

Improved Survival of Baby Boomer Women with Early-stage Uterine Cancer: A Surveillance, Epidemiology and End Results (SEER) Study

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Abstract. *Aim: To study the prognostic impact of baby boomer (BB) generation on survival end-points of patients with early-stage endometrial carcinoma (EC). Patients and Methods: Data were obtained from the SEER registry between 1988–2009. Inclusion criteria included women who underwent hysterectomy for stage I-II EC. Patients were divided into two birth cohorts: BB (women born between 1946 and 1964) and pre-boomers (PB) (born between 1926 and 1945). Results: A total of 30,956 patients were analyzed. Considering that women in the PB group were older than those of the BB generation, the statistical analysis was limited to women 50-59 years of age at the time of diagnosis (n=11,473). Baby boomers had a significantly higher percentage of endometrioid histology (p<0.0001), higher percentage of African American women (p<0.0001), lower tumor grade (p<0.0001), higher number of dissected lymph nodes (LN) (p<0.0001), and less utilization of adjuvant radiation therapy (p=0.0003). Overall survival was improved in women in the BB generation compared to the PB generation (p=0.0003) with a trend for improved uterine cancer-specific survival (p=0.0752). On multivariate analysis, birth cohort (BB vs. PB) was not a significant predictor of survival end-points. Factors predictive of survival included: tumor grade, FIGO stage, African-American race, and increased number of dissected LN. Conclusion: Our study suggests that the survival of BB women between 50-60 years of age is better compared to women in the PB generation. As more BB patients are diagnosed with EC, further research is warranted.*

Endometrial cancer (EC) is the most common gynecological malignancy in the United States with an estimated 49,560 women diagnosed with the disease and 8,190 deaths in 2013 (1). The baby boomer (BB) generation is distinguished by an increase in birth rates following World War II, and is one of the largest generations in US history. The BB includes people born between 1946 and 1964 (2).

The incidence of obesity, a major risk factor for many diseases including uterine carcinoma (3-7), is increasing in the BB generation. Several investigators suggested that women in the BB generation are relatively more obese compared to earlier generations (8-10). A recently published single-institution study showed that women with uterine endometrioid carcinoma who were born between 1946 and 1964 were more obese compared to pre-boomer (PB) patients born between 1926 and 1964. However, there were no differences in overall survival between BB and PB patients (11).

There is a paucity of population-based studies in the literature evaluating the outcome of BB women with EC. The National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) provides a database to examine this issue. Considering that more than 85% of patients with endometrial carcinoma present with International Federation of Gynecology and Obstetrics (FIGO) stage I-II carcinoma (12), the purpose of the present study was to describe patient demographics, tumor characteristics and survival in BB women and compare it to PB women who underwent hysterectomy for early-stage EC.

Patients and Methods

This study used public-use data from the SEER Program (13), which was initiated by the National Cancer Institute in 1973 to report population-based estimates of cancer incidence, mortality, and survival in the U.S. This analysis was limited to the original SEER 9 registries which include the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah; the metropolitan areas of Atlanta, Detroit, and San Francisco-Oakland; and the 13-county area of

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Seattle-Puget Sound (14). The populations in these areas are generally representative of the US population as a whole, although somewhat more urban and racially diverse. The SEER program's standard is 98% for completeness of case ascertainment (15). Medical records are abstracted for all patients diagnosed in the defined geographic regions for demographics, primary tumor site, histology, stage at diagnosis, and first course of cancer treatment. The microscopically confirmed morphologies were divided into two groups, endometrioid and non-endometrioid type, using the International Classification of Diseases (ICD-O-3) coding system for corpus uteri (16). The endometrioid group encompassed the following codes: 8010, 8020, 8050, 8140, 8210, 8260, 8380, 8382, 8383, 8480, and 8481; the non-endometrioid group encompassed the following codes: 8070, 8071, 8072, 8120, 8130, 8255, 8310, 8323, 8441, 8460, 8461, 8560, 8570, 8940, and 8950.

