



Disparities in surgery for early-stage cancer: the impact of refusal

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Abstract

Background For early-stage cancer surgery is often curative, yet refusal of recommended surgical interventions may be contributing to disparities in patient treatment. This study aims to assess predictors of early-stage cancers surgery refusal, and the impact on survival.

Methods Patients recommended surgery with primary stage I and II lung, prostate, breast, and colon cancers, diagnosed between 2007–2014, were identified in the Surveillance, Epidemiology and End Results database ($n=498,927$). Surgery refusal was reported for 5,757 (1.2%) patients. Associations between sociodemographic variables and surgery refusal by cancer type were assessed in adjusted multivariable logistic regression models. The impact of refusal on survival was investigated using adjusted Cox-Proportional Hazard regression in a propensity score-matched cohort.

Results Increasing age ($p < 0.0001$ for all four cancer types), non-Hispanic Black race/ethnicity (OR_{adjBREAST} 2.00, 95% CI 1.68–2.39; OR_{adjCOLON} 3.04, 95% CI 2.17–4.26; OR_{adjLUNG} 2.19, 95% CI 1.77–2.71; OR_{adjPROSTATE} 2.02, 95% CI 1.86–2.20; vs non-Hispanic White), insurance status (uninsured: OR_{adjBREAST} 2.75, 95% CI 1.89–3.99; OR_{adjPROSTATE} 2.10, 95% CI 1.72–2.56; vs insured), marital status (OR_{adjBREAST} 2.16, 95% CI 1.85–2.51; OR_{adjCOLON} 1.56, 95% CI 1.16–2.10; OR_{adjLUNG} 2.11, 95% CI 1.80–2.47; OR_{adjPROSTATE} 1.94, 95% CI 1.81–2.09), and stage (OR_{adjBREAST} 1.94, 95% CI 1.70–2.22; OR_{adjCOLON} 0.13, 95% CI 0.09–0.18; OR_{adjLUNG} 0.71, 95% CI 0.52–0.96) were all associated with refusal; patients refusing surgery were at increased risk of death compared to patients who underwent surgery.

Conclusions More vulnerable patients are at higher risk of refusing recommended surgery, and this decision negatively impacts their survival.

Keywords Cancer surgery · Early-stage · Surgery · Refusal · Survival

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Introduction

Breast, colon, lung, and prostate cancer account for nearly half of all new cancer diagnoses, and 45.1% of all annual cancer-related deaths [1]. Despite the fact that surgery is often curative in these cancers [2–8], and notwithstanding clinical recommendations, disparities exist among those who receive cancer directed surgeries, with African American patients less likely to receive breast [2], colorectal [3], and lung cancers surgeries [4, 5]. Patients without private insurance [6] and those who are unmarried [7] are less likely to undergo cancer surgery as well. Unfortunately, it remains unclear why these more vulnerable populations are less likely to receive surgery as cancer treatment.

It has been suggested that some of these patients refuse recommended surgery, and that there may be disparities in refusal. A previous analysis found age, race, marital status, and income level to be associated with surgery refusal

for multiple cancer types [8]. Another study reported that age, ethnicity, marital status, stage, and insurance status to be associated with refusal of surgery for breast cancer [9]. However, these analyses included patients of advanced stage, where health fragility due to regional or distant metastasis might be a contributing factor in treatment refusal. Moreover, while these studies showed surgery refusal to be associated with increased risk of overall [9] and cancer-specific [8] mortality, surgery alone in late stage cancers may not be effective given the severity of the disease, and the impact of refusing surgery may be underestimated in these studies. Understanding which patients are more likely to refuse physician-recommended surgical intervention for early-stage cancer, when surgery is most likely to be curative, and evaluating the impact of refusal on cancer-related outcomes would be of great clinical value, and might introduce avenues whereby cancer outcome disparities might be addressed.

This study aims to identify clinical and demographic predictors of early-stage surgery refusal, and to assess the impact of surgery refusal on survival.

Materials and methods

Database and selection

The Surveillance, Epidemiology, and End Results (SEER) program, sponsored by the National Institute of Health's National Cancer Institute, aggregates cancer incidence and survival data from cancer registries in several regions throughout the country. The SEER database was retrospectively queried to identify patients with primary, AJCC Stage I or Stage II lung, prostate, breast, or colon cancer diagnosed between 2007 and 2014. ($n = 767,438$).

