

Octogenarians with triple negative breast cancer

Daisy L. Spoer^{1,2}, Niloofar Ghyasi², Teagan L. Thorson³, Samuel S. Huffman^{1,2}, Lauren E. Berger^{1,4}, Christian X. Lava^{1,2}^, Chung-Fu Lin², Monika K. Masanam³, Lindy M. Rosal³, Marc E. Boisvert³, Patricia B. Wehner³, Ian T. Greenwalt³, Jennifer D. Son³, Rafael J. Convit⁵, Eleni Tousimis⁶, David H. Song¹, Kenneth L. Fan^{1,2}, Lucy M. De La Cruz¹

¹Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA; ²Georgetown University School of Medicine, Washington, DC, USA; ³Division of Breast Surgery, Department of Surgery, MedStar Washington Hospital Center, Washington, DC, USA; ⁴Plastic and Reconstructive Surgery Division, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA; ⁵Department of Plastic and Reconstructive Surgery, MedStar Washington Hospital Center, Washington, DC, USA; ⁶Scully-Welsh Cancer Center, Vero Beach, FL, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Lucy M. De La Cruz, MD. Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, 3800 Reservoir Road, NW, Washington, DC 20007, USA. Email: lucy.delacruz@medstar.net.

Background: As the global population ages, we can expect increases in cancer incidence in older individuals. Treatment patterns for triple-negative breast cancer (TNBC) vary by age group, where older individuals (≥70 years) receive standard of care [(SOC): i.e., chemotherapy, radiation, or surgery] less often than their younger counterparts. Deciding to recommend these treatments for individuals over 80 years can be challenging without evidence-based guidance. Thus, we aimed to investigate the relevance of patient and oncologic factors in pursuing SOC for octogenarians with TNBC.

Methods: We performed a retrospective chart review of patients aged 80 years or older with TNBC who underwent breast resection across three institutions between 2018 and 2022. Covariates collected from electronic medical reports included pathologic stage, adjuvant therapy received, Eastern Cooperative Oncology Group (ECOG) performance status, surgical and non-surgical treatments, and oncologic outcomes. Individuals receiving SOC were compared to those who received informed-deferred (ID) treatment.

Results: Of the 76 octogenarians receiving oncologic resection, 21 (27.6%) TNBC confirmed on pathology. Fifty-seven percent received SOC, and 42.9% received ID. Poorer performance, measured by ECOG score, was statistically associated with ID. ID involved deferral of both chemotherapy and radiation. We did not observe associations between age, cancer stage, surgical treatment, or oncologic outcomes between SOC and ID groups. The reasons for ID comprised shared-decision making deferral, decompensation/hospice driven, and patient preference.

Conclusions: This pilot study emphasizes individuals ≥80 years of age may benefit from SOC. The appropriateness of chemotherapy should be directed by tumor biology and potentially functional status, rather than age alone. Geriatric evaluation tools may be helpful in guiding shared-decision making and future research is needed to determine the optimal screening method for informing patient-centered recommendations for TNBC non-surgical therapy.

Keywords: Breast cancer (BC); chemotherapy; octogenarian; radiation; triple-negative

[^] ORCID: 0000-0001-5665-9822.

Received: 04 August 2023; Accepted: 24 October 2023; Published online: 08 November 2023. doi: 10.21037/abs-23-58

View this article at: https://dx.doi.org/10.21037/abs-23-58

Introduction

Breast cancer (BC) is the most common cancer worldwide (1,2). The risk of BC increases with age, and the prevalence is expected to increase as the global population lives longer (3-7). Triple-negative BC (TNBC) is an aggressive subtype defined by a lack of ERBB2 amplification (formerly HER2) and hormone receptor overexpression [e.g., estrogen receptors (ER) or progesterone receptors (PR)]. Without these receptor targets, patients with TNBC cannot benefit from the established endocrine or ERBB2-targeted medications. The standard of care (SOC) to TNBC often includes neoadjuvant chemotherapy, although treatment decisions are highly individualized. TNBC SOC treatment relies on surgical resection, chemotherapy, and radiation (8,9).

Despite increasing overall and BC-specific survival, these treatments are employed less often in older populations (aged ≥70 years) (9-14). The age-related discrepancies are most pronounced for chemotherapy, where the administration can be 41–47% lower in individuals over 70 years compared to their younger counterparts (9,11-14).

The treatment for TNBC should be discussed as a shared decision between patients and providers, but without clear

Highlight box

Key findings

 Patients aged ≥80 with triple-negative breast cancer (TNBC) achieve similar mortality outcomes to those <80 years old when receiving standard of care [(SOC): i.e., chemotherapy, radiation, or surgery].

What is known and what is new?

- Treatment patterns for TNBC vary by age group, where older individuals (≥70 years) receive SOC less often than their younger counterparts.
- The appropriateness of chemotherapy should be directed by tumor biology and potentially functional status, rather than age alone.

What is the implication, and what should change now?

Treatment decisions for those with advanced disease should be
personalized based on coexisting conditions, patient preferences,
and geriatric evaluation tools. Further, declining functional
performance may indicate a potential need for subsequent
treatment cessation, and patients should be appropriately counseled
on this as a possibility.

guidance may be subject to bias. Between 70 and 80 years of age, median survival shortens, functional status declines, and comorbidities rise. In combination, these factors may decrease the tolerance to chemotherapy-related toxicity (15-28). However, the infrequent use of chemotherapy in individuals ≥70 years may be a product of provider hesitation rather than patient refusal (not administered: n=8,391: recommended 32% vs. not recommended 68%) (29). As benefiting from chemotherapy is multifactorial, the algorithm for patient selection should be highly individualized.

