

Endometrial Carcinoma in the Baby Boomer Generation. Tumor Characteristics and Clinical Outcome

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Abstract. *Background:* Baby boomers (BB) entering retirement represent a significant burden on medical resources. The unique lifestyle characteristics engendered by the BB may lead to different endometrial cancer characteristics that bear understanding. We sought to characterize BB with endometrioid carcinoma after hysterectomy and compare the results to those of prior to the baby boomers (PB). *Patients and Methods:* After reviewing our prospectively maintained database of 1,450 patients with endometrial cancer, we identified 595 patients who underwent hysterectomy for 1988 International Federation of Gynecologic Oncology (FIGO) stage I-II uterine endometrioid carcinomas, who were born between 1926 and 1964. Their medical records were reviewed in this Institutional review board (IRB)-approved study. Patients with non-endometrioid carcinoma and those who received preoperative therapy were excluded. Patients were defined as BB (born 1946-1964) or PB (born in 1926-1945). The two groups were compared regarding patients' demographics, tumor characteristics and survival. Following a univariate analysis, multivariable modeling was carried out using Cox regression analysis. *Results:* All patients underwent hysterectomy with a minimum of two years' follow-up. There were 234 patients (39%) in the BB group and 361 patients (61%) in the PB group. Median follow-up for the study cohort was 56 months. BB had higher body mass index ($p=0.027$), lower tumor grade ($p=0.002$), earlier FIGO stage ($p=0.023$),

higher number of dissected lymph nodes ($p=0.008$), less lymphovascular space involvement ($p<0.034$), less utilization of adjuvant therapy ($p<0.001$), and younger age at diagnosis ($p=0.002$). However, there was no significant difference found between the BB and PB in regards to local control, disease-specific survival and overall survival. For the study cohort, FIGO stage and tumor grade were independent predictors of recurrence-free and disease-specific survival. There was a trend towards shorter overall survival for the PB women ($p=0.063$). *Conclusion:* Although tumor characteristics were more favorable in the BB group of women, local control and survival end-points were not statistically different compared to those of the PB group. As more BB are diagnosed with endometrial carcinoma, further research is warranted to further elucidate the characteristic differences in endometrial carcinoma, if any, in this generation.

Endometrial cancer is the most common gynecological malignancy in the United States and ranks second in gynecological cancer mortality following ovarian cancer (1). The baby boomer (BB) generation is distinguished by a dramatic increase in birth rates following World War II, and is one of the largest generations in the US history. The BB includes people born between 1946 and 1964 (2). The aging of BB will result in profound changes in the demographics in the US, with a likely increase in the prevalence of uterine carcinoma. Some investigators suggested that women in the BB generation are relatively more obese and became so at younger ages than did their predecessors (3, 4). Obesity and increased body mass index (BMI) are well-known etiological factors for uterine carcinoma (5-9).

Considering that more than 84% of patients with endometrial carcinoma present with (FIGO) stage I-II endometrioid carcinoma (10), the purpose of the present study was to describe patients' demographics, tumor characteristics and treatment outcome in BB women and compare it to pre-boomer (PB) women with early-stage endometrial carcinoma who underwent hysterectomy for their endometrial carcinoma.

Presented at the Annual meeting of American Society of Clinical Oncology (ASCO). Chicago, Illinois June 2012.

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Key Words: Endometrial carcinoma, baby boomers, early stage, obesity, outcome, prognosis.

Patients and Methods

After Institutional Review Board approval, we retrospectively reviewed the medical records of 1,450 consecutive patients in our prospectively maintained endometrial cancer database. We identified 595 women with endometrioid carcinoma who were born between 1926 and 1964. All study patients underwent hysterectomy, salpingo-oophorectomy, with or without peritoneal cytology and pelvic and paraaortic lymph node dissection for 1988 FIGO stage I-II disease, between 1987 and 2009.

Patients with non-endometrioid and mixed histologies were excluded from this analysis. Patients who received preoperative radiation treatment or systemic chemotherapy before relapse were also excluded.

Adjuvant radiation treatment (RT) was prescribed at the discretion of the treating physician for patients believed to be at high risk for tumor recurrence such as those with cervical stromal involvement, higher tumor grade, deep myometrial involvement and those with lower uterine segment involvement. Adjuvant RT was in the form of intravaginal brachytherapy (VB) or pelvic external beam RT, or a combination of both. None of the patients received adjuvant chemotherapy.