Selection of cases who were recommended surgery: Cases in which patients were not recommended surgery either because it was not part of the planned first course of treatment or contraindicated ($n_{\text{excluded}} = 199,497$), if it was unknown whether the surgery was recommended ($n_{\text{excluded}} = 2,335$), if surgery was recommended but unknown if the procedure was actually performed ($n_{\text{excluded}} = 3,744$), or if the surgery was recommended but not performed, either because patients died prior to surgery ($n_{\text{excluded}} = 224$) or for unknown reasons ($n_{\text{excluded}} = 17,186$) were excluded. This first selection left 544,452 patients who were recommended surgery.

Other exclusions: Cases without a microscopically confirmed cancer diagnosis ($n_{\text{excluded}} = 613$), who were under 18 years ($n_{\text{excluded}} = 53$), and male breast cancers ($n_{\text{excluded}} = 1,937$) were excluded from the study; patients with unknown data for insurance status ($n_{\text{excluded}} = 11,686$), race/ethnicity ($n_{\text{excluded}} = 2,758$), and urban/rural residence ($n_{\text{excluded}} = 596$) were excluded. This left 526,809 eligible

patients. Lastly, only those histological types amenable to surgical resection were included. This was adenocarcinoma for colon and prostate cancers, ductal, lobular, and tubular histologies for breast cancer, and non-small cell histology for lung cancer ($n_{\text{excluded}} = 27,882$). This resulted in 274,346 breast, 69,490 colon, 36,763 lung, and 118,328 prostate cancer patients (Fig. 1).

Outcomes and predictor variables

The primary outcome was patient's refusal of recommended surgery, specifically defined as "Patient or Patient's Guardian refused", derived from the NAACCR definition as "Surgery of the primary site was not performed; it was recommended by the patient's physician, but was refused by the patient, the patient's family member, or the patient's guardian. The refusal was noted in the patient record". We compared these individuals to those for whom surgery was recommended and performed.

Predictors of interest included age, sex, race and ethnicity, stage (AJCC defined), alternative treatments (chemotherapy or radiation treatment), health insurance, residence in proximity to an urban area, marital status, and in the case of breast cancer, histology (derived from ICD-O-3 codes). Race/ethnicity was categorized based on the combined information from race (White, Black, Asian-American/Pacific Islander and Native America/Alaskan Native) and ethnicity (Hispanic) as non-Hispanic whites, non-Hispanic blacks, Hispanics, and other non-Hispanic races (Asian-Americans/Pacific Islanders/Alaskan-Natives/Native-Americans). Ages were categorized as < 50, 50–64, 65–79, 80+ years. Marital status was condensed to reflect whether patients identified they were single and never married, separated, divorced, or widowed, and compared this category with patients who indicated they were married or had an unmarried domestic partner. Insurance data in SEER became available in 2007; for the purposes of our study, it was defined as the presence or access to some type of health insurance, either private or Medicaid/Medicare. County of residence was classified using SEER's Urban–Rural Continuum, adopted from the US Department of Agriculture's Economic Research Service (ERS) [10]. Metro counties were defined as including at least one urbanized area of $\geq 50,000$ population. Suburban counties are classified as adjacent to a Metro area if physically adjoining a Metropolitan county and with at least 2% of its employed labor force commuting to Metro counties.

Statistical analysis

Univariate associations were assessed using Chi-square tests for categorical variables and Wilcoxon rank sum test for continuous variables. An adjusted multivariable logistic regression model assessed associations between sociodemographic

