Examining the Completeness of Breast Cancer Pathology Reports Registered in the Population-Based Cancer Registration System in Iran during 2016 to 2018

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Abstract

Background: Ensuring the comprehensive and accurate representation of data within cancer registries holds paramount significance across various facets of public health decision-making. This study delves into the evaluation of data completeness in breast cancer (BC) pathology reports within a population-based cancer registration system in Iran, spanning the period from 2016 to 2018.

Methods: Employing a retrospective and descriptive analytical approach, we harnessed secondary data extracted from pathology reports encompassing breast cancer diagnoses, which were duly recorded in the Integrated Cancer Information Management System database during 2016-2018. A total of 4000 pathology reports were thoughtfully selected from each of the three years. The spectrum of pathology information encompassed tumor type, site grade, size (T), and involvement of lymph nodes (N). Summary statistics were provided as percentages of categorical variables and mean with standard deviation of continuous variables. A comparison of categorical variables was performed using the Chi-squared test.

Results: The participants' mean age was 51.8±12.5 years. Among the 12,000 studied patients, 5744 (47.9%) were ≤ 50 years old, 5233 (43.6%) were 50-69 years old, and 1023 (8.5%) were >60 years old. The completeness of BC pathology reports varied for different variables. Interestingly, the completeness of these variables increased with older age groups. The proportion of specific tumor types differed significantly among age groups (P = 0.001). Notably, the prevalence of invasive ductal carcinoma was higher in the ≤ 50 years age group compared to the older cohorts. Likewise, notable variations in tumor sizes were observed (P = 0.009), with a higher prevalence of missing tumor size data noted in the age group ≤ 50 years. On the other hand, pathologic T stage also demonstrated age-dependent variations (P = 0.014), indicating a higher prevalence of missing stages in the ≤ 50 years age group. Finally, tumor grade exhibited a statistically significant difference (P < 0.001), with a higher proportion of grade 1 tumors observed in the 50-69 years age group.

Conclusion: Tumor grade had the highest completeness rate, while tumor size, pathologic T stage, and pathologic N stage had the lowest. Therefore, a good understanding of completeness of pathology reports, as well as improvement in the registration of stage, integrated system at the national level for BC is warranted.

Keywords: Completeness, Pathology report, Breast cancer, Iran

Conflicts of Interest: None declared

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Introduction

Breast cancer (BC) stands as one of the most frequently diagnosed malignancies in females, with a projected count...
of over 2.2 million new cases worldwide in 2020. Notably, BC ranks as the fifth leading cause of cancer-related mortality in women and also affects a noteworthy proportion of men. GLOBOCAN 2020 findings underscore an age-standardized incidence rate (ASIR) of 35.8 per 100,000 person-years for BC, constituting 12.9% of all new cancer cases (1). The trajectory of ASIR has exhibited a slight increase from 1990 to 2019 (2). Predictions for the year 2040 anticipate a surge in new BC cases surpassing 3 million, accompanied by over 1 million deaths, amplifying the impending disease burden (3). Distinct regional variations in BC incidence emerge, with East Asia reporting the highest incident cases and North America witnessing the highest ASIR attributed to BC in 2019. Notably, North Africa and the Middle East have experienced a significant surge in BC incidence over the past three decades, particularly impacting younger populations in developing nations (2, 4).

Of particular concern is Iran, where cancer holds the second rank among chronic noncommunicable diseases, and BC alone accounts for 21.4% of all prevalent cancers (5). Iranian females have experienced a remarkable rise in ASIR for BC between 1990 and 2019 (6). GLOBOCAN reports have further highlighted BC's ascendency as the leading cancer type in Iran in terms of new cases, fatalities, and 5-year prevalence in 2020, posing a substantial public health challenge (1, 7). A comprehensive understanding of BC's distribution across provinces has been garnered through extensive studies in Iran over the past decades, revealing uniform incidence rates (8-16). Notably, a cross-sectional study rooted in Iran's cancer registry report identified the highest BC incidence in Isfahan, Yazd, Gilan, and Alborz province (17).

