriched, denoting bad prognosis of this molecular class.*

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I. Introduction

Breast cancer is nowadays the most frequent malignant tumour in females. Its morbidity and mortality continue to increase, despite remarkable progresses in the field of early diagnosis and adjuvant therapy. In the United States (US), breast cancer is the most common among females representing 30% of all cancers, the second most common cause of cancer deaths in women(1).

In Egypt, according to population-based registry, breast cancer is the most common cancer among females (25.8%- 32.9%) and second common. At National Cancer Institute (NCI) Cairo University, breast cancer ranked the first type of cancer in females (38.8%) and in both genders (19.6%) according to NCI Hospital-based registry (2).

A variety of clinical and pathological factors are routinely used to categorize patients with breast cancer to assess prognosis these include patient age, tumor size, hormone receptor status, and HER2 status. Although these risk categories have been of great value for assessment of prognosis, their role in determining prognosis and evaluating risk in an individual patient with breast cancer is more limited, as patients with similar combinations of features may have very different clinical outcomes. Better methods, therefore, are required to precisely assess prognosis and determine the most appropriate treatment for patients on an individual basis (3).

Long-term follow-up of patients with breast cancer have shown that a particular subtype of carcinoma or a specific grade has only a minor impact on prognosis and brings little information about the therapeutic strategy. Also, it is very well known that patients with the same pathologic subtype and grade frequently have a different outcome (4).

A significant improvement was achieved in the last decade by investigating some useful markers Estrogen receptor (ER), Progesteron receptor (PR), Ki67, and Human Epidermal Growth Factor Receptor 2 (HER2). It was found that patients with breast cancer can be stratified based on the expression of these markers, as demonstrated by immunohistochemistry and/or gene analysis (5).

There have been accumulated evidences that hormone receptors and HER2 expression have direct impact on therapy and no significant correlation was found with conventional subtypes of breast carcinomas (6).Gene expression analysis has demonstrated distinct molecular classes of breast cancer based on the degree of

expression of a selected number of genes, which can be translated into more prognostically and therapeutically useful information than what can be provided by existing histological classification systems (7).

Perou et al.(2000) were the first to provide a classification system based on gene expression analysis, and this consisted of four major molecular classes of breast cancer: luminal-like, basal-like, normal-like, and HER-2 positive(8). Bhargava et al.(2009) defined LUMA and LUMB as pure hormone receptor positive, the differentiating feature between them being the strong intensity of ER positivity in LUMA tumours. Cheang et al. (2009) added that a Ki67 proliferation index of more than 13.25% is a hallmark of LUMB tumours. Ki67 is a nuclear marker of cell proliferation, and its expression correlates proportionally to poorer clinical outcomes.

Molecular profiling, immune-histochemical analysis of hormone receptors and human epidermal growth factor receptor-2 (HER2) overexpression have been used to characterize breast cancers beyond the conventional use of grade, histology. The resulting taxonomy defines the breast cancer intrinsic subtypes. Different molecular subtypes also enhanced our ability to predict clinical outcome and response to therapy (9).

Understanding different subtypes of breast cancer clarify the different risks of relapse and response to adjuvant therapies. This demonstrates that breast cancer subtypes are associated with unique patterns of metastatic spread with notable differences in relapse and survival(10)

In a large cohort study of women diagnosed with invasive breast cancer in Toronto from 1987 to 1997, patients who were diagnosed with triple-negative breast tumors (TNBC), the risk of recurrence within 5 years of diagnosis were significantly higher compared with non–triple-negative subtypes, ($p<0.001$). Patterns in recurrence of breast cancer were seen during the first 5-7 years following diagnosis peaking at 3 years and quickly declining. The same study also reported that women with TNBC experienced a local recurrence at higher rates before a distant recurrence(11).

II. Patients and Methods

The aim was to evaluate molecular classification of breast cancer for prognosis and treatment outcome expresses as disease free survival at National Cancer Institute, Cairo University, through classifying non-metastatic breast cancer patients into five molecular subclasses.

