



Cohort Study

Association of socioeconomic status with the clinical management and outcomes in young patients (≤ 35 years) diagnosed with breast cancer: A retrospective analysis



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A B S T R A C T

Background: Very young breast cancer at 35 years or younger is rare and tends to be aggressive. The management of very young breast cancer should be equally aggressive, and early diagnosis is critical. We hypothesized that socioeconomic status (SES) is associated with how very young breast cancer (VYBC) patients are diagnosed and treated in our community.

Methods: We retrospectively analyzed a database for invasive breast cancer or ductal carcinoma in-situ (DCIS) diagnosed ≤ 35 years old (VYBC) from both a government-run county hospital (CH) and a neighboring private hospital (PH) for 82 months. Inclusion criteria composed of female patients diagnosed with invasive breast cancer and DCIS at ≤ 35 years of age at diagnosis were examined in our analysis. Patient diagnoses and severity, treatment, and outcomes were compared between the two facilities. The methods are consistent with the STROCSS guidelines.

Results: The incidence of VYBC was a significantly higher percentage of new breast cancers diagnosed in the CH at 5.4% as compared to the PH at 1.9% (OR: 2.94; $p < 0.001$). CH had a significantly higher proportion of Medicaid payers (73% CH vs. 21% PH, $p < 0.001$). Mean time from patient's initial symptoms until a tissue diagnosis was significantly longer at the county hospital at 9.6 months vs 2.1 months at the private hospital ($p < 0.01$). Stage I tumors were only found in 13% of county hospital patients versus 67% at the private hospital ($p < 0.001$). Approximately 63% of the patients at the government-run county facility had a relative delay in diagnosis, contributing to higher stage at presentation. The rate of mastectomy surgery was high at both institutions: CH 83% vs. PH 76% ($p = NS$).

Discussion: The results of our study suggest a significant healthcare difference between county and private hospital systems among very young breast cancer patients. Patients at the county hospital system had a longer delay to diagnosis leading to worse outcomes. This difference may be a reflection of barriers in health literacy or access to medical care.

1. Introduction

Most breast cancers occur at an average age of 62 years [1]. Very young breast cancer at 35 years or younger is rare and has distinct biological behavior [2]. Young patients frequently present with aggressive, poorly differentiated tumors that are often triple-negative or human epidermal growth factor receptor-2 (HER2)-positive and commonly driven by genetic mutation such as the breast cancer gene (BRCA) [1,3–5]. Studies even suggest that hormone-positive, HER2-negative tumors in young patients carry a worse prognosis when compared to similar tumors in an older population [2,6]. Surgical treatment in young women often involves high rates of mastectomies and adjuvant and neoadjuvant chemotherapy although breast-conserving therapy and radiation in indicated cases do not lead to lower survival [7–9]. Previous studies demonstrate a delay in diagnosis

among young women [1,10,11]. Factors contributing to delayed diagnosis include younger age, lower perceived risk, cost, and lack of higher education [10,12]. We hypothesized that socioeconomic status contributes to differences that may exist in how very young breast cancer patients are diagnosed and treated in our community.

This study examined female patients with invasive breast cancer or DCIS diagnosed at age 35 years or younger. We compared patients from neighboring government-run county hospital and a private hospital systems to discern differences between disease characteristics and treatment patterns.

2. Materials & methods

We retrospectively queried a prospectively maintained database over 82 months spanning 2013–2019 for invasive breast cancer or ductal

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carcinoma in-situ (DCIS) diagnosed ≤ 35 years old (very young breast cancer, VYBC) from both a county hospital (CH) and a neighboring private hospital (PH). Inclusion criteria was composed of female patients in this database who were diagnosed with invasive breast cancer or DCIS at age 35 years or younger. Male patients, female patients older than 35 years at time of diagnosis or patients with diagnoses other than invasive ductal carcinoma or DCIS were excluded from the study. Data on patient insurance, clinical presentation at diagnosis, tumor composition, treatment, and outcomes were compared. The data distributions of the two groups were assumed normal and similar, so two-tailed student's t-tests were done. Statistical significance was set at 0.5. SPSS Premium Grad Pack Version 23 was used for statistical analysis. Institutional Review Board approval was obtained for this study via Ventura County Institutional Review Board Study 272: Breast cancer under 40 (IRB #272).