In the context of BC management, the accurate recording of surgical findings, injury identification, diagnosis, and prognosis plays a pivotal role in facilitating informed patient treatment decisions. A surgical identification injury report necessitates the documentation of cancer presence, type, grade, size, local extent, vascular involvement, margin status, and, at times, tumor markers. Pathological factors, including tumor invasion, prognosis, treatment responses, and outcome prediction, heavily influence treatment decisions (18, 19). Vital to the selection of optimal and effective treatment approaches is the comprehension of tumor spread and severity at diagnosis. This mandates that pathology reports be characterized by timeliness, precision, comprehensiveness, and utility. In addition to precision, the promptness and turnaround time of cancer pathology reports hold significance. The completeness of a cancer pathology report serves as a pivotal indicator of overall quality. Accurate presentation of these facets within a pathology report, alongside pertinent information for diagnosis and prognosis, fosters the selection of the most fitting treatment modality for the afflicted individual (20-23).

A comprehensive pathology report concerning breast surgical specimens assumes critical importance in discerning the benign or malignant nature of lesions, ensuring surgery's completeness, gauging the risk of cancer recurrence, and guiding the selection of suitable treatments (24-26). An adept breast cancer team involves a radiologist, surgeon, histopathologist, physician, and radiation oncologist. The patient undergoes sequential evaluation by a radiologist, followed by a breast surgeon and subsequently a histopathologist. The surgeon and histopathologist's close collaboration is essential to furnish an accurate and all-encompassing pathology report for breast cancer surgery. Histopathological reports relating to breast cancer furnish oncologists with pivotal insights indispensable for patient care, allowing the determination of disease stage, prognosis estimation, future treatment strategy formulation, and outcome prediction. Within this multidisciplinary paradigm, the surgeon assumes a critical role, as the quality of a surgical pathology report hinges on its precision and comprehensiveness (27). Upholding international standards and quality within clinical laboratories assumes paramount significance. A breast surgeon's responsibility encompasses the procurement of appropriately labeled specimens, their comprehensive reporting, and engagement with histopathologists to yield meticulous analyses. The meticulous interpretation of surgical pathology reports by oncologists forms an integral aspect of patient management decisions (26). Furthermore, maintaining clinical laboratory quality entails satisfying physicians' expectations and providing surgical pathology reports that meet their standards (28, 29).

Given the absence of studies on this topic in Iran, this research delves into the completeness of breast cancer pathology reports registered in the population-based cancer registration system from 2016 to 2018. The study aims to scrutinize the efficiency of the pathology report registration system with the expectation that the identification of existing shortcomings will catalyze improvements in pathology report quality, thereby enhancing the development of tailored cancer treatment protocols.

Methods

Data sources

This study adopts a cross-sectional pathology-based approach to investigate patients with breast cancer. The dataset comprises 8940, 10091, and 12127 pathology reports registered in 2016, 2017, and 2018, respectively. The chosen sample size encompasses 12000 pathology reports. Employing a simple random sampling methodology, 4000 pathology reports were systematically selected for each year from the Integrated Cancer Information Management System, also known as Sima Cancer.

The primary data sources within the population-based cancer registration system encompass pathology centers, hospitals, and the death registration unit under the purview of the vice-chancellor of health. Pathology reports find their repository within the Integrated Cancer Information Management System (Sima Cancer), an entity established by the Ministry of Health, Treatment, and Medical Education. This system encompasses comprehensive patient details, including personal information such as name, surname, gender, place of residence, date of birth, and occupation, as well as insurance specifics such as insurance type, insurance number, and validity date. The registration of cancer case reports bifurcates into two segments: the first section pertains to tumor-related information, encompassing tumor type, tumor site, tumor size, maximum tumor diameter,
pathologic T stage, pathologic N stage, number of resected lymph nodes, number of implicated lymph nodes, surgical margin status, lymphatic vascular invasion, peripheral nerve invasion, gene mutation data, cancer grade, estrogen receptor status, progesterone receptor status, and human epidermal growth factor receptor 2 status. The second section pertains to cancer registration sources, encompassing affiliations with universities and centers. The current study implements the Framework for Specialist Minimum Data Set Development for Specific Cancers in Clinical Cancer Registration to design and employ the minimum data set of the pathology report (28). Ethical clearance for this study was granted by the Research Ethics Committee of Iran University of Medical Sciences, Tehran, Iran (IR.IUMS.REC. 1400.878).