A retrospective cohort study of all non-metastatic breast cancer patients diagnosed and/or treated at National Cancer Institute, Cairo University from January to December 2003. Clinical and Epidemiologic data werereviewed from medical records of all ages, all women consecutively presented with primary invasive breast cancer and undergoing treatment at National Cancer Institute, Cairo University from January to December 2003. Patients with distant metastasis detected at the time of surgery or within 4 months of surgery were excluded.

Follow up data: to calculate 10 years disease free survival DFS, patients' cohort of 2003 were followed up to end of 2014.

Pathologic data:all studied cases reviewed to confirm the diagnosis, status of ER, PR, and other tumor characteristics. The Pathological data were collected from pathology department. Immune-staining was performed on paraffin embedded tissue sections according to standard protocols. Evaluating IHC expression of markers ER, PR, Her2 neu, CK5/6, EGFR, and Ki67 were done.

End point disease-free survival (DFS) was calculated from date of surgical resection to the date of any of the following events: loco-regional recurrence, distant metastasis, or death. Treatment outcome is expressed as DFS.

III. Results

The distribution of molecular classification in our study group was found to be: luminal A representing 34%, luminal B 16.5%, luminal B Her2 enriched 10.7%, Her-2 enriched 12.4% and triple negative 26.4%. With a long term follow up of 10 years and after majority of patients have developed either local and / or systemic recurrences of the tumor. We found that more than half of patients had systemic recurrences 52.1%, while local recurrences occurred only in 37.2%

For local recurrences, pairwise comparisons revealed that patients with luminal Her-2 enriched, Her-2 enriched and triple negative were significantly more prone to local recurrences than those with luminal A, p value=0.04, 0.02 and 0.04 respectively. For any recurrences, pairwise comparisons between different molecular classes showed that only triple negative patients were more liable to any type of recurrences than luminal A, constituting 81.3% versus 36.6%. $p = 0.01$.

Disease free survival: After a median follow up period of 44.55 months ranges from (1.72 – 141.09 moths). The median DFS time in the present study was 35.68 with a range of (1.12 – 131.06). We found that the median disease-free survival (DFS) of female patients with breast cancer at NCI, 2003 was 47.4 months and the cumulative survival proportion was 61.3%, 47.9% and 20.9% at 3rd year, 5th year and 10th year, respectively.

Though median DFS of patients with luminal A class is 110.3 month which appears longer than those with Her-2 enriched and triple negative (48.9 and 35.9 month respectively), yet it's not significant $p = 0.132$.

The median time to local recurrence (TLR) in the present study was 88.4 months. Local recurrence free rate was 76.2 % at 3rd year, 68 % at 5th year and 39.9% at 10th year.

The time to local recurrence (TLR) was significantly different between different molecular classes, p= 0.005. The 5- years local recurrence rate of patients with luminal classes A was significantly higher 83.7 % than those with luminal Her-2 enriched, Her-2 enriched and triple negative (65.8%, 40.6% and 59.7% respectively), p=0.012, 0.001 and 0.004 respectively. Also, patients with luminal Her-2 enriched had a significantly higher 5- years local recurrence rate 65.8% than those with Her-2 enriched 40.6%, p=0.029.

The median time to distant metastasis (TDM) was 68.1 months. Distant metastasis rate was 67.1% at 3rd year, 53.4 % at 5th year and 31.3% at 10th year.

Though median TDM of patients with luminal classes A and B seem longer (110.3 and 62.9 months respectively) than those with Her-2 enriched and triple negative (48.9 and 39.9 months respectively), yet it's not significant p=0.26.