This study aimed to further characterize this process by analyzing a retrospective cohort of individuals over or equal to 80 years old receiving surgical treatment for TNBC. In doing so, we sought to expand on the relevance of age, functional status, and oncologic characteristics in deferring standard treatments in octogenarians with TNBC to support further refinements in shared decision-making. We present this article in accordance with the STROBE reporting checklist (available at https://abs.amegroups.com/article/view/10.21037/abs-23-58/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the MedStar Health Research Institute (MHRI) Institutional Review Board (STUDY00004989) and individual consent for this retrospective analysis was waived.

Data source and patient population

A retrospective cohort was identified from consecutive adult patients receiving oncologic resection for BC treatment across three institutions between January 2018 and October 2022. Patients were eligible for inclusion in this study if they were the following: 80 years old or older, underwent surgical breast resection [e.g., breast-conserving surgery (BCS), mastectomy, or modified radical mastectomy] for an associated preoperative diagnosis of BC. The eligible patients were screened by two reviewers to be included if their operation was confirmed to be a primary resection with a histopathological diagnosis of TNBC. Patients were

excluded if they had the following: ER, PR, or EBBR2 receptor-positive cancer, under 80 years at the time of surgery, or no available data indicating receptor status. The study size was determined by the absolute number of consecutive patients who met inclusion criteria during the study duration.

Retrospective review

The electronic medical records of included patients were reviewed for data on patient characteristics, BC details, surgical treatment, non-surgical treatment, and oncologic outcomes. The records were prospectively maintained until January 2023 unless patients were lost to follow-up.

The patient characteristics extracted for analysis included age, performance status, and preoperative diagnosis. Performance status was calculated as a proxy for comorbidity burden and was assessed using the "Eastern Cooperative Oncology Group (ECOG)" performance scale, which is graded on a scale from "0" to "V" (30). ECOG performance status assessments were conducted prior to surgery. The oncologic covariates comprised details on the patient's BC, surgical treatment, non-surgical treatment, and reason for deferral. The assessment of BC included data on tumor and nodal grade, stage, and surgical treatments. The pathological tumor (T) grade, nodal (N) grade and tumor-node-metastasis (TNM) stage were extracted per the American Joint Committee on Cancer (AJCC) staging manual 2017.

The surgical treatments were categorized into resection, lymph node dissection, and reconstruction. The surgical approaches to BC resection included (I) BCS (e.g., lumpectomy); (II) simple mastectomy; and (III) radical mastectomy. The nodal dissection was categorized into sentinel lymph node biopsy (SLNB) and axillary nodal dissection (ALND). When applicable, the type of breast reconstruction was recorded. The variables for nonsurgical treatments included the indications, timing, and utilization of (neo)adjuvant chemotherapy and radiation therapy. Chemotherapy is typically considered for larger tumors, lymph node involvement, triple-negative or HER2positive BC, high-grade tumors, or when there is a risk of metastasis. Radiation therapy is recommended postsurgery (e.g., lumpectomy, mastectomy) to reduce the risk of local recurrence, especially when there is lymph node involvement, incomplete tumor removal, or in cases of inflammatory BC (8,9).

The oncologic outcomes included the follow-up

duration, re-operation, all-cause mortality, BC-related mortality, and time to postoperative mortality. Patients were categorized for comparative analysis according to compliance with the American Society of Clinical Oncology (ASCO) and incorporation of the International Society of Geriatric Oncology (SIOG) guidelines (31). Patients were determined to have received "SOC" if their treatment aligned with ASCO recommendations [Supplemental Digital Content (SDC 1); Table S1] (32,33). Patients who deferred treatments of indicated chemotherapy or radiation were categorized as informed-deferred ("ID"). The reason for deferral was recorded when available.

Statistical analysis

Patients underwent complete case analysis, which omitted missing electronic medical record (EMR) data, and analysis was performed on what remained. Descriptive statistics were calculated for all patient data. Shapiro-Wilk testing of normality was performed to assess the distribution of continuous variables. Normally distributed continuous variables were described by means and standard deviations, and non-normally distributed variables were reported using median and interquartile range (IQR). Frequencies and percentages explained categorical variables. All continuous variables were compared using bivariate analysis with Mann-Whitney tests and unpaired two-tailed t-testing as appropriate. Pearson's chi-squared (χ^2) or Fisher's exact tests (n<7) were employed for categorical variables as appropriate. All statistical analysis was performed using StataBE Software (StataCorp LLC, College Station, TX, USA), with a significance set as P<0.05. Results are reported per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies.

Results

Patient demographics and comorbidities

We identified 124 patients who fulfilled the criteria for eligibility. Of these individuals, 21 patients met the criteria for inclusion in this study. The composite cohort comprised females (21, 100.0%) with a mean age of 85.6±3.9 years with a histopathological diagnosis of TNBC who underwent primary surgical resection during the study period. Of the composite cohort, 12 received SOC (57.1%), and 9 received ID (42.9%).