Completeness Assessment
The focal point of this study revolves around the assessment of completeness, achieved by ascertaining the frequency and proportion of available data within clinical pathology reports across distinct age categories (≤ 50, 50-60, and > 60 years). The Chi-squared test emerged as the method of choice for assessing differences between these groups. All data were meticulously entered and subjected to analysis utilizing STATA 13.0 (StataCorp LLC, College Station, TX). Statistical significance was attributed to P-values below 0.05.

Results
This study embarks on a comprehensive examination of surgical pathology reports concerning 12,000 individuals diagnosed with breast cancer within the period of 2016 to 2018. The encompassed age spectrum spans from 15 to 96 years, with an average age of 51.8±12.5 years. Notably, the highest frequency of age distribution was noted among individuals below the age of 50. Among the studied patients, 11,817 (98.5%) were females, while 183 (1.5%) were males. The analysis embraced 2,709 pathologies from government centers and 9,291 reports from private centers. Health insurance coverage was evident for 94.6% of the patients, while 5.4% remained uninsured (Table 1).

The scrutiny of surgical pathology reports originating from breast cancer patients revealed intriguing frequency distributions among the evaluated parameters. The disclosure of cancer grade demonstrated full coverage at 100% for all 12,000 reports. Notably, favorable figures were observed for tumor site (10942; 91.2%), tumor grade (9575; 79.8%), tumor size (4427; 36.9%), tumor type (9575; 79.8%), lymphatic vascular invasion (4200; 35.0%), perineural invasion (3429; 28.6%), margin status (4345; 36.2%), ER status (1370;11.4%), PR status (1358;11.3%), and Her2 status (786;6.6%).

The frequency distribution of tumor size across all age groups, manifesting as 27 (0.4%), 26 (0.5%), and 8 (0.8%) instances. The frequency distribution of tumor size revealed age-specific disparities, with the highest frequencies noted in age groups ≤ 50 (3721; 64.8%), 50-69 (3415; 65.3%), and >60 years (650; 63.5%). Similarly, the upper outer quadrant emerged as the predominant tumor site across all age groups, with respective figures of 4273 (74.4%), 3824 (72%), and 751 (73.5%). Conversely, the middle quadrant depicted the lowest frequency across these groups, constituting 23 (0.4%), 26 (0.5%), and 8 (0.8%) instances. The frequency distribution of tumor size and tumor location, and tumor type across different age groups, the highest frequency of invasive ductal carcinomas was consistently observed in the age ranges ≤ 50 (3721; 64.8%), 50-69 (3415; 65.3%), and >60 years (650; 63.5%). Similarly, the upper outer quadrant emerged as the predominant tumor site across all age groups, with respective figures of 4273 (74.4%), 3824 (72%), and 751 (73.5%). Conversely, the middle quadrant depicted the lowest frequency across these groups, constituting 23 (0.4%), 26 (0.5%), and 8 (0.8%) instances. The frequency distribution of tumor size and tumor location, and tumor type across different age groups, the highest frequency of invasive ductal carcinomas was consistently observed in the age ranges ≤ 50 (3721; 64.8%), 50-69 (3415; 65.3%), and >60 years (650; 63.5%). Similarly, the upper outer quadrant emerged as the predominant tumor site across all age groups, with respective figures of 4273 (74.4%), 3824 (72%), and 751 (73.5%). Conversely, the middle quadrant depicted the lowest frequency across these groups, constituting 23 (0.4%), 26 (0.5%), and 8 (0.8%) instances. The frequency distribution of tumor size and tumor location, and tumor type across different age groups, the highest frequency of invasive ductal carcinomas was consistently observed in the age ranges ≤ 50 (3721; 64.8%), 50-69 (3415; 65.3%), and >60 years (650; 63.5%). Similarly, the upper outer quadrant emerged as the predominant tumor site across all age groups, with respective figures of 4273 (74.4%), 3824 (72%), and 751 (73.5%). Conversely, the middle quadrant depicted the lowest frequency across these groups, constituting 23 (0.4%), 26 (0.5%), and 8 (0.8%) instances. The frequency distribution of tumor size and tumor location, and tumor type across different age groups, the highest frequency of invasive ductal carcinomas was consistently observed in the age ranges ≤ 50 (3721; 64.8%), 50-69 (3415; 65.3%), and >60 years (650; 63.5%). Similarly, the upper outer quadrant emerged as the predominant tumor site across all age groups, with respective figures of 4273 (74.4%), 3824 (72%), and 751 (73.5%). Conversely, the middle quadrant depicted the lowest frequency across these groups, constituting 23 (0.4%), 26 (0.5%), and 8 (0.8%) instances. The frequency distribution of tumor size and tumor location, and tumor type across different age groups, the highest frequency of invasive ductal carcinomas was...
Examining the Completeness of Breast Cancer Pathology Reports