3. Results

Table 1 shows the important outcomes of our study. The incidence of VYBC was a significantly higher proportion of new breast cancers diagnosed in the CH at 5.4% ($n = 30$ of 558 new cancers) as compared to the PH at 1.9% ($n = 21$ of 1100 new cancers) (OR: 2.94; $p < 0.001$). CH had a significantly higher proportion of Medicaid (73% CH vs. 21% PH, $p < 0.001$). DCIS alone was found in 10% ($n = 3/30$) of CH and 5% ($n = 1/21$) of PH patients ($p = NS$). CH cancers had a higher average Ki67 (53% CH vs. 37% PH, $p = 0.04$). HER2-positive or triple-negative cancers were found in 52% of CH patients (14 of 27) and 65% of PH patients (13 of 20) ($p = NS$). Neoadjuvant chemotherapy was commonly used (38% CH vs. 50% PH, $p = NS$). Self-palpated mass was the presenting symptom in 87% at CH and 90% at PH ($p = NS$). Time from patient's initial symptoms until a tissue diagnosis was significantly longer at CH (mean 9.6 months CH vs 2.1 months PH, $p < 0.01$). Stage I tumors was only found in 13% of CH patients versus 67% at PH ($p < 0.001$). Of the CH patients, 63% had a delay in diagnosis of ≥ 2 months attributable to patient delay in seeking care after symptoms started whereas 27% were due to physician/radiology delays. The rate of mastectomy surgery was high at both institutions. At the CH a large majority, 83% ($n = 25$), underwent a mastectomy, and 68% ($n = 17$) of those also had a contralateral prophylactic mastectomy so were bilateral mastectomies. The PH also had a very high rate of mastectomy surgery with 76% undergoing a mastectomy ($n = 16$ of 21) and 56% ($n = 9$) of those were bilateral mastectomies (mastectomy rate 83% CH vs. 76% PH, $p = NS$). VYBC should all have qualified for genetic testing. At the CH, 100% of the patients were offered genetic testing and 37% ($n = 11$) tested positive for deleterious genetic mutations. The PH had a lower rate of genetic testing with only 29% (6 of 21) having documented testing - of those tested 5 of 6 (83%) were positive. We were unable to determine

Table 1
Comparison of outcomes between County Hospital and Private Hospital.

Variable	County Hospital (CH)	Private Hospital (PH)	P-value
Incidence of VYBC	5.4%	1.9%	<0.001*
Medicaid insured	73.0%	21.0%	<0.001*
DCIS alone	10.0%	5.0%	NS
Average Ki67%	53.0%	37.0%	0.04*
HER2+ or TNBC	52.0%	65.0%	NS
Neoadjuvant chemotherapy	38.0%	50.0%	NS
Self-palpated mass	87.0%	90.0%	NS
Time to tissue diagnosis	9.6 months **	2.1 months**	<0.01*
Stage I at diagnosis	13.0%	67.0%	<0.001*
Mastectomy performed	83.0%	76.0%	NS
Rate of genetic mutation	37.0%	83.0%	NS

Note. *Significance level set at < 0.05 , **Mean time in number of months. Triple Negative Breast Cancer (TNBC), Very Young Breast Cancer (VYBS), Human Epidermal Growth Factor Receptor 2 (HER2), Ductal Carcinoma in Situ (DCIS), Not Significant (NS).

the cause of the lower rate of testing at the PH but if no genetic testing result or evidence of referral to a genetic counselor was found, we considered this a non-tested patient.

4. Discussion

The CH had a higher incidence of VYBC and more Medicaid reflecting an overall younger and less-insured population. (Fig. 1). VYBC are biologically aggressive tumors, and early diagnosis is paramount. Our study showed that VYBC in both CH and PH patients has aggressive behavior with over half of all patients being HER2 or triple-negative or requiring neoadjuvant chemotherapy. Previous literature mirrors this finding as younger women have higher-grade tumors, less hormone positivity, more HER2 overexpression, and more lymph node involvement [13]. Although we did not study long-term survival, the literature has found that even for estrogen receptor-positive and HER2 negative tumors in young women that the prognosis is worse when compared to similar tumors in older patients [2,14]. When facing a VYBC patient, innovative treatment strategies, such as optimal ovarian suppression and novel therapies, should be considered even in those tumors with what would normally be considered less aggressive phenotypes.