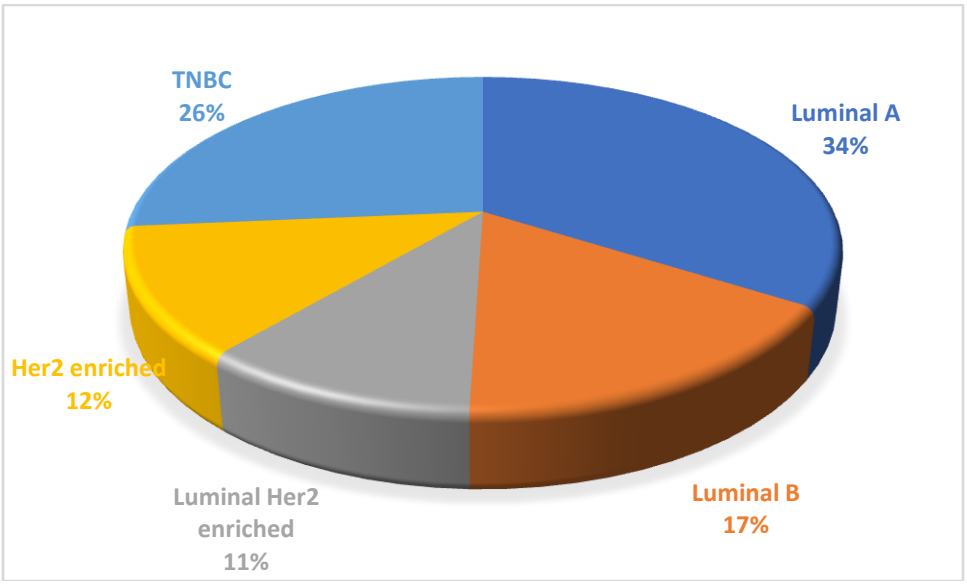

Figure 1. Distribution of molecular classification of non-metastatic breast cancer during 2003.

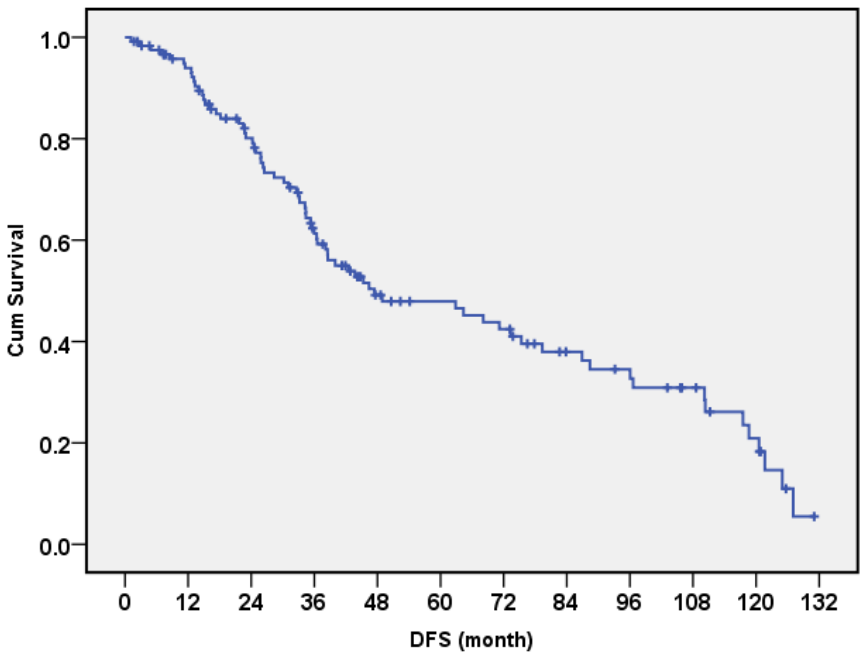

Figure 2. Disease free survival of non-metastatic breast cancer who were managed at NCI, 2003.

Table 1. Recurrence of breast cancer according to molecular classification:

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Recurrence Status		Total	Luminal A N= 41	Luminal B N= 20	Luminal Her2 enrihed N= 13	Her2 enriched N= 15	Triple Negative N= 32	P value
		No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	
Systemic recurrence	No	58 (47.9)	27 (65.9)	8 (40.0)	4 (30.8)	7 (46.7)	12 (37.5)	0.068
	Yes	63 (52.1)	14 (34.1)	12 (60.0)	9 (69.2)	8 (53.3)	20 (62.5)	
Local recurrence	No	76 (62.8)	35 (85.4)	13 (65.0)	6 (46.2)	6 (40.0)	16 (50.0)	0.003
	Yes	45 (37.2)	6 (14.6) (a)	7 (35.0) (ab)	7 (53.8) (b)	9 (60.0) (b)	16 (50.0) (b)	
Any recurrence	No	49 (40.5)	26 (63.4)	7 (35.0)	4 (30.8)	6 (40.0)	6 (18.8)	0.003
	Yes	72 (59.5)	15 (36.6) (a)	13 (65.0) (ab)	9 (69.2) (ab)	9 (60.0) (ab)	26 (81.3) (b)	