The patient characteristics and cancer details are displayed in *Table 1*. The comparative analysis of ID and SOC patients revealed critical differences between the groups. Specifically, the ID group had a higher mean age of (87.4±3.6 years) than those of the SOC group (84.3±3.6 years), though this was not statistically significant (P=0.060). The frequencies of ECOG scores differed significantly between groups (P=0.042). The distribution for ECOG scores 0, I, and II in the SOC group was 5 (41.7%), 6 (50.0%), and 1 (8.3%), respectively. This was found to be significantly different from those in the ID group, in which the distribution of ECOG scores was 0 (2, 22.2%), I

(2, 22.2%), and III (4, 44.4%). In comparing the frequencies at each ECOG score, ECOG III was observed to be significantly associated with treatment deferral (P=0.014). There were no significant differences in the pathologic/treatment TNM stages (P=0.861), tumor grade (T) (P=0.504), node grade (N) (P=0.825), laterality (P=0.323), or breast quadrant (P=0.611).

The operations were performed in equal frequency over the five included years, with most procedures performed by one of six surgeons (Surgeon 1; 12, 57.1%) at one of three included hospitals (Hospital 2; 16, 76.2%), with no significant differences between groups (P>0.05). The

Table 1 Patient characteristics & oncologic history

Variables	Total (n=21)	SOC (n=12; 57.1%)	ID (n=9; 42.9%)	P value
Patient demographics				
Age, mean ± SD	85.6±3.9	84.3±3.6	87.4±3.6	0.060
Comorbidities, n (%)				
ECOG				0.042
0	7 (33.3)	5 (41.7)	2 (22.2)	0.642
1	8 (38.1)	6 (50.0)	2 (22.2)	0.642
2	1 (4.8)	1 (8.3)	0	>0.99
3	4 (19.0)	0	4 (44.4)	0.014
Pathologic stage, n (%)				
pT or yT				0.504
Tmi	1 (4.8)	1 (8.3)	0	
T1a	3 (14.3)	1 (8.3)	2 (22.2)	
T1b	1 (4.8)	1 (8.3)	0	
T1c	5 (23.8)	4 (33.3)	1 (11.1)	
T2	8 (38.1)	3 (25.0)	5 (55.6)	
T2a	1 (4.8)	1 (8.3)	0	
T3	2 (9.5)	1 (8.3)	1 (11.1)	
pN or yN				0.825
х	2 (9.5)	1 (8.3)	1 (11.1)	
N0	11 (52.4)	5 (41.7)	6 (66.7)	
N1(mic)	2 (9.5)	2 (16.7)	0	
N1	1 (4.8)	1 (8.3)	0	
N1a	3 (14.3)	2 (16.7)	1 (11.1)	
N1c	1 (4.8)	1 (8.3)	0	
N2a	1 (4.8)	0	1 (11.1)	

Table 1 (continued)

Table 1 (continued)

Variables	Total (n=21)	SOC (n=12; 57.1%)	ID (n=9; 42.9%)	P value
pTNM or yTNM stage				0.861
Stage 1A	8 (38.1)	5 (41.7)	3 (33.3)	
Stage 1B	1 (4.8)	1 (8.3)	0	
Stage 2A	5 (23.8)	2 (16.7)	3 (33.3)	
Stage 2B	3 (14.3)	2 (16.7)	1 (11.1)	
Stage 3A	1 (4.8)	1 (8.3)	0	
Stage 4	1 (4.8)	0	1 (11.1)	
Laterality				0.323
BL	1 (4.8)	1 (8.3)	0	
L	9 (42.9)	4 (33.3)	5 (55.6)	
R	7 (33.3)	3 (25.0)	4 (44.4)	
Breast quadrant				0.611
Central	5 (23.8)	2 (16.7)	3 (33.3)	
Upper-outer	8 (38.1)	6 (50.0)	2 (22.2)	
Upper-inner	3 (14.3)	2 (16.7)	1 (11.1)	
Lower-inner	1 (4.8)	0	1 (11.1)	
Multifocal	4 (19.0)	2 (16.7)	2 (22.2)	
Hospital and temporal character	ristics, n (%)			
Treatment year				0.743
2018	4 (19.0)	1 (8.3)	3 (33.3)	
2019	4 (19.0)	2 (16.7)	2 (22.2)	
2020	4 (19.0)	3 (25.0)	1 (11.1)	
2021	5 (23.8)	3 (25.0)	2 (22.2)	
2022	4 (19.0)	3 (25.0)	1 (11.1)	
Hospitals				0.472
Hospital 1	3 (14.3)	1 (8.3)	2 (22.2)	
Hospital 2	16 (76.2)	9 (75.0)	7 (77.8)	
Hospital 3	2 (9.5)	2 (16.7)	0	
Surgeons				0.430
Surgeon 1	12 (57.1)	6 (50.0)	6 (66.7)	
Surgeon 2	1 (4.8)	1 (8.3)	0	
Surgeon 3	1 (4.8)	0	1 (11.1)	
Surgeon 4	2 (9.5)	2 (16.7)	0	
Surgeon 5	1 (4.8)	0	1 (11.1)	
Surgeon 6	4 (19.0)	3 (25.0)	1 (11.1)	

SOC, standard of care; ID, informed-deferred; SD, standard deviation; ECOG, Eastern Cooperative Oncology Group; pT, pathological tumor; yT, post-therapy pathological tumor; pN, pathological lymph node; yN, post-therapy pathological lymph node; pTNM, pathological staging incorporating information about primary tumor, regional lymph nodes, and distant metastasis; yTNM, post-therapy pathological staging incorporating information about primary tumor, regional lymph nodes, and distant metastasis; BL, bilateral; L, left; R, right.

surrounding population characteristics did not differ significantly between SOC and ID.