Table 3. Association between surgery pathology report information (tumor type, tumor sit and tumor size) and age groups during 2016-2018

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>≤ 50</th>
<th>50-60</th>
<th>≥60</th>
<th>Total</th>
<th>X²</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>305</td>
<td>(5.3)</td>
<td></td>
<td></td>
<td>235</td>
<td>(4.5)</td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>3721</td>
<td>(64.8)</td>
<td></td>
<td></td>
<td>3415</td>
<td>(65.3)</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>243</td>
<td>(4.2)</td>
<td></td>
<td></td>
<td>238</td>
<td>(4.5)</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
<td>208</td>
<td>(3.6)</td>
<td></td>
<td></td>
<td>183</td>
<td>(3.5)</td>
</tr>
<tr>
<td>Others</td>
<td>91</td>
<td>(1.6)</td>
<td></td>
<td></td>
<td>123</td>
<td>(2.3)</td>
</tr>
<tr>
<td>Not report/ missing</td>
<td>1176</td>
<td>(20.5)</td>
<td></td>
<td></td>
<td>1039</td>
<td>(19.9)</td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central portion of breast</td>
<td>797</td>
<td>(13.9)</td>
<td></td>
<td></td>
<td>738</td>
<td>(14.1)</td>
</tr>
<tr>
<td>Lower inner quadrant</td>
<td>23</td>
<td>(0.4)</td>
<td></td>
<td></td>
<td>26</td>
<td>(0.5)</td>
</tr>
<tr>
<td>Lower outer quadrant</td>
<td>45</td>
<td>(0.8)</td>
<td></td>
<td></td>
<td>64</td>
<td>(1.2)</td>
</tr>
<tr>
<td>Nipple</td>
<td>46</td>
<td>(0.8)</td>
<td></td>
<td></td>
<td>61</td>
<td>(1.2)</td>
</tr>
<tr>
<td>Upper inner quadrant</td>
<td>54</td>
<td>(0.9)</td>
<td></td>
<td></td>
<td>51</td>
<td>(1.0)</td>
</tr>
<tr>
<td>Upper outer quadrant</td>
<td>4273</td>
<td>(74.4)</td>
<td></td>
<td></td>
<td>3824</td>
<td>(72.0)</td>
</tr>
<tr>
<td>Not report/ missing</td>
<td>506</td>
<td>(8.8)</td>
<td></td>
<td></td>
<td>469</td>
<td>(9.0)</td>
</tr>
</tbody>
</table>

Table 4. Association between surgery pathology report information (pathologic T category, pathologic N category and tumor grade) and age groups during 2016-2018