Table 2. Disease free survival and Time to local recurrence of breast cancer according to molecular classification

survival	Luminal A N= 41	Luminal B N=20	Luminal Her2 enriched N=13	Her2 enriched N=15	TNBC N=32	P value
DFS						
5 years	**62.7 ± 0.09**	**50.9 ± 0.11**	**51.9 ± 0.14**	**41.9 ± 0.16**	**32.9 ± 0.1**	
10 years	**46.4 ± 0.12**	_____	_____	**20.9 ± 0.17**	**13.1± 0.1**	**0.132**
Median	**110.3**	**62.8**	**64.4**	**48.9**	**35.9**	
TLR						
5 years	**83.7 ± 0.07**	**73.9 ± 0.11**	**65.8 ± 0.14**	**40.6 ± 0.16**	**59.7 ± 0.1**	
10 years	**77.3 ± 0.09**	**39.6 ± 0.16**	_____	**20.3 ± 0.16**	**28.7 ± 0.1**	**0.005**
Median		**88.4**	**64.4**	**48.9**	**71.2**	

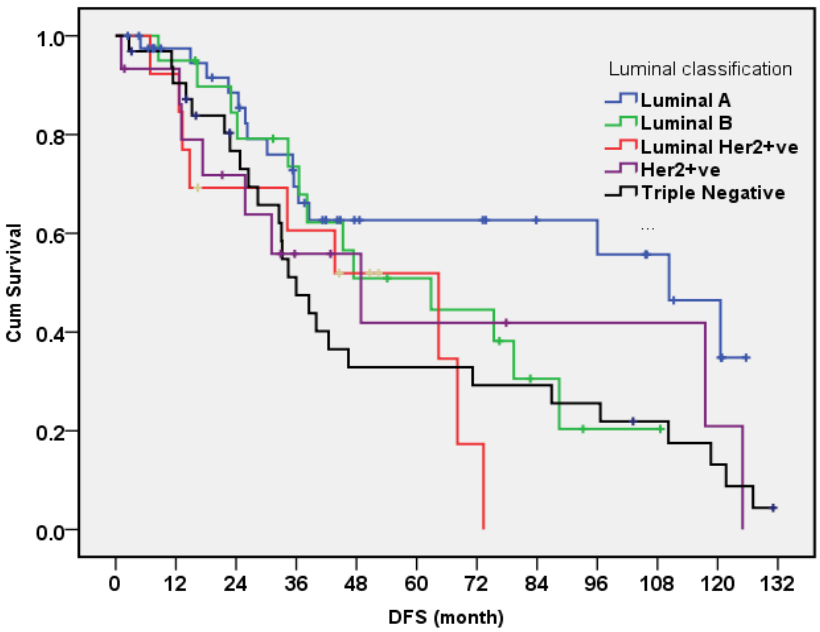

Figure 3. Disease free survival according to molecular classification.