Surgical treatment

The oncologic treatment characteristics and outcomes are summarized in *Table 2*. The most common surgical regimens in the composite cohort included resection performed with BCS (12, 57.1%) and nodal dissection performed as SLND (16, 76.2%). Nine patients (42.9%) underwent breast reconstruction, most often performed via local tissue rearrangement oncoplastic procedures (8, 38.1%). In the SOC group, the most common methods of surgical resection were BCS (9, 75.0%) with SLNB (11, 91.7%). This differed from the ID group, in which more patients underwent mastectomy (6, 66.7%; P=0.087) with a nearly equal distribution of SLNB (5, 55.6%) and ALND (4, 44.4%; P=0.119). The proportion of patients who underwent concomitant oncoplastic breast reconstruction was not significantly different between the two groups.

Non-surgical treatment

Collectively, chemotherapy was indicated in 18 individuals (85.7%) and administered in 10 (47.6%). Despite the two groups having similar indications for chemotherapy (SOC 75.0% vs. ID 88.9%, P=0.229), it was administered

significantly less often in the ID group (1, 11.1%) than the SOC group (9, 75.0%, P=0.008). Chemotherapy was most often deferred as a shared medical decision between the patient and providing oncologist (4, 44.4%).

Radiation was indicated in 17 (81.0%) and administered in 13 (61.9%). The indications for radiation were similar between groups, with significantly less radiation administered in the ID group (2, 22.2%) than in the SOC group (11, 91.7%; P=0.002). Radiation was often deferred due to patient preferences (2, 22.2%).

Oncologic outcomes

By a mean follow-up of 22.2 months, the composite cohort had an all-cause mortality rate of 19.0% (4) and breast-cancer specific mortality rate of 4.8% (1) with a median time to the mortality event of 30.5 months (IQR, 18 months). There were no significant differences in mortality between SOC and ID groups.

Discussion

The standard treatment for TNBC relies on surgery, chemotherapy, and with or without radiation (9). Yet, older individuals (≥70 years) receive chemotherapy and radiation less often than their younger counterparts (9,12,34). In this study, of 21 octogenarians with surgically treated

Table 2 Oncologic treatment characteristics and outcomes

Variables	Total (n=21)	SOC (n=12)	ID (n=9)	P value
Surgical treatment, n (%)				
Surgical approach				0.087
BCS	12 (57.1)	9 (75.0)	3 (33.3)	
Mastectomy	5 (23.8)	3 (25.0)	6 (66.7)	
Nodal dissection				0.119
SLNB	16 (76.2)	11 (91.7)	5 (55.6)	
ALND	5 (23.8)	1 (8.3)	4 (44.4)	
Breast reconstruction, n (%)				
Immediate breast reconstruction	9 (42.9)	6 (50.0)	3 (33.3)	0.429
Surgical approach				0.272
Tissue rearrangement	8 (38.1)	6 (50.0)	2 (22.2)	
Reduction mammaplasty	1 (4.8)	0	1 (11.1)	

Table 2 (continued)

Table 2 (continued)

Variables	Total (n=21)	SOC (n=12)	ID (n=9)	P value
Non-surgical treatment, n (%)				
Chemotherapy indicated				0.229
Not indicated	4 (19.0)	3 (25.0)	1 (11.1)	
Indicated	17 (81.0)	9 (75.0)	8 (88.9)	
Chemotherapy				0.008
Not administered	11 (52.4)	3 (25.0)	8 (88.9)	
Administered	10 (47.6)	9 (75.0)	1 (11.1)	
Chemotherapy timing				0.035
None	11 (52.4)	3 (25.0)	8 (88.9)	
Neoadjuvant	1 (4.8)	1 (8.3)	0	
Adjuvant	7 (33.3)	6 (50.0)	1 (11.1)	
Both	2 (9.5)	2 (16.7)	0	
Reason deferring chemotherapy				-
Shared decision-making	NA	NA	4 (44.4)	
Decompensation, BCR	NA	NA	1 (11.1)	
Decompensation, non-BCR	NA	NA	2 (22.2)	
Radiation indicated				0.272
Not indicated	4 (19.0)	1 (8.3)	3 (33.3)	
Indicated	17 (81.0)	11 (91.7)	6 (66.7)	
Radiation				0.002
Not administered	8 (38.1)	1 (8.3)	7 (77.8)	
Administered	13 (61.9)	11 (91.7)	2 (22.2)	
Radiation localization				0.005
None	8 (38.1)	1 (8.3)	7 (77.8)	
Partial breast	1 (4.8)	1 (8.3)	0	
Whole breast	12 (57.1)	10 (83.3)	2 (22.2)	
Reason deferring radiation				-
Patient preference	NA	NA	2 (22.2)	
Decompensation, BCR	NA	NA	1 (11.1)	
Decompensation, non-BCR	NA	NA	1 (11.1)	
Oncologic outcomes				
Follow up, months, mean ± SD	22.2±14.8	23.2±14.2	21.0±16.2	0.7486
All-cause mortality (deceased), n (%)	4 (19.0)	1 (8.3)	3 (33.3)	0.272
Breast-cancer-related mortality (deceased), n (%)	1 (4.8)	0	1 (11.1)	0.272
Date deceased, months, median [IQR]	30.5 [18]	29 [0]	32 [33]	>0.99

SOC, standard of care; ID, informed-deferred; BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy; ALND, axillary nodal dissection; BCR, breast-cancer related; SD, standard deviation; IQR, interquartile range.