Inclusion criteria for the study included women with histologically-confirmed EC diagnosed between January 1, 1988 and December 31, 2009 as a first primary, who underwent hysterectomy as a primary management for their EC for 1988 FIGO stages I-II with at least one year follow-up after hysterectomy and were born between 1926 and 1964. Patients who underwent preoperative radiation treatment, those with uterine sarcoma and those with missing FIGO stage data or unknown age were excluded from the study. The public-use SEER dataset, which only contains aggregated de-identified data, was used for this analysis and an IRB approval was not required.

This resulted in a study cohort of 30,956 women who met the inclusion and exclusion criteria for the study. For the purpose of data analysis, patients were divided into two birth cohorts: BB (women born between 1946 and 1964) and PB (born between 1926 and 1945). To mitigate the adverse prognostic significance of old age on clinical outcomes as reported by many investigators (17-20) and considering that women in the PB group are relatively older than those of the BB generation, a subgroup analysis was performed including only women who were 50-59 years of age at the time of diagnosis. In addition to overall survival and uterine cancer-specific survival, the following factors were evaluated: birth cohort (BB vs. PB), race, 1988 FIGO stage, tumor grade, tumor histology (endometrioid vs. non-endometrioid), number of lymph nodes dissected, and the use of any form of adjuvant radiation treatment.

The two groups were compared regarding patient demographics, tumor characteristics and survival using Chi-square test for categorical variables and two-sample t-test for continuous variables. The analysis started by testing the individual factor effect (univariate analysis), followed by the multivariable modeling. The Cox regression model was used for multivariate analysis.

A two-sided *p*-value less than 0.05 was considered statistically significant and all statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

The study cohort included 30,956 women. There were 11,102 women in the BB group (36%) and 19,854 in the PB group (64%) (Table I). Table II shows patient characteristics included in this study. Considering that women in the PB group were relatively older than those of the BB generation, the statistical analysis was performed including only women 50-59 years of age at diagnosis. This resulted in 11,473 women in this birth cohort (51% were BB women and 49% were PB).

Table I. Number and age distribution of the study cohort.

Birth cohort	Age Groups					Total
	<40	40-49	50-59	60-69	70+	
Pre-boomers	0	573	5677	10220	3384	19854
Baby boomers	749	4026	5796	532	0	11102
Total	749	4599	11473	10751	3384	30956

The median age for BB was 54 years compared to 56 years in PB ($p < 0.0001$), median follow-up was 54 (range=12-167) and 158 (range=12-263) months, respectively. Within this cohort, baby boomers had a significantly higher percentage of endometrioid histology ($p < 0.0001$), higher percentage of African American women ($p < 0.0001$), lower tumor FIGO grade ($p < 0.0001$), higher number of dissected lymph nodes ($p < 0.0001$), and less utilization of adjuvant radiation therapy ($p = 0.0003$).

Overall survival was improved in women in the BB compared to the PB generation. Actuarial 5-year overall survival was 97.7% for BB compared to 95.4% for PB women ($p = 0.0003$), with a trend for improved uterine cancer-specific survival (actuarial 5-year uterine cancer-specific survival of 98.2% vs. 95.5%, respectively, $p = 0.0752$).

On multivariate analysis, these variables were included: birth cohort, race, FIGO grade, histological type, FIGO stage, number of dissected lymph nodes and the utilization of adjuvant radiotherapy. After adjusting for other prognostic factors, birth cohort (BB vs. PB) was not a significant predictor of survival end-points. The following factors were predictive of overall and uterine cancer-specific survival; FIGO grade, FIGO stage, African American race, and increased number of dissected lymph nodes. Hazard ratios and corresponding 95% confidence intervals for variables included in the model are shown in Table III.

Discussion

To our knowledge, we believe that this report is the first in the literature in using large US population database to study patient demographics, tumor characteristics and survival in women of the BB generation who were diagnosed with early-stage EC. Our study suggests that BB women who underwent hysterectomy for 1988 FIGO stage I-II uterine carcinoma had more favorable prognostic features *e.g.* lower FIGO grade, lower FIGO stage, less non-endometrioid histology and a significantly higher number of dissected lymph nodes compared to PB women. Taking into account the differing age distribution between the generational

Table II. *Patients' characteristics and age distribution of the 30,956 women with early-stage endometrial carcinoma.*