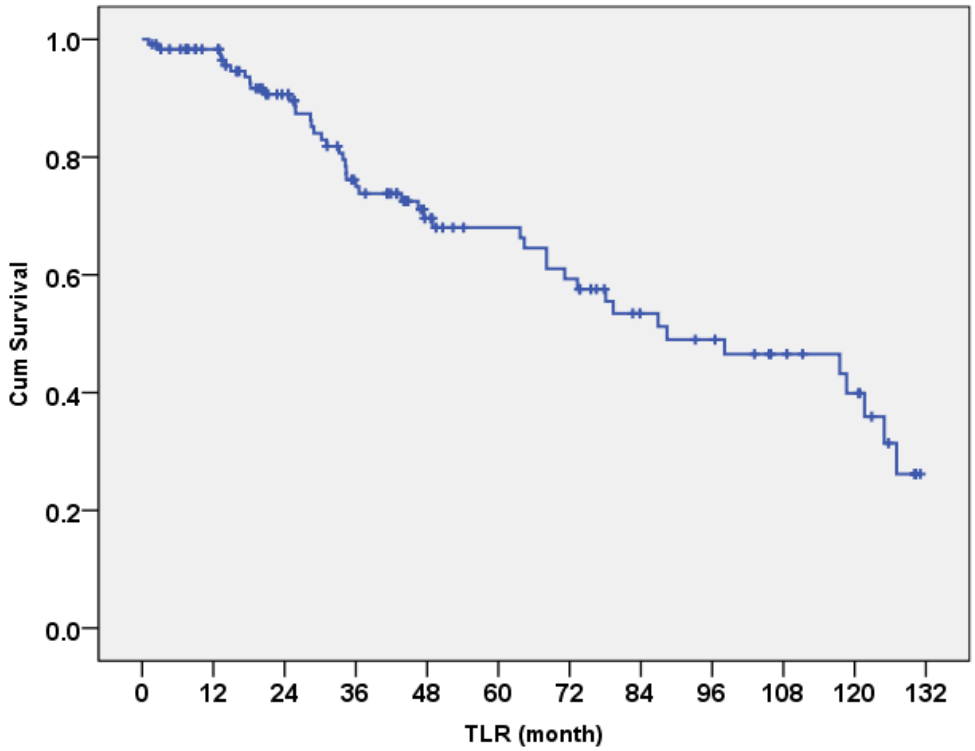

Figure 4. Time to local recurrence of non-metastatic breast cancer who were managed at NCI, 2003.

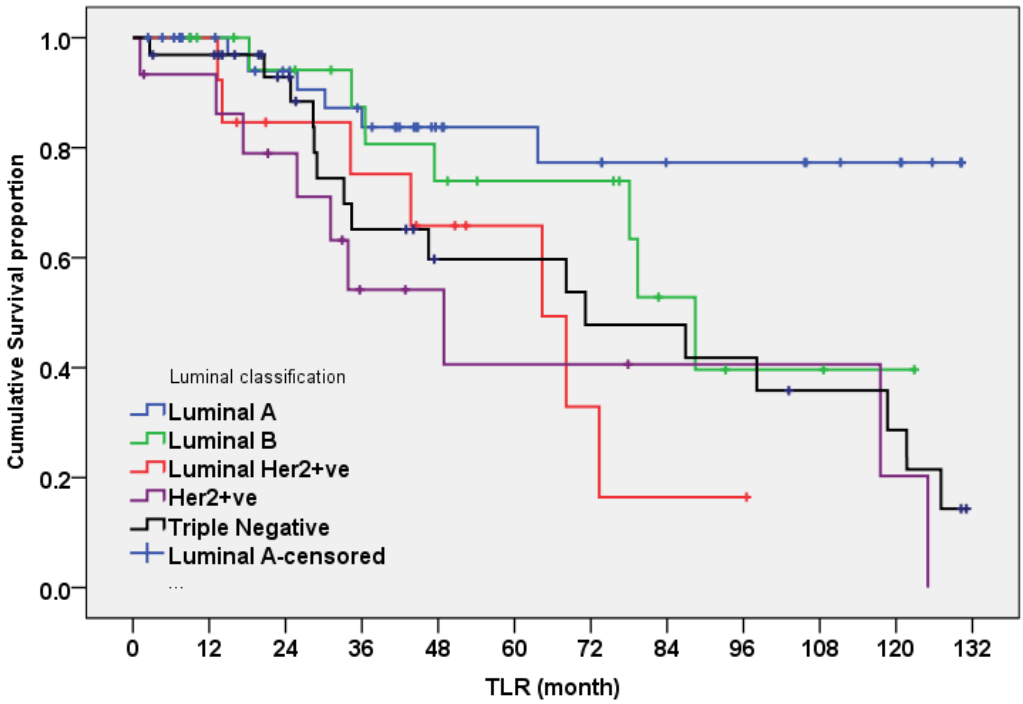

Figure 5. Time to local recurrence according to molecular classification.