TNBC, we observed that 57.1% received all indicated nonsurgical treatments (SOC, 12) and 42.9% received nonstandard care (ID, 9). Receiving ID was associated with having lower performance status (ECOG III), avoidance of chemotherapy, and avoidance of radiation. The two groups had no differences in all-cause or breast-cancerrelated mortality rates. These results build on previous literature and suggest that individuals with TNBC over 80 years may pursue chemotherapy and radiation, and achieve comparable all-cause and BC-mortality outcomes as those less than 80 years. Moreover, the functional status may be more relevant than age in the decision to defer treatment (35-37).

Non-selective systemic chemotherapy confers numerous toxicities that are observed to be more pronounced in individuals who are older or increasingly frail (10,25,29,38). The long-term survival in elderly individuals (>70 years) with TNBC is thought to be reduced due to the infrequent use of chemotherapy and radiation (11,13,14,34,39,40). However, most of our patients (18, 85.7%) had indications for chemotherapy. Across our institutions, physicians typically perform an independent risk-benefit analysis before discussing care goals with patients and their families. While the SOC is considered for most patients, physicians and patients engage in informed, shared decision-making to minimize undue harm. Through this approach, 57.1% of patients opted for all indicated treatment modalities, and 42.9% deferred at least one treatment method. The reasons for deferral included the shared decision to forgo, patient preference, and decompensation (breast and non-BCrelated).

Contrary to previous studies, we observed that age, T/N grade, or TNM stage of cancer was not significantly associated with deferral (34,41). Instead, treatment deferral was associated with poorer functional status, whereby ECOG III was significantly associated with treatment deferral (P=0.0140). These findings reinforce the notion that functional status is a potentially important factor to be integrated into treatment decision-making algorithms and that age should not necessarily be an independent contraindication to chemotherapy (36).

To conduct an evidence-based geriatric assessment, ASCO recommends the following chemotherapy risk prediction models: (I) the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score and (II) the Cancer and Aging Research Group (CARG) chemotherapy toxicity score (42,43). More recently, CARG-BC was shown to predict unplanned modifications in treatment

and chemotherapy toxicities (44). The accuracy in the risk calculation for CARG-BC may be explained by its inclusion of medical and physical functioning and exclusion of age. Beyond this, our results suggest that a scale measuring daily functioning (i.e., ECOG) may provide additional information relevant in the decision to pursue treatment (43,45). CRASH is one such scale that incorporates ECOG, and may support patient-centered geriatric assessments. Further research is needed to determine the comparative predictive nature of these scoring systems to support their universal integration in this decision-making process for older adults with TNBC.

Treatment-related disparities in BC vary according to socioeconomic and psychological factors (35,46-48). When our patients were offered standard therapy for TNBC, subsequent deferral of chemotherapy and radiation occurred due to preference, concern for adverse side effects, and hospice-driven refusal. In these settings, providers should be mindful of the logistical and internal barriers to care, including financial/logistical access, health literacy, and psychological distress. In individuals over 70 years with primary operable TNBC, increasing age, Black race, increasing grade, T stage, N stage, and radiation or chemotherapy independently predict overall survival (12). As differences in chemotherapy use vary according to race and sociocultural factors, improving these outcomes will require further exploration of this topic for the affected sub-populations. Looking to the future, research should seek to describe the themes in patientreported deferral to determine the relevance of external and internal barriers to receiving chemotherapy when indicated. Identifying how sociodemographic barriers to care influence patient-decision making may inform healthcare-driven interventions to support those who may have otherwise not received treatment.

In contrast with the systemic approach to TNBC, the geriatric population (92.8%) frequently undergoes surgical resection for TNBC (9). Surgery independently lowers the risk of BC-related death but may be avoided in certain patients due to increasing age, comorbidity, and concern for a postoperative psychological decline. However, individuals deferring chemotherapy and radiation may benefit from surgical interventions, particularly if combined with psychosocial interventions. If the tumor was relatively small and localized, surgery was the preferred initial treatment, followed by adjuvant therapy to reduce the risk of recurrence. Mastectomy has been considered palliative therapy for individuals over 70 years with locally

advanced hormone receptor-negative BC (T3/4 M0) (49). Surgical removal of TNBC tumors prior to progression into a fungating wound may enhance the quality of life of individuals, even if chemotherapy and radiation are deferred. Concurrently performing oncoplastic or aesthetic flat closure further promotes patient wellbeing while respecting patient autonomy and oncologic medical decision-making (50-55). Additionally, concurrent oncoplastic may influence survival by increasing the excised margins at the time of lumpectomy (51-55). The multidisciplinary teams in our network of institutions function to integrate social work, psychological support, and plastic and reconstructive surgery with the surgical and nonsurgical treatment of BC. Expanding the armamentarium for non-traditional treatment for individuals at high risk for chemotherapy toxicity may be an important avenue to explore to optimize the quality of life for older (≥80 years) individuals with TNBC (56,57).