The following factors were evaluated; age, race, BMI, birth cohort (BB vs. PB), tumor FIGO grade, FIGO stage, depth of myometrial invasion, lymphovascular space involvement (LVSI), lower uterine segment involvement (LUSI), and use of adjuvant RT.

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). The two groups were compared regarding patients' demographics, tumor characteristics and survival, using Chi-square test for categorical variables and two-sample *t*-test for continuous variables. Kaplan Meier plots were generated for each group for recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS). The analysis started testing the individual factor effect (univariate analysis), followed by the multivariable modeling. The Cox regression model was used for multivariate analysis.

Univariate comparisons were performed using Wilcoxon rank-sum and Fisher's exact tests. A two-sided *p*-value <0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.2.

To mitigate the adverse prognostic significance of old age on clinical outcomes, as reported by many investigators (11-14) 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 50-60 years of age at the time of diagnosis.

Results

There were 234 women (39%) in the BB group and 361 women (61%) in the PB group. Median follow-up for the study cohort was 56 months. All patients had a minimum of two years follow-up. Baby boomers had a higher BMI ($p=0.027$), lower tumor grade ($p=0.002$), earlier FIGO stage ($p=0.023$), higher number of dissected lymph nodes ($p=0.008$), less frequent LVSI ($p=0.034$), less utilization of adjuvant therapy ($p=0.001$), and younger age at diagnosis ($p=0.002$). Table I shows the patients' characteristics included in this study.

All patients underwent hysterectomy and salpingo-phorectomy, 80% had peritoneal cytological examination and 71% underwent pelvic lymphadenectomy.

VB was delivered using ^{192}Ir high-dose rate (HDR) in three to five fractions with a target volume of the upper 3-4 cm of the vagina. The median dose was 37.5 Gy, prescribed to the vaginal surface. The treatment was delivered once or twice per week using a single-channel vaginal cylinder. The dose of pelvic external beam RT ranged from 44 Gy to 50.4 Gy in daily treatments.

Despite the relatively favorable prognostic features in the BB group, there was no significant difference found between BB and PB groups in regards to recurrence-free or disease-specific survival. The five-year RFS for women in the BB was 91% vs. 90% for PB women ($p=0.9834$) (Figure 1). Similarly the five-year DSS was 97% vs. 95% ($p=0.1945$), respectively) (Figure 2).

As expected, considering that women in the PB group were relatively older than women in the BB group, there was a trend for improved five-year OS in the BB group at 91% vs. 86% ($p=0.0613$) (Figure 3).

In an attempt to mitigate the adverse prognostic impact of old age, a subset analysis was performed including only women 50-60 years of age at diagnosis. This resulted in 230 patients. There were 131 PB in this group (57%) and 99 BB (43%). The only two persistent significant differences between the two groups in this age cohort were increased BMI ($p=0.040$) and increased number of dissected lymph nodes ($p=0.032$) in the BB group.

On multivariate analysis, significant predictors of RFS and DSS included LVSI, ($p<0.001$), and FIGO grade ($p=0.002$). For OS, independent prognostic factors included LVSI ($p<0.001$), age as a continuous variable ($p<0.001$), FIGO grade ($p=0.002$), and lower uterine segment involvement ($p=0.010$). On univariate analysis, birth cohort (BB vs. PB) was not found to be a significant predictor of RFS, DSS or OS.

Discussion

To our knowledge, this is the first report examining patients' demographics, tumor characteristics and treatment received in women of the BB generation who were diagnosed with early-stage endometrioid carcinoma. Our study suggests that BB women who underwent hysterectomy for 1988 FIGO stage I-II uterine endometrioid carcinoma have similar RFS and DSS despite their more favorable prognostic features *e.g.* younger age, lower FIGO grade, stage and less frequent involvement of the lower uterine segment and less LVSI.

Additionally, after controlling for the confounding effect of old age, the subset analysis of the study cohort showed no clear difference in outcome between the BB and PB groups.

In agreement with other investigators (3, 4), our study suggests a significant increase in BMI in women in the BB

Table I. Patient characteristics of the study cohort.