IV. Discussion

Distribution of molecular classification:

In studying molecular classification of 121 females with non-metastatic breast cancer who were manged at NCI, Cairo University during 2003, we found the distribution of molecular classification to be: luminal A representing (34%), luminal B (16.5%), luminal B Her2 enriched (10.7%) Her-2 enriched (12.4%) and TNBC was (26.4%). This is similar to what was reported in a study done by Ihemelandu et al. 2007, on

142 African-American women. He found that luminal A constituted 50%, luminal B 14.1%, Her-2 enriched 12.7%, while triple negative represents 23.2%.

It was reported that the use of immune-histochemistry (IHC) as a proxy for DNA microarray classification. Studies established that it could reliably identify the major molecular classes of invasive breast carcinoma (13). This method represents a feasible alternative because many of the cases of breast cancer occur in places where analysis of prognostic factors needs to be economical, easy, and reproducible (14)

Another study showed the frequency of luminal A, luminal B, luminal B Her2 enriched, Her2 enriched and triple negative subtypes to be 35.5%, 22.5%, 13.1%, 13.7% and 15.2% respectively (15) .These figures were comparable to our results except for TNBC which were higher in our study. According to the American Breast Cancer Facts and Figures during 2015 distribution of molecular classes were totally different from previous studies as they found that luminal A represented 74%, Luminal B 10%, HER2-enriched 4% and TNBC 12% (16).

Exceptionally higher figures of TNBC was also found by an Egyptian study, which showed that TNBC frequency was (28.5%) (17).

Recurrence of breast cancer and molecular classes:

Breast cancer cohort of 2003 at NCI, Cairo was followed up till end of 2014. More than half of patients in the current study had systemic recurrences (52.1%), local recurrences in 37.2% and 59.5% had either local, systemic or both.

A study in Saudi Arabian women diagnosed at King Abdul-Aziz University, Jeddah, during years 2000-2008, found that 19% of breast cancer patients developed recurrences either local or distant and 15% of patients developed distant metastasis in different organs as liver, lungs or bones. (18). Rate of either local or distant recurrences in breast cancer Turkish patients was 30% in a study done as surveillance of the radiology imaging procedures, during the period January 2005 - July 2013 including 477 patients. Rate of local recurrences was 10.7% and distant metastasis occurred in 25.4% of patients (19). Another study in Turkey showed little higher figures to previous one as they reported the rate of both local and distant recurrences to be 37.8% (20).

In the present study, it was clear that recurrence rates either local, systemic or both were much higher than that found in other studies. That discrepancy could reflect differences in patient risk and prognosis including, age at diagnosis, stage at diagnosis, molecular classes, which is reflected on differences in treatment outcome and prognosis. Local recurrence was related to molecular classification. Results revealed that patients with luminal Her-2 enriched, Her-2 enriched and TNBC were more prone to local recurrences than those with luminal A, (adjusted p value=0.008, <0.001 and 0.004 respectively). Pairwise comparisons between different molecular classes showed that only TNBC was highly significantly liable to any type of recurrences than luminal A, constituting 81.3% and 36.6% respectively, $p<0.001$. This was similar to that reported in a recent study that TNBC had a particularly aggressive biological course, that strongly associated with local or distant recurrences, visceral metastases, and death in comparison with the other subtypes (21).

Incidence of distant metastases was 12.6 % in a large cohort of breast cancer patients who were referred to the Breast Unit of the University Hospital Mu´tua Terrassa and Hospital of Terrassa, University of Barcelona, between January 1, 1997 and January 31, 2014. It studied 1822 breast cancer patients. (22). Similar to what was found in the present study, Garcia et al, found that TNBC patients were significantly prone to metastasis (66.8%) compared to Luminal A class (20.1%). They also reported that Luminal A subtype patients showed significantly less rate of metastases than the rest of all other molecular classes, including luminal B HER2+ve patients ($p< 0.001$). The same study also found that luminal B patients showed significantly less rate of metastases than Her2 +ve ($p = 0.05$) and TNBC ($p<0.001$). There were no differences between Her2 +ve and TN patients (0.06)(22).

The bad prognosis of TNBC patients shown as higher rates of recurrences in those patients, which might be explained by either a more aggressive, rapid growth rate or intrinsic differences among women diagnosed with triple-negative breast cancer. Other studies provide additional evidence on differences between hormone receptor positive and hormone receptor negative breast cancer, not only in presentation, prognosis, and treatment, but also in etiology and natural history (23).