This pilot study emphasizes that SOC treatment offerings should be directed by tumor biology and individual patient profiles rather than age alone (8,29,58). Treatment decisions for those with advanced disease should be personalized based on coexisting conditions, patient preferences, and geriatric evaluation tools. Further, declining functional performance may indicate a potential need for subsequent treatment cessation, and patients should be appropriately counseled on this as a possibility.

Limitations

The findings of this study are inherently limited by its retrospective design. The number of available cases seen across these three institutions limited the analysis of treatment considerations. We did not assess factors such as race, insurance type, and education, which have all previously been demonstrated to predict decreased treatment utilization. We found drawing conclusions on these factors challenging in such a small sample size (20,35,36,38,59-61). Additionally, all included patients underwent surgical treatment for TNBC, which may introduce a bias by excluding those who were either not offered or chose not to undergo surgical resection. Further, we did not separate patients according to their adjuvant chemotherapy regimens and the radiotherapy cycles or dose. Nevertheless, this study provides guarded optimism for the use of performance-based scoring systems to support the decision-making process in the non-operative management of TNBC in individuals over 80 years old.

These findings reinforce the continued importance of patient-centered oncologic counseling and identifying the barriers to care to optimize an elderly patient's ability to receive live-prolonging treatment.

Conclusions

This retrospective cohort of octogenarians with TNBC study revealed that 57.1% accepted all standard treatment modalities. Non-standard care was associated with ECOG grade III functional performance, chemotherapy deferral, and radiation therapy. This study of consecutive patients sheds light on areas of BC research for further exploration. It outlines a treatment protocol that may expand access to life-prolonging treatment in octogenarians with TNBC.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://abs.amegroups.com/article/view/10.21037/abs-23-58/rc

Data Sharing Statement: Available at https://abs.amegroups.com/article/view/10.21037/abs-23-58/dss

Peer Review File: Available at https://abs.amegroups.com/article/view/10.21037/abs-23-58/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://abs.amegroups.com/article/view/10.21037/abs-23-58/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the MedStar Health Research Institute (MHRI) Institutional Review Board (STUDY00004989) and individual consent for this retrospective analysis was waived.

Open Access Statement: This is an Open Access article

distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the noncommercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

- WCRF International. Global cancer statistics for the most common cancers in the world. WCRF International. 2023. Available online: https://www.wcrf.org/cancer-trends/ worldwide-cancer-data/
- 2. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. CA Cancer J Clin 2022;72:7-33.
- 3. Giaquinto AN, Sung H, Miller KD, et al. Breast Cancer Statistics, 2022. CA Cancer J Clin 2022;72:524-41.
- 4. SEER 22 areas (San Francisco C, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, Georgia excluding ATL/RG, Idaho, New York, Massachusetts, Illinois and Texas). Data from: Breast SEER Incidence Rates by Age at Diagnosis, 2015-2019. 2022. Available online: https://seer.cancer.gov/statfacts/html/breast.html
- The American Cancer Society. Breast Cancer Facts & Figures 2022-2024. American Cancer Society; 2022. Available online: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2022-2024-breast-cancer-fact-figures-acs.pdf
- United Nations. World Population Prospects 2022: Summary of Results. 2022. Available online: https:// www.un.org/development/desa/pd/sites/www.un.org. development.desa.pd/files/wpp2022_summary_of_results. pdf
- 7. Smith BD, Smith GL, Hurria A, et al. Future of cancer incidence in the United States: burdens upon an aging, changing nation. J Clin Oncol 2009;27:2758-65.
- 8. Kaplan DA. Overview of the Updated NCCN
 Guidelines on Triple-Negative Breast Cancer. Accessed
 11/15/22, 2022. Available online: https://www.
 hmpgloballearningnetwork.com/site/jcp/jcp-special-report/overview-updated-nccn-guidelines-triple-negative-breast-cancer

- Yoon J, Knapp G, Quan ML, et al. Cancer-Specific Outcomes in the Elderly with Triple-Negative Breast Cancer: A Systematic Review. Curr Oncol 2021;28:2337-45.
- 10. Brown L, Carr MJ, Sam C, et al. Tolerance and Outcomes of Neoadjuvant Chemotherapy in Geriatric Breast Cancer Patients. J Surg Res 2023;283:329-35.
- 11. Kozak MM, Xiang M, Pollom EL, et al. Adjuvant treatment and survival in older women with triple negative breast cancer: A Surveillance, Epidemiology, and End Results analysis. Breast J 2019;25:469-73.
- 12. Tang Z, Ji Y, Min Y, et al. Prognostic Factors and Models for Elderly (≥70 Years Old) Primary Operable Triple-Negative Breast Cancer: Analysis From the National Cancer Database. Front Endocrinol (Lausanne) 2022;13:856268.
- Zhu W, Perez EA, Hong R, et al. Age-Related Disparity in Immediate Prognosis of Patients with Triple-Negative Breast Cancer: A Population-Based Study from SEER Cancer Registries. PLoS One 2015;10:e0128345.
- Syed BM, Green AR, Nolan CC, et al. Biological characteristics and clinical outcome of triple negative primary breast cancer in older women - comparison with their younger counterparts. PLoS One 2014;9:e100573.
- 15. Extermann M, Overcash J, Lyman GH, et al. Comorbidity and functional status are independent in older cancer patients. J Clin Oncol 1998;16:1582-7.
- National Center for Health Statistics. Life Expectancy in the U.S. Dropped for the Second Year in a Row in 2021. Available online: https://www.cdc.gov/nchs/pressroom/ nchs_press_releases/2022/20220831.htm
- 17. Malorni L, Shetty PB, De Angelis C, et al. Clinical and biologic features of triple-negative breast cancers in a large cohort of patients with long-term follow-up. Breast Cancer Res Treat 2012;136:795-804.
- Gradishar WJ, Moran MS, Abraham J, et al. Breast Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2022;20:691-722.
- 19. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R, Davies C, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet 2012;379:432-44.
- 20. Jauhari Y, Dodwell D, Gannon MR, et al. The influence of age, comorbidity and frailty on treatment with surgery and systemic therapy in older women with operable triple negative breast cancer (TNBC) in England: A population-based cohort study. Eur J Surg Oncol 2021;47:251-60.