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>≤ 50</th>
<th>50-60</th>
<th>≥60</th>
<th>Total</th>
<th>X²</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic T stage*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TX</td>
<td>23</td>
<td>(0.4)</td>
<td></td>
<td></td>
<td>19</td>
<td>(0.4)</td>
</tr>
<tr>
<td>T1</td>
<td>421</td>
<td>(7.2)</td>
<td></td>
<td></td>
<td>447</td>
<td>(6.6)</td>
</tr>
<tr>
<td>T2</td>
<td>1124</td>
<td>(19.6)</td>
<td></td>
<td></td>
<td>1109</td>
<td>(21.2)</td>
</tr>
<tr>
<td>T3</td>
<td>232</td>
<td>(4.0)</td>
<td></td>
<td></td>
<td>167</td>
<td>(3.2)</td>
</tr>
<tr>
<td>T4</td>
<td>27</td>
<td>(0.5)</td>
<td></td>
<td></td>
<td>29</td>
<td>(0.6)</td>
</tr>
<tr>
<td>Not report/ missing</td>
<td>3917</td>
<td>(68.2)</td>
<td></td>
<td></td>
<td>3462</td>
<td>(66.2)</td>
</tr>
<tr>
<td>Pathologic N stage**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NX</td>
<td>47</td>
<td>(0.8)</td>
<td></td>
<td></td>
<td>50</td>
<td>(1.0)</td>
</tr>
<tr>
<td>N0</td>
<td>722</td>
<td>(12.6)</td>
<td></td>
<td></td>
<td>699</td>
<td>(13.4)</td>
</tr>
<tr>
<td>N1</td>
<td>557</td>
<td>(9.7)</td>
<td></td>
<td></td>
<td>502</td>
<td>(9.6)</td>
</tr>
<tr>
<td>N2</td>
<td>320</td>
<td>(5.6)</td>
<td></td>
<td></td>
<td>293</td>
<td>(5.6)</td>
</tr>
<tr>
<td>N3</td>
<td>148</td>
<td>(2.6)</td>
<td></td>
<td></td>
<td>144</td>
<td>(2.8)</td>
</tr>
<tr>
<td>Not report/ missing</td>
<td>3949</td>
<td>(68.8)</td>
<td></td>
<td></td>
<td>3543</td>
<td>(67.7)</td>
</tr>
<tr>
<td>Tumor grade***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>2621</td>
<td>(45.6)</td>
<td></td>
<td></td>
<td>2625</td>
<td>(50.2)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>1649</td>
<td>(28.7)</td>
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<td></td>
<td>1420</td>
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<td>Grade 3</td>
<td>1474</td>
<td>(25.7)</td>
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<td></td>
<td>1188</td>
<td>(22.0)</td>
</tr>
</tbody>
</table>

Discussion

A population-based cancer registry serves as a critical tool to accumulate accurate and comprehensive information concerning new cancer cases within a specific population. In this context, developing countries rely on such registries as a pivotal component of their health information systems. The assessment of data quality spans a spectrum of attributes, including accuracy, validity, reliability, accessibility, usefulness, confidentiality, completeness, comparability, correctness, and timeliness. The international pathology community has published guidelines aimed at enhancing the quality of pathology reports. Prior research from diverse nations has underscored the issue of incomplete pathology reports that lack essential information crucial for clinical decision-making. In Iran, the National Cancer Registry constitutes the primary source of cancer statistics, rendering an appraisal of data completeness crucial for accurate clinical decision-making and patient welfare. Within the scope of this study, a comprehensive evaluation of the completeness of pathology reports associated with breast cancer was undertaken. The findings revealed high proportions of completeness, particularly for

represented the lowest. Remarkably, tumor grade demonstrated its highest frequency in grade 1 across all age groups, accounting for 2621 (45.6%), 2625 (50.2%), and 531 (51.9%) patients. Notably, 8049 patients lacked pathologic T stage reporting, and 8195 patients were without pathologic N stage documentation in the pathology reports. A significant statistical association was found between pathologic T stage and age (X²(10) = 31.10, P = 0.014) and tumor grade (X²(4) = 32.39, P = 0.0001) with age, although no substantial correlation emerged between pathologic N stage and age (X²(10) = 5.22, P = 0.816) (Table 4).

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Med J Islam Repub Iran. 2024 (29 May); 38:61.
tumor grade (100%), tumor site (91.2%), and tumor type (79.8%). Notably, some literature has highlighted the efficacy of synoptic reporting and templates in fostering completeness within surgical pathology reports (25, 34).