Variable	Age 40-49 years			Age 50-59 years			Age 60-69 years		
	Pre-boomers N (%)	Baby boomers N (%)	<i>p</i> -Value	Pre boomers N (%)	Baby boomers N (%)	<i>p</i> -Value	Pre boomers N (%)	Baby boomers N (%)	<i>p</i> -Value
Race			0.0008			<0.0001			0.0005
White	496 (86.6%)	3192 (79.3%)		4993 (88.0%)	4885 (84.3%)		8979 (87.9%)	440 (82.9%)	
Black	17 (3.0%)	189 (4.7%)		233 (4.1%)	288 (5.0%)		602 (5.9%)	47 (8.9%)	
Other	58 (10.1%)	662 (15.4%)		433 (7.6%)	586 (10.1%)		603 (5.9%)	38 (7.2%)	
Unknown	2 (0.3%)	23 (0.6%)		18 (0.3%)	37 (0.6%)		36 (0.4%)	6 (1.1%)	
FIGO stage*			0.3450			0.9619			0.7716
I	527 (92.0%)	3654 (90.8%)		5264 (92.7%)	5373 (92.7%)		9390 (91.9%)	486 (91.5%)	
II	46 (8.0%)	372 (9.2%)		413 (7.3%)	423 (7.3%)		830 (8.1%)	45 (8.5%)	
Histology			0.1118			<0.0001			0.0306
Endometrioid	526 (91.8%)	3767 (93.6%)		5232 (92.2%)	5519 (95.2%)		9351 (91.5%)	500 (94.2%)	
Non-endometrioid	47 (8.2%)	259 (6.4%)		445 (7.8%)	277 (4.8%)		869 (8.5%)	31 (5.8%)	
FIGO Grade			0.3001			<0.0001			0.0323
Well-differentiated	314 (54.8%)	2249 (55.9%)		2860 (50.4%)	2979 (51.4%)		4487 (43.9%)	243 (45.8%)	
Moderately differentiated	176 (30.7%)	1072 (26.6%)		1790 (31.5%)	1479 (25.5%)		3340 (32.7%)	136 (25.6%)	
Poorly differentiated	48 (8.4%)	325 (8.1%)		608 (10.6%)	517 (8.9%)		1243 (12.2%)	49 (9.2%)	
Undifferentiated	5 (0.9%)	55 (1.4%)		99 (1.7%)	83 (1.4%)		219 (2.1%)	11 (2.1%)	
Unknown	30 (5.2%)	325 (8.1%)		320 (5.6%)	738 (12.7%)		931 (9.1%)	92 (17.3%)	
Adjuvant RT			0.0345			0.0003			0.2140
No	461 (80.5%)	3368 (83.7%)		4448 (78.4%)	4698 (81.1%)		7534 (73.7%)	405 (76.3%)	
Yes	110 (19.2%)	631 (15.7%)		1186 (20.9%)	1058 (18.3%)		2588 (25.3%)	122 (23.0%)	
Unknown	2 (0.3%)	27 (0.7%)		43 (0.8%)	40 (0.7%)		98 (1.0%)	4 (0.8%)	
LN examined			<0.0001			<0.0001			<0.0001
None	416 (72.6%)	2415 (60.0%)		3677 (64.8%)	2637 (45.5%)		5383 (52.7%)	163 (30.7%)	
0-10	82 (14.3%)	670 (16.6%)		911 (16.0%)	1148 (19.8%)		1936 (18.9%)	111 (20.9%)	
11 or more	44 (7.7%)	783 (19.4%)		777 (13.7%)	1861 (32.1%)		2420 (23.7%)	251 (47.3%)	
Unknown	31 (5.4%)	158 (3.9%)		349 (5.6%)	150 (2.6%)		481 (4.7%)	6 (1.1%)	

FIGO: International Federation of Gynecology and Obstetrics, LN: lymph nodes; RT: radiation treatment; LN: lymph nodes.