- 21. Reinisch M, von Minckwitz G, Harbeck N, et al. Side effects of standard adjuvant and neoadjuvant chemotherapy regimens according to age groups in primary breast cancer. Breast Care (Basel) 2013;8:60-6.
- 22. Dreyer G, Vandorpe T, Smeets A, et al. Triple negative breast cancer: clinical characteristics in the different histological subtypes. Breast 2013;22:761-6.
- 23. Dotan E, Walter LC, Browner IS, et al. NCCN Guidelines® Insights: Older Adult Oncology, Version 1.2021. J Natl Compr Canc Netw 2021;19:1006-19.
- 24. Abdel-Qadir H, Austin PC, Lee DS, et al. A Population-Based Study of Cardiovascular Mortality Following Early-Stage Breast Cancer. JAMA Cardiol 2017;2:88-93.
- 25. Muss HB, Berry DA, Cirrincione C, et al. Toxicity of older and younger patients treated with adjuvant chemotherapy for node-positive breast cancer: the Cancer and Leukemia Group B Experience. J Clin Oncol 2007;25:3699-704.
- Gray E, Marti J, Wyatt JC, et al. Chemotherapy effectiveness in trial-underrepresented groups with early breast cancer: A retrospective cohort study. PLoS Med 2019;16:e1003006.
- Land LH, Dalton SO, Jensen MB, et al. Impact of comorbidity on mortality: a cohort study of 62,591 Danish women diagnosed with early breast cancer, 1990-2008.
 Breast Cancer Res Treat 2012;131:1013-20.
- 28. Guo Q, Lan T, Lu Y, et al. Effectiveness of adjuvant chemotherapy for elderly patients with triple-negative breast cancer. Biomol Biomed 2023;23:502-9.
- 29. Crozier JA, Pezzi TA, Hodge C, et al. Addition of chemotherapy to local therapy in women aged 70 years or older with triple-negative breast cancer: a propensity-matched analysis. Lancet Oncol 2020;21:1611-9.
- Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5:649-55.
- Lichtman SM, Wildiers H, Launay-Vacher V, et al.
 International Society of Geriatric Oncology (SIOG) recommendations for the adjustment of dosing in elderly cancer patients with renal insufficiency. Eur J Cancer 2007;43:14-34.
- 32. Tanzola M. ASCO Guideline Rapid Update Addresses the Use of Neoadjuvant Pembrolizumab in High-Risk Early-Stage Triple-Negative Breast Cancer. Updated May 25, 2022. Available online: https://ascopost.com/issues/may-25-2022/asco-guideline-rapid-update-addresses-the-use-of-neoadjuvant-pembrolizumab-in-high-risk-early-stage-triple-negative-breast-cancer/#:~:text=In%20t-he%202022%20ASCO%20Guideline,stage%20

- triple%2Dnegative%20breast%20cancer
- 33. Korde LA, Somerfield MR, Hershman DL, et al. Use of Immune Checkpoint Inhibitor Pembrolizumab in the Treatment of High-Risk, Early-Stage Triple-Negative Breast Cancer: ASCO Guideline Rapid Recommendation Update. J Clin Oncol 2022;40:1696-8.
- Zhou C, Xu L, Du Z, et al. Geriatric Early-Stage Triple-Negative Breast Cancer Patients in Low-risk Population: Omitting Chemotherapy Based on Nomogram. Clin Breast Cancer 2022;22:771-80.
- Cho B, Han Y, Lian M, et al. Evaluation of Racial/Ethnic Differences in Treatment and Mortality Among Women With Triple-Negative Breast Cancer. JAMA Oncol 2021;7:1016-23.
- 36. Dias LM, Bezerra MR, Barra WF, et al. Refusal of medical treatment by older adults with cancer: a systematic review. Ann Palliat Med 2021;10:4868-77.
- 37. Tzikas AK, Nemes S, Linderholm BK. A comparison between young and old patients with triple-negative breast cancer: biology, survival and metastatic patterns. Breast Cancer Res Treat 2020;182:643-54.
- 38. Chan WL, Marinho J, Chavarri-Guerra Y, et al. Systemic treatment for triple negative breast cancer in older patients: A Young International Society of Geriatric Oncology Review Paper. J Geriatr Oncol 2022;13:563-71.
- Kaplan HG, Malmgren JA, Atwood MK. Triple-negative breast cancer in the elderly: Prognosis and treatment. Breast J 2017;23:630-7.
- 40. Rocco N, Rispoli C, Pagano G, et al. Breast cancer surgery in elderly patients: postoperative complications and survival. BMC Surg 2013;13 Suppl 2:S25.
- 41. Xiu M, Zhang P, Li Q, et al. Chemotherapy Decision-Making and Survival Outcomes in Older Women With Early Triple-Negative Breast Cancer: Evidence From Real-World Practice. Front Oncol 2022;12:867583.
- 42. Extermann M, Boler I, Reich RR, et al. Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. Cancer 2012;118:3377-86.
- 43. Shachar SS, Hurria A, Muss HB. Breast Cancer in Women Older Than 80 Years. J Oncol Pract 2016;12:123-32.
- 44. Magnuson A, Sedrak MS, Gross CP, et al. Development and Validation of a Risk Tool for Predicting Severe Toxicity in Older Adults Receiving Chemotherapy for Early-Stage Breast Cancer. J Clin Oncol 2021;39:608-18.
- 45. Trapani D. Adjuvant Chemotherapy in Older Women With Early Breast Cancer. J Clin Oncol 2023;41:1652-8.
- 46. Yousefi Afrashteh M, Masoumi S. Psychological well-