In our study, a significant delay was observed between the initial onset of suspicious findings noticed by the patient and a tissue diagnosis (9.6 months at the CH vs. 2.1 months at the PH, Fig. 1). At the CH, this is attributable in 63% of cases by patient delay in seeking or obtaining medical care. CH patients were five times less likely to be diagnosed with Stage I disease. Stage I tumors were only found in 13% of CH patients versus 67% at PH ($p < 0.001$) (Fig. 1). A study of young breast cancer patients in a California state-wide tumor registry showed that African American women, those with public or no insurance, and those with low socioeconomic status had a longer treatment delay time and this led to a worse prognosis [15]. Since many of the biologic behaviors of the tumors in VYBC patients were similar between the hospital systems in our study, the higher stage at presentation seen in the CH is likely attributable in part to delays in diagnosis and treatment. While there is no "easy fix" for an issue such as this, efforts can be focused on sweeping education of patients and healthcare providers of the existence and unique factors of breast cancer in this young population.

We found that the vast majority of VYBC patients among both systems found their tumors by self-palpation. This is expected, as these patients were all younger than 35 and unlikely to have screening breast imaging at that age. As expected, we found that patients in the safety-net county hospital system had more government-based insurance and likely many of these were uninsured prior to diagnosis and were only granted emergency Medicaid after a cancer diagnosis (Fig. 1). Poor access to primary care physicians and a lower level of health literacy would be expected in a young population at a county safety-net hospital and the patient-driven delay in seeking care more reflects a health care delivery issue rooted in socio-economic disparity. We, unfortunately, do not have a way to capture health literacy in a retrospective study such as this. We also expected a certain percentage of delay between initial symptoms and tissue diagnosis to be due to a low suspicion for breast cancer in such a young patient population by health care providers. Of the CH patients with a delay in diagnosis of ≥ 2 months, 27% were due to physician/radiology delays. Previous literature has also shown that even after young breast cancer patients have accessed medical care, the low level of suspicion on the part of healthcare providers still leads to delays in diagnosis especially in the postpartum period or if a nonspecific billing code is used [11]. There is also room to improve awareness among healthcare providers that county hospital systems have a significant proportion of very young patients with breast masses that turn out to be cancerous - an incidence of 5% found over 7 years in our study.

It is expected that a woman who develops breast cancer at a young age would be at risk for harboring a genetic mutation. NCCN guidelines recommend genetic testing of any patient diagnosed with breast cancer under the age of 45 [16]. At the CH, all VYBC patients had genetic

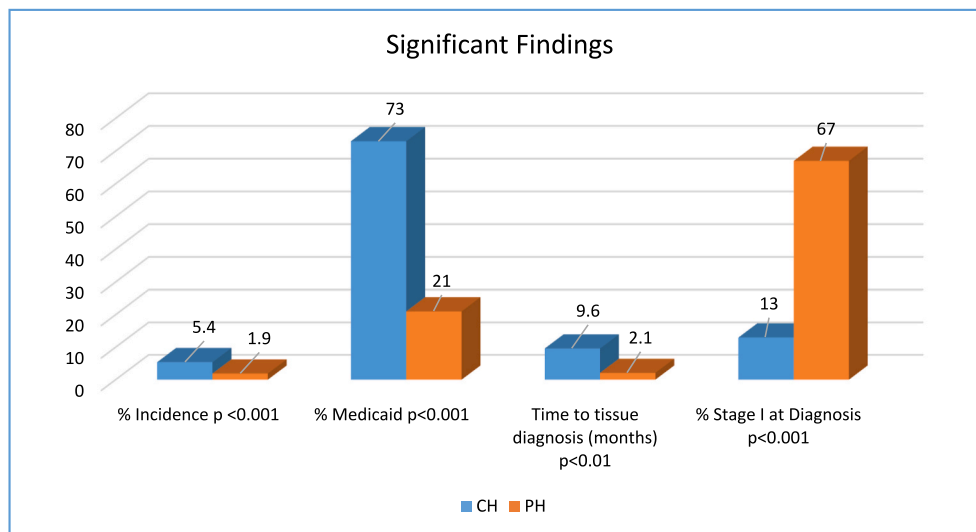


Fig. 1. Significant Findings between CH and PH patient populations.