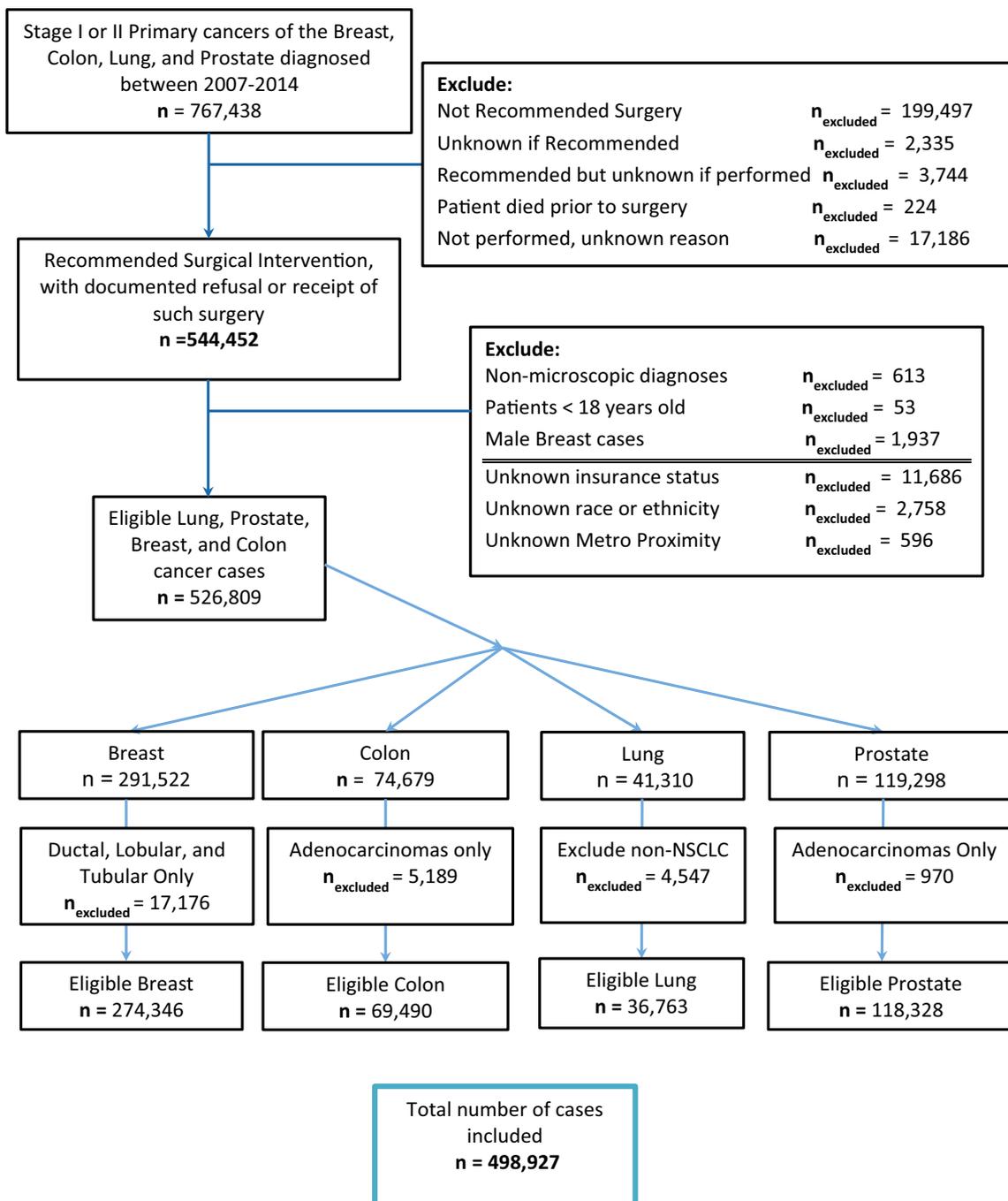


Fig. 1 Patient selection

(age, sex, race/ethnicity, health insurance, marital status, metro proximity), clinical (stage, treatment with chemotherapy or radiation), and year of diagnosis with surgery refusal within each cancer type.

Adjusted Cox-Proportional Hazard regression analysis was used to investigate the association between treatment type (recommended surgery, refusal of recommended surgery but treatment with chemotherapy or radiotherapy,

surgery refusal and no chemotherapy or radiotherapy) and cancer-specific survival as derived from SEER’s cause-specific death classification, and was stratified by cancer type. Patients without complete follow-up information were excluded. Hazard models were adjusted for age, sex, race and ethnicity, stage, surgical refusal, insured status, county of residence, marital status, and for breast cancer, histology. In prostate cancer, we were unable to adjust for stage,

given that stage I prostate cancer were few ($n = 793$) with no instances of refusal.

Additionally, propensity score-matched analysis was conducted to adjust for baseline differences between those undergoing and refusing recommended cancer surgery. Propensity scores were created using a logistic regression model based on age, sex, race/ethnicity, stage, size, insurance status, marital status, and county of residence. The logit of the propensity score was then used for 1:1 greedy matching, with a caliper set at 0.2, creating a balanced cohort, for a final sample of 1,882 breast, 466 colon, 1,496 lung, and 7,528 prostate cancer patients ($N_{\text{BREASTexcluded}} = 272,464$; $N_{\text{COLONexcluded}} = 69,024$; $N_{\text{LUNGexcluded}} = 35,267$; $N_{\text{PROSTATEexcluded}} = 110,800$). Cox-proportional hazards survival analysis was then conducted.