A striking observation arose concerning the relationship between age groups and the completeness of key variables within pathology reports. The data indicated an augmented completeness trend as age progressed. This phenomenon could be attributed to the heightened vulnerability to breast cancer with advancing age, greater data availability for individuals beyond 50 years, and a higher disease prevalence within this segment, collectively contributing to improved pathology report completeness (35). On the contrary, the detection rate of breast cancer among younger women is lower compared to their older counterparts. Consequently, the assessment of data completeness is more intricate in this demographic due to limited research and data availability, exacerbated by the possibility of younger women being less attuned to breast cancer risk factors and hence less likely to seek medical attention or undergo regular screenings, thereby leading to incomplete data (36, 37).

It is noteworthy that the completeness of breast cancer pathology reports across different age groups is influenced by multifarious factors including data collection resources, population distribution within age groups, the nature of the collected data, cancer type, and the studied population. Factors such as data collection method—whether derived from medical records, surveys, or self-reported information—contribute significantly to the completeness of the data. For instance, data accuracy from medical records hinges upon the meticulousness of the records. Similarly, survey-based or self-reported data relies on participants' willingness to provide accurate information (38). Studies in the United States and the United Kingdom have exhibited divergent trends in the completeness of cancer data across age groups, showcasing the intricate interplay between these variables (39, 40).

Delving into the pathology reports, our findings revealed high levels of completeness for tumor grade (100%) and tumor site (above 90%) across all age groups. Corresponding to a Brazilian study evaluating hospital-based cancer registries by Lopes-Júnior et al., reported notably high completeness for tumor site (97.5%), potentially owing to the objective nature of this parameter's interpretation (41). However, a different picture emerged for tumor size, pathologic T category, and pathologic N category, revealing suboptimal levels of completeness. This outcome likely results from a complex interplay of factors, including age, comorbidity, patient and physician preferences, and the alignment with prevailing clinical guidelines, collectively contributing to reduced completeness of pathology reports (42-44). This deficit in completeness has the potential to undermine clinical decision-making, strategic planning, resource allocation, and the validity of assessments (45, 46). Variability in the completeness of pathologic T and N stages across different studies is attributed to diverse factors including resource availability, data collection quality, and reporting systems (47). Some countries, such as Denmark and the Netherlands, have achieved pathologic T and N completeness exceeding 90% for various cancers including breast cancer (48, 49). Ramos et al.'s study, however, uncovered pathologic T and N completeness exceeding 50% for breast cancer (47). In essence, comprehensive, reliable, and timely information is the cornerstone of effective decision-making and appropriate treatment provision, constituting integral components of a functional health system.

Several limitations warrant acknowledgment in this study. The presence of illegible handwriting in medical records introduces the potential for missing data, thus complicating the interpretation of observed disparities. The irregular and disjointed nature of documentation within medical records also poses a challenge to data interpretation. Additionally, while this study evaluates the level of surgery pathology report completeness, the actual validity of registrations remains unexplored. Lastly, the study's short duration precludes the execution of trend analysis on incomplete data. Despite these limitations, the study's national representation of the Iranian population makes it a significant contribution to the field, providing unprecedented insights into breast cancer pathology report completeness across age groups.

Conclusion
To the best of our knowledge, this study marks the inaugural examination of the completeness of breast cancer data by age group in Iran. The findings underscore the importance of comprehending pathology report completeness and urge for improvements in stage registration for breast cancer. Furthermore, the establishment of a dedicated integrated system at the national level, capable of harmonizing data from hospitals, clinics, pathology laboratories, and death certificates, is essential to ensuring a comprehensive and accurate representation of breast cancer statistics.

List of Abbreviations
BC: Breast Cancer
ASIR: Age-standardized Incidence Rate
ER: Estrogen Receptor
PR: Progesterone Receptor
Her2: Human epidermal growth factor 2
SD: Standard Deviation

Authors' Contributions
All the authors have contributed to the study design, data collection, data analysis, and manuscript editing.

Ethical Considerations
This study was approved by the ethics committee of Iran University of Medical Sciences with the ethics code IR.IUMS.REC.1400.878.

Acknowledgment
All the authors thank all those who contributed to this study.

Conflict of Interests
The authors declare that they have no competing interests.
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