Molecular classes and disease-free survival:

For disease free survival DFS, the median follow-up time for breast cancer patients was 44.55 (1.72 – 141.09) months in the present study and median DFS time was 35.68 with a range of (1.12–131.06). Median disease-free survival for Luminal A class was 110.3 months as compared to 62.8 months for Luminal B, 48.9 months for Her2 +ve and 35.9 months for TNBC. For the whole study group, 5 years DFS estimate was 47.9%±0.05. Though at 5 years estimate of DFS of luminal A class looked higher (62.7%) as compared to Her-2 enriched and TNBC (41.9% and 32.9% respectively), yet not statistically significant, $p = 0.13$.

Estimates of DFS by Garcia et al, 2015 looked comparable to the present study (though ours were not significant), where they reported that luminal A subtype had significantly higher median DFS (80.7 months) than luminal B (58.2 months), Her2 +ve (60.7 months), and TNBC (63.8 months) ($p = 0.006$, $p = 0.008$ and $p<0.001$ respectively). Luminal B patients did not differ from Her2 +ve , but were significantly different from TNBC ($p< 0.001$) (22). Differences in significance of results could be explained by the large cohort studied by Garcia et al, 2015 compared to the present study.

Another study showed differential DFS according to molecular subtypes, where patients with luminal A tumours had the most favourable prognosis, with 5 years DFS (87.4%) which is significantly better than Her-2 enriched (65.5%) (24). For TNBC according to a study done in Iran on 180 TNBC patients, 5 years DFS was 71% (25) compared to 32.9% in the present study.

For time to local recurrence TLR, the five-year TLRin our study is 68% ± 0.05. This was less than that reported by Jia et al, 2014 which was 90.5%. In that study loco-regional recurrence occurred less frequently for luminal A tumours and consecutively they had the higher TLR (93.2%) when compared with the other molecular subtypes, p=0.016 (24). This is in comparison to the present study results, as the five years' TLR in Luminal A was 83.7 %, Luminal B 73.9%, Her2 +ve 40.6% and TNBC 59.7%. While three years TLR was Luminal A was 87.2 %, Luminal B 87.4%, Her2 +ve 54.2% and TNBC 65.1%, p value= 0.005.

A recent study in 2018 showed that three years TLR in Luminal A was 100%, Luminal B 93.3%, Her2 +ve 87.5% and TNBC 96.4% (26).

V. Conclusion

A cohort on females with non-metastatic breast cancer were managed at NCI during the year 2003 and evaluated according to molecular classes. Most common class was Luminal A (34%), and least was Luminal B HER2 enriched (10.7%).TN and HER2 enriched being more aggressive tumours were significantly associated with higher recurrence rate than other luminal classes ($p = 0.003$). The median DFS was 47.4 months. The median TLR of all patients was 88.4 months. The 5-year TLR was significantly longer in luminal class A (83.7%) than HER2 enriched (40.6%), p=0.001.