testing and 37% tested positive for deleterious genetic mutations. The PH had a lower rate of genetic testing but found that, of the 29% of overall VYBC patients tested, 83% were positive. We could not determine why the private hospital had less documented genetic testing although one would expect all VYBC patients should be strongly considered for genetic testing in the current era. Based on our findings, one could expect anywhere from 40 to 80% of those genetic tests may be positive although we are increasingly discovering new mutations such as CDH1, PALB2, and PTEN that drive young-onset breast cancer so the incidence of deleterious genetic mutations is likely to go up in the future [16].

Mastectomy surgery was performed frequently in VYBC patients at both institutions. At the CH, 83% underwent a mastectomy and 68% of those had a contralateral prophylactic mastectomy so were bilateral mastectomies. The PH also had a very high rate of mastectomy surgery with 76% undergoing a mastectomy and 56% of those were bilateral mastectomies. The decision to undergo mastectomy, either unilateral or bilateral, was equivalent between county hospital and private hospital patients in our study. This rate is higher than what would be expected for bilateral prophylactic mastectomy based solely on genetic testing. Bilateral mastectomy rates are increasing in general over the past several decades. The high rate of mastectomy partially reflects a higher stage of disease in VYBC patients, but also this trend shows a more unilateral and bilateral mastectomy rate even in patients considered candidates for breast conservation surgery and without deleterious genetic mutations [17]. Many treating physicians likely fear future recurrence risk when dealing with a very young breast cancer patient regardless of genetic testing results. To delve into this issue, the POSH study (Prospective study of Outcomes in Sporadic vs. Hereditary breast cancer) looked at over 3000 women with breast cancer under the age of 40 in the UK. The POSH study found that surgical extent was less important for distant disease-free intervals than ensuring negative surgical margins and appropriate use of radiotherapy [18]. In a properly selected VYBC patient, breast-conserving therapy with radiation should not be deemed inferior in terms of survival. Unfortunately, the data does show a higher local recurrence risk after breast-conserving surgery which is a difficult hurdle to overcome in discussions about long-term outcomes given the lack of competing factors for mortality in these young patients [18]. As most breast surgeons know, however, the decision for bilateral mastectomy is often patient-driven more than data-driven. This phenomenon seems to affect both county and private hospital patients equivalently in our study.

Weaknesses of our study include the retrospective nature. We found it difficult to ascertain the cause of delays in diagnosis or treatment.

Surrogates such as the time between initial physician contact or patient-reported symptoms and tissue diagnosis were used as objective data. The time from initial patient symptoms was gleaned from chart review but is subject to reporter and recall bias. The CH has an integrated electronic medical record system so that data from various specialties such as surgery and medical oncology could be found in a single location. The PH used more private physician offices, many of which did not use an integrated electronic medical record system making chart review more challenging and likely is the cause of data fall-out such as in the case of genetic testing in the PH patients. Additionally, the low incidence of VYBC led to relatively small patient numbers, which weakened our statistical analysis.

5. Conclusions

VYBC has distinct biological and socioeconomic factors. The results of our study suggest a significant difference among very young breast cancer patients between CH and PH systems in our community as the CH patients suffered longer times to diagnosis and higher stage disease at diagnosis. This disparity seems largely driven by patient delays in seeking or obtaining care and may reflect barriers in health literacy or initial access to medical care. We also found a trend towards aggressive surgery such as bilateral mastectomies that affected patients in both types of healthcare delivery systems. Widespread education about the incidence and treatment of breast cancer in this unique patient population should be targeted not only at the public but also towards healthcare providers.

Ethical approval

Ventura County Board of Education #272.

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None.

Author contribution

Dr. Shawn Steen: principal investigator.
 Dr. Zoe Birnbaum: writing of the manuscript.
 Dr. Graal Diaz: statistician.
 Dr. Thomas Duncan: provider and analysis.
 Dr. Garrett Jones: data collector.
 Dr. Javier Romero: provider and analysis.

Research registration number

1. Name of the registry: Ventura County Board of Education Institutional Review Board
2. Unique Identifying number or registration ID: #272
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Dr. Shawn Steen.

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Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104524>.

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