Table III. *Cox multivariate analysis of survival endpoints.*

Variable	All-cause survival Adjusted model			Uterine cancer survival Adjusted model		
	HR	95% CI	<i>p</i> -Value	HR	95% CI	<i>p</i> -Value
Baby boomers ^a	0.83	0.66-1.05	0.1150	1.04	0.77-1.41	0.8106
African American race ^b	2.85	2.05-3.96	<0.0001	2.27	1.47-3.51	0.0002
Grade - Moderately differentiated ^c	2.08	1.59-2.72	<0.001	3.46	2.25-5.34	<0.001
Grade - poorly differentiated ^c	3.87	2.79-5.35	<0.0001	9.46	5.96-15.04	<0.0001
Grade - undifferentiated ^c	5.26	3.09-8.96	<0.0001	9.93	4.97-19.86	<0.0001
Non-endometrioid histology ^d	1.25	0.88-1.76	0.2163	1.55	1.04-2.32	0.0302
FIGO stage II ^e	1.62	1.19-2.20	0.0024	1.82	1.26-2.63	0.0016
Number of lymph nodes examined ^f	0.98	0.96-0.99	0.0004	0.98	0.96-0.99	0.0064
Adjuvant radiation treatment ^g	1.31	0.63- 3.03	0.210	1.20	0.84-2.93	0.296

Compared to a: Pre-baby boomers, b: white race, c: well differentiated grade, d: endometrioid histology, e: FIGO stage I, f: continues variable, g: no radiation treatment.

cohorts, the subset analysis for women 50-59 years of age showed improved overall survival and a trend for a better uterine cancer-specific survival of the BB compared to the PB women after treatment.

Our results agree with that of a recently reported single-institution study (11), EC in women in the BB generation was associated with lower FIGO grade, earlier FIGO stage, increased number of dissected lymph nodes and less

utilization of adjuvant radiation treatment. In the past few years, more women with EC are being diagnosed with early FIGO stage, with lower tumor grade (21) and greater-grade endometrioid histology (22). Additionally, the number of dissected lymph nodes during surgical staging is increasing (21-23). Our results suggest that BB women live longer compared to PB women. The trend of improving survival for women with EC diagnosed in the past few decades was also reported by other investigators in US and in Europe (21, 23, 24). The suggested improved survival of women in BB generation could be attributed to all of the aforementioned favorable prognostic factors in this birth cohort, in addition to more accurate staging and treatment of patients. The recent trends of improved surgical staging may result, at least in theory, in better identification and exclusion of patients with high FIGO stages. This might be another possible contributor to the higher survival of women in the BB generation.

The incidence of EC has been rising in the USA (25) and in Europe (26). According to a recent SEER report, there was a significant increase in the incidence of patients with uterine cancer between 2006 and 2009 compared to an earlier time period (25). This increase has been attributed to increasing obesity, life expectancy and tamoxifen use in women with breast cancer (26).

The first members of the BB generation reached the age of 65 in 2011. In the coming decades, if obesity prevalence continues to climb as the BB generation ages, it is likely that more women will be diagnosed with EC (27-29). The impact of obesity and related EC in the BB generation may exacerbate the shortage of oncologists (30-32) in the USA.

A major limitation of the current study is the retrospective nature of its design with its inherent biases. While useful, several limitations in the SEER database must be acknowledged. SEER contains data from 26% of the US population but does not provide coverage for the entire US. In addition, SEER lacks data on the pattern of recurrences, comorbidity, and important risk factors such as body mass index. Other clinically important pathological parameters *e.g.* the presence of lymphovascular space involvement and depth of myometrial invasion, are only available for cases diagnosed in recent years; SEER also lacks data on adjuvant chemotherapy post-hysterectomy (33).

The strength of this study is that we believe it to be the first population-based analysis of the baby boomer generation with EC. We attempted to eliminate the confounding effect of older age in the PB generation by performing a subset analysis of women of 50-59 years of age. Additionally, we included only women with early-stage EC who are less likely to receive systemic chemotherapy, a variable that is not captured in the SEER database. Furthermore, all patients underwent hysterectomy. The BB generation is just entering the age when uterine carcinoma

becomes common and this study represents an early report on this generation. As more women in the BB generation age, patient's demographics and uterine cancer characteristics should be explored.

Conclusion

Women of similar age groups and early-stage EC of the BB generation had more favorable prognostic factors and longer overall survival compared to women of the PB generation. As more BB women are diagnosed with uterine carcinoma, further studies are warranted to further characterize the prognosis of uterine cancer in this generation.

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