References

[1]. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA Cancer J Clin. 2011;61(4):212–36.
[2]. www.cancerregistry.gov.eg
[3]. Schnitt SJ. Classification and prognosis of invasive breast cancer: from morphology to molecular taxonomy. Mod Pathol. 2010;23 Suppl 2:S60–4.
[4]. Journal R, Raica M, Jung I, Cîmpean AM, Suciu C, Mureşan AM. From conventional pathologic diagnosis to the molecular classification of breast carcinoma: are we ready for the change? Rom J Morphol Embryol. 2009 Jan;50(1):5–13.
[5]. Dabbs DJ, Chivukula M, Carter G, Bhargava R. Basal phenotype of ductal carcinoma in situ: recognition and immunohistologic profile. Mod Pathol. 2006;19(11):1506–11.
[6]. Reis-Filho JS, Westbury C, Pierga J-Y. The impact of expression profiling on prognostic and predictive testing in breast cancer. J Clin Pathol. 2006;59(3):225–31.
[7]. Cancer EB. O ncologist. Gynecol Oncol. 2007;0:1–10.
[8]. Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. 2000 Aug 17;406(6797):747–52.
[9]. Carey LA. Molecular intrinsic subtypes of breast cancer. In: Daniel H, editor. Uptodate. 2011.
[10]. Chen C, Yuan JP, Wei W, Tu Y, Yao F, Yang XQ, et al. Subtype classification for prediction of prognosis of breast cancer from a biomarker panel: Correlations and indications. Int J Nanomedicine. 2014;9(1):1039–48.
[11]. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: Clinical features and patterns of recurrence. Clin Cancer Res. 2007;13(15):4429–34.
[12]. Ihemelandu CU, Leffall LD, Dewitty RL, Naab TJ, Mezghebe HM, Makambi KH, et al. Molecular Breast Cancer Subtypes in Premenopausal and Postmenopausal African-American Women: Age-Specific Prevalence and Survival. J Surg Res. 2007;143(1):109–18.
[13]. Peppercorn J, Perou CM, Carey L a. Molecular subtypes in breast cancer evaluation and management: divide and conquer. Cancer Invest. 2008;26(1):1–10.
[14]. Zepeda-Castilla EJ, Recinos-Money E, Cuéllar-Hubbe M, Robles-Vidal CD, Maafs-Molina E. [Molecular classification of breast cancer]. Cir Cir. 2008;76(1):87–93.
[15]. Li J, Chen Z, Su K, Zeng J. Clinicopathological classification and traditional prognostic indicators of breast cancer. Int J Clin Exp Pathol. 2015;8(7):8500–5.
[16]. DeSantis C, Siegel R, Jemal A. Breast cancer facts and figures. American Cancer Society. Elsevier; 2015. 352-359 p.
[17]. El-Hawary AK, Abbas AS, Elsayed AA, Zalata KR. Molecular subtypes of breast carcinoma in Egyptian women: clinicopathological features. Pathol Res Pract. 2012 Jul 15;208(7):382–6.
[18]. Buhmeida A, Al-maghrabi J, Merdad A, Al-thubaity F, Chaudhary A, Gari M, et al. Nuclear Morphometry in Prognostication of Breast Cancer in Saudi Arabian Patients : Comparison with European and African Breast Cancer. 2010;2192:2185–91.
[19]. Ursaru M, Jari I, Negru D, Scripcariu V. Local and Distant Recurrences - A Comparative Study on Conservative and Radical Surgery for Breast Cancer. 2015;(1):38–42.
[20]. Shahriari-Ahmadi A, Arabi M, Payandeh M, Sadeghi M. The recurrence frequency of breast cancer and its prognostic factors in Iranian patients. Int J Appl Basic Med Res. 2017;7(1):40.
[21]. Tun NM, Villani G, Ong K, Yoe L, Bo ZM. Risk of having BRCA1 mutation in high-risk women with triple-negative breast cancer: a meta-analysis. Clin Genet. 2014 Jan;85(1):43–8.

[22]. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S, et al. Differential patterns of recurrence and specific survival between luminal A and luminal B breast cancer according to recent changes in the 2013 St Gallen immunohistochemical classification. Clin Transl Oncol. 2015;17(3):238–46.
[23]. Bouchardy C, Benhamou S, Fioretta G, Verkooijen HM, Chappuis PO, Neyroud-Caspar I, et al. Risk of second breast cancer according to estrogen receptor status and family history. Breast Cancer Res Treat. 2011 May;127(1):233–41.
[24]. Jia W-J, Jia H-X, Feng H-Y, Yang Y-P, Chen K, Su F-X. HER2-enriched tumors have the highest risk of local recurrence in Chinese patients treated with breast conservation therapy. Asian Pac J Cancer Prev. 2014;15(1):315–20.
[25]. Yousefi Kashi AS, Yazdanfar S, Akbari M-E, Rakhsha A. Triple Negative Breast Cancer in Iranian Women: Clinical Profile and Survival Study. Int J Cancer Manag. 2017 May 2;10(8).
[26]. Wadasadawala T, Mondal M, Paul SN, Parmar V, Nair N, Shet T, et al. Should molecular subtype be recommended as one of the selection criteria for accelerated partial breast irradiation? Preliminary results from an Asian cohort. J Contemp Brachytherapy. 2018;10(1).

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