Variable	Response	Pre boomers (N=361, 61%)	Boomers (N=234, 39%)	p-Value	
Median age in years (range)		64 (44-83)	53 (43-63)	0.002	
Median BMI (range)		34.4 (18-46.1)	36.5 (26-49.8)	0.027	
Race	Caucasian	267 (74%)	173 (74%)	0.983	
	AA	94 (26%)	60 (26%)		
Median follow-up in months, (range)		79 (32-276)	32 (24-210)	<0.001	
FIGO tumor grade	1	243 (67%)	189 (81%)	0.002	
	2	81 (22%)	31 (13%)		
	3	37 (10%)	14 (6%)		
	1988 FIGO stage	IA	51 (14.2%)		49 (21%)
	IB	206 (57%)	141 (60%)		
	IC	64 (18%)	22 (9%)		
	IIA	15 (4%)	8 (3%)		
	IIB	25 (7%)	14 (6%)		
	LUS involvement	Yes	69 (19%)	33 (14%)	0.118
LVSI	Yes	44 (12%)	16 (7%)	0.034	
Lymph node dissection	Yes	250 (69%)	171 (73%)	0.327	
Median number of pelvic lymph nodes dissected (range)		10 (0-40)	12 (0-59)	0.008	
Median number of para-aortic lymph nodes dissected (range)		2 (0-12)	3 (0-23)	0.671	
Peritoneal cytology*	Yes	285 (79%)	192 (82%)	0.454	
Adjuvant RT	Yes	139 (39%)	53 (23%)	<0.001	
Type of RT				0.747	
Pelvic		19 (14%)	5 (9%)		
Brachytherapy		50 (36%)	21 (40%)		
Combination		68 (50%)	27 (51%)		
Recurrence	Yes	26 (7%)	12 (5%)	0.312	

BMI, Body mass index; AA, African-American; FIGO, International Federation of Gynecologic Oncology; LUS, lower uterine segment; LVSI, lymphovascular space involvement; RT, radiation treatment. *None with positive peritoneal cytology.

generation compared to those of the PB. Similarly to other studies (15, 16), increased BMI in our study did not impact on the prognosis of patients in either group.

However, BB women are likely to present at a younger age, with earlier stages disease, with lower FIGO grade and lacking other adverse pathological features. Hence, as in our analysis, they may have similar outcomes to PB women who may present at older age with a higher incidence of adverse prognostic factors requiring adjuvant RT. We believe that adjuvant RT may have resulted in the overall outcome being the same in the two cohorts examined in our study. The only factors predictive of RFS and DSS were FIGO grade and stage.

It is possible that the two birth cohorts overlap when it comes to the age at diagnosis and outcome, considering that many confounding factors might play a major role in the response-to-treatment. For example, older women in the PB generation may be diagnosed in their 70s and undergo a complete surgical staging that may influence the need for adjuvant therapy and ultimately alter the prognosis. On the other hand, women in the BB group may have been

diagnosed at an earlier age before the trends of complete surgical staging and increased lymphadenectomy assumed standard of care status.

In the coming decades, the increased BMI in the BB generation is likely to contribute to more women being diagnosed with endometrial carcinoma. The impact of obesity and related endometrial carcinoma in the BB generation may exacerbate the shortage of gynecological oncologists (17) and radiation oncologists (18) in the USA.

A major limitation of the current study is the retrospective nature of its design with its inherent biases. The BB generation is just entering the age when uterine carcinoma becomes common and thus this analysis represents an early experience of this generation. We attempted to eliminate the confounding effect of older age in the PB generation by performing a subset analysis for women of 50-60 years of age. Additionally, we included only women with early-stage endometrioid carcinoma. Furthermore, all patients underwent hysterectomy and they underwent similar adjuvant treatments in our study.