- being and death anxiety among breast cancer survivors during the Covid-19 pandemic: the mediating role of self-compassion. BMC Womens Health 2021;21:387.
- 47. Chiu HC, Lin CY, Kuo YL, et al. Resilience among women with breast cancer surviving longer than five years: The relationship with illness perception and body image. Eur J Oncol Nurs 2023;62:102254.
- 48. Liu Y, Liu W, Ma Y, et al. Research on body image cognition, social support and illness perception in breast cancer patients with different surgical methods. Front Psychol 2022;13:931679.
- 49. Pan H, Zhang K, Wang M, et al. Palliative Local Surgery for Locally Advanced Breast Cancer Depending on Hormone Receptor Status in Elderly Patients. Clin Breast Cancer 2019;19:e247-60.
- 50. Hadjittofi C, Almalki H, Mirshekar-Syahkal B, et al. Simple oncoplastic breast defect closure improves longterm cosmetic outcome of breast conserving surgery for breast cancer: A randomised controlled trial. Breast 2022;65:104-9.
- 51. Weber WP, Shaw J, Pusic A, et al. Oncoplastic breast consortium recommendations for mastectomy and whole breast reconstruction in the setting of post-mastectomy radiation therapy. Breast 2022;63:123-39.
- 52. Pinto CA, Peleteiro B, Pinto CS, et al. Breast cancer patient-reported outcomes on level 1 and level 2 oncoplastic procedures using BREAST-Q(®). J Cancer Res Clin Oncol 2023;149:3229-41.
- 53. Oberhauser I, Zeindler J, Ritter M, et al. Impact of Oncoplastic Breast Surgery on Rate of Complications, Time to Adjuvant Treatment, and Risk of Recurrence.

doi: 10.21037/abs-23-58

Cite this article as: Spoer DL, Ghyasi N, Thorson TL, Huffman SS, Berger LE, Lava CX, Lin CF, Masanam MK, Rosal LM, Boisvert ME, Wehner PB, Greenwalt IT, Son JD, Convit RJ, Tousimis E, Song DH, Fan KL, De La Cruz LM. Octogenarians with triple negative breast cancer. Ann Breast Surg 2024;8:16.

- Breast Care (Basel) 2021;16:452-60.
- 54. Nanda A, Hu J, Hodgkinson S, et al. Oncoplastic breast-conserving surgery for women with primary breast cancer. Cochrane Database Syst Rev 2021;10:CD013658.
- 55. Metz G, Snook K, Sood S, et al. Breast Radiotherapy after Oncoplastic Surgery-A Multidisciplinary Approach. Cancers (Basel) 2022;14:1685.
- 56. Islam N, Bhuiyan AKMMR, Alam A, et al. Coping strategy among the women with metastatic breast cancer attending a palliative care unit of a tertiary care hospital of Bangladesh. PLoS One 2023;18:e0278620.
- 57. Campagna V, Mitchell E, Krsnak J. Addressing Social Determinants of Health: A Care Coordination Approach for Professional Case Managers. Prof Case Manag 2022;27:263-70.
- 58. Curigliano G, Pravettoni G. Use of chemotherapy in elderly patients with early-stage triple-negative breast cancer. Lancet Oncol 2020;21:1543-5.
- 59. Fwelo P, Yusuf ZI, Adjei A, et al. Racial and ethnic disparities in the refusal of surgical treatment in women 40 years and older with breast cancer in the USA between 2010 and 2017. Breast Cancer Res Treat 2022;194:643-61.
- Eckhert E, Lansinger O, Ritter V, et al. Breast Cancer Diagnosis, Treatment, and Outcomes of Patients From Sex and Gender Minority Groups. JAMA Oncol 2023;9:473-80.
- 61. Jabbal IS, Bilani N, Yaghi M, et al. Geographical Disparities and Factors Associated With the Decision to Decline Chemotherapy in Breast Cancer. JCO Oncol Pract 2022;18:e1417-26.

Supplementary

Table S1 ECOG performance status

Grade	ECOG performance status
0	Fully active, able to carry on all pre-disease performance without restriction
I	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
II	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
III	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
IV	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
V	Dead

ECOG, Eastern Cooperative Oncology Group.