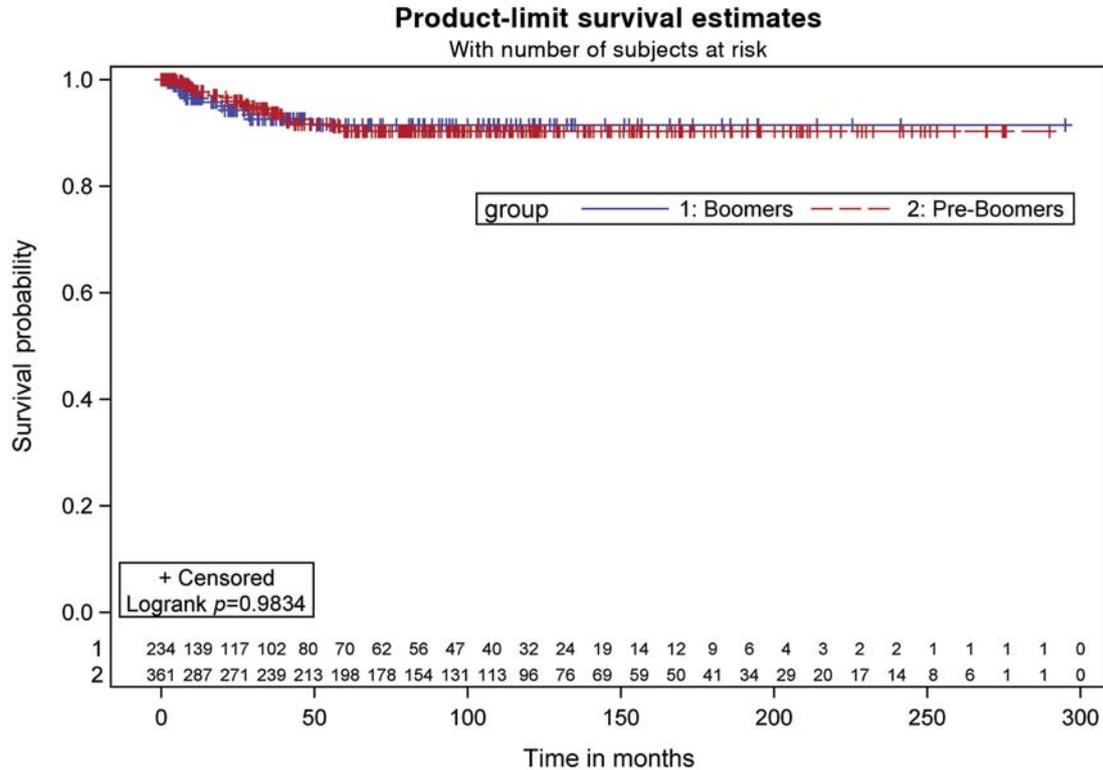


Figure 1. Recurrence-free survival for the study cohort.

As more women in the BB generation age, patients' demographics and uterine cancer characteristics should be explored in the years to come. A robust analysis using a larger and mature data set *e.g.* SEER data, is warranted in the near future to shed more light on the difference between birth cohort generations, if any.

Conclusion

Despite favorable prognostic features in women with early-stage endometrioid carcinoma who were born between 1946 and 1964 (BB generation), there was no difference in RFS, DSS compared to women born between 1926 and 1945 (PB generation). As more BB women are diagnosed with uterine carcinoma, further studies are warranted to characterize this generation's impact on prognosis of uterine cancer.

Conflicts of Interest

The Authors declare that there are no conflicts of interest.

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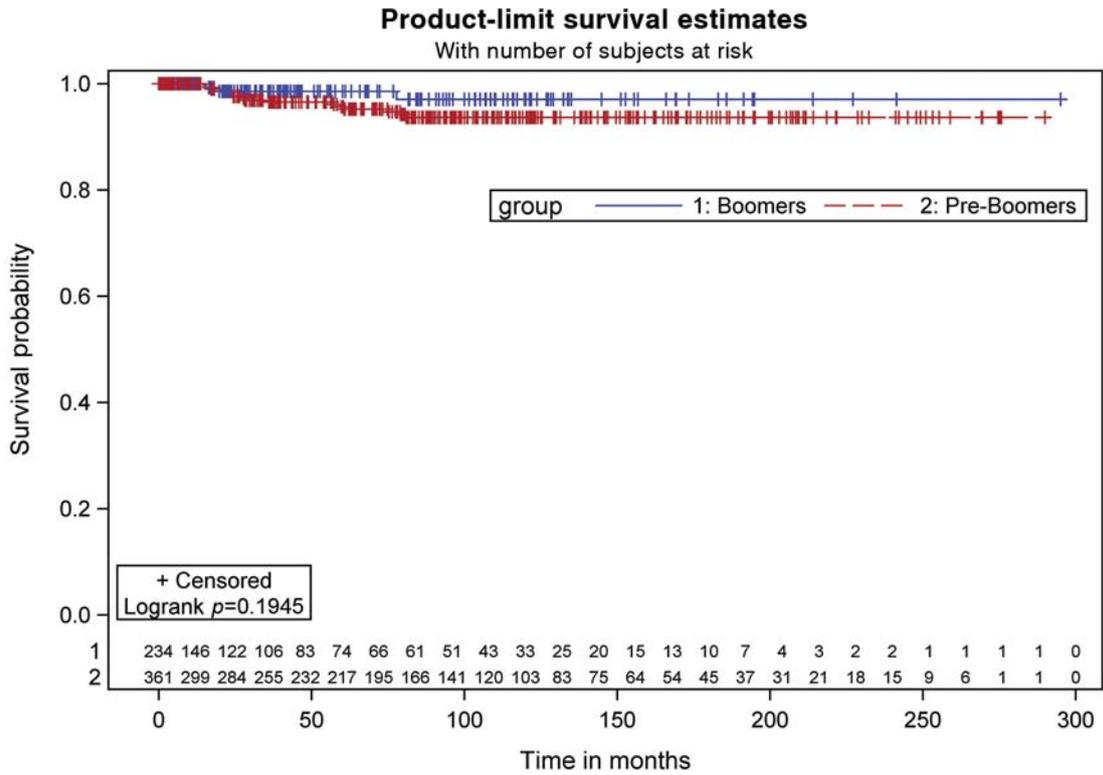


Figure 2. Disease-specific survival for the study cohort.

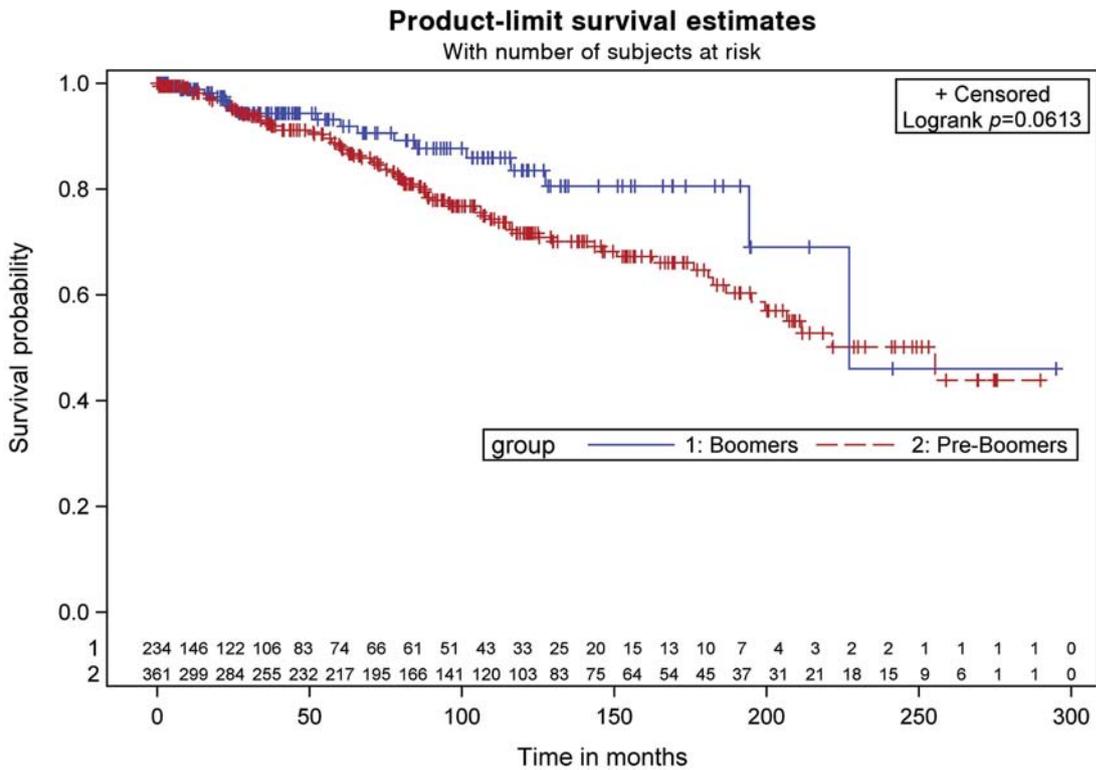


Figure 3. Overall survival for the study cohort.

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Received December 4, 2012

Revised January 14, 2013

Accepted January 14, 2013