Results

Of the 498,927 cases of early-stage cancer who met selection criteria, 5757 (1.2%) refused recommended surgeries. This included 754 (2.0%) refusals in lung cancer, 3,821 (3.2%) refusals in prostate cancer, 947 (0.35%) refusals in breast cancer, and 235 (0.34%) cases of refusal in colon cancer.

Breast cancer

Patients who refused surgery for breast cancer were more likely to be older ($p < 0.0001$), non-White race/ethnicity ($p < 0.0001$), lack health insurance ($p < 0.0001$), live without a life partner ($p < 0.0001$), and have a stage II diagnosis ($p < 0.0001$) (Table 1).

In multivariate analysis, predictors of refusal included older age (50–64 years: $OR_{\text{adj}} 0.99$, 0.79–1.22; 65–79 years: $OR_{\text{adj}} 1.32$, 1.05–1.64; 80+ years $OR_{\text{adj}} 7.51$, 6.10–9.24 vs. < 50 years), non-White race/ethnicity (non-Hispanic Black: $OR_{\text{adj}} 2.00$, 95% CI 1.68–2.39; non-Hispanic other race: $OR_{\text{adj}} 1.56$, 1.25–1.95 vs non-Hispanic White), lack of insurance ($OR_{\text{adj}} 2.75$, 95% CI 1.89–3.99), lack of a life partner ($OR_{\text{adj}} 2.16$, 95% CI 1.85–2.51), and stage II diagnoses ($OR_{\text{adj}} 1.94$, 95% CI 1.70–2.20). County of residence (suburban county vs metro county: $OR_{\text{adj}} 0.68$, 95% CI 0.49–0.95) was inversely associated with surgery refusal (Table 2).

Colon cancer

Patients who refused surgery for colon cancer were more likely to be older ($p < 0.0001$), a non-White race/ethnicity ($p < 0.0001$), to live without a life partner ($p < 0.0001$), and to have a Stage II diagnosis ($p = 0.035$) (Table 1).

Predictors of refusal included older age (65–79 years: $OR_{\text{adj}} 5.26$, 95% CI 1.28–21.71; 80+ years $OR_{\text{adj}} 35.28$,

8.68–143.48 vs. < 50 years), non-Hispanic Black race/ethnicity ($OR_{\text{adj}} 3.04$, 95% CI 2.17–4.26), and lack of life partner ($OR_{\text{adj}} 1.56$, 95% CI 1.16–2.10). Stage II diagnosis was associated with decreased risk of surgery refusal ($OR_{\text{adj}} 0.13$, 95% CI 0.09–0.18) (Table 2).

Lung cancer

Patients who refused surgery for lung cancer were more likely to be older ($p < 0.0001$), non-White race/ethnicity ($p < 0.0001$), to live without a life partner ($p < 0.0001$), and to have been stage II at diagnosis ($p = 0.042$) (Table 1).

After adjustment, predictors of lung cancer refusal included older age (50–64 years: $OR_{\text{adj}} 2.42$, 95% CI 1.06–5.51; 65–79 years $OR_{\text{adj}} 4.21$, 1.87–9.48; 80+ years $OR_{\text{adj}} 16.60$, 7.34–37.56 vs. < 50 years), non-White race/ethnicity (non-Hispanic Black: $OR_{\text{adj}} 2.19$, 95% CI 1.77–2.71; non-Hispanic Other Race: $OR_{\text{adj}} 1.43$, 1.10–1.88 vs non-Hispanic White), lack of a life partner ($OR_{\text{adj}} 2.11$, 95% CI 1.80–2.47), and county of residence (living in rural county vs metro county: $OR_{\text{adj}} 1.37$, 95% CI 1.01–1.84). Patients with a stage II diagnoses ($OR_{\text{adj}} 0.71$, 95% CI 0.52–0.96) were less likely to refuse surgical intervention (Table 2).

Prostate cancer

Patients who refused surgery for prostate cancer were more likely to be older ($p < 0.0001$), non-White race/ethnicity ($p < 0.0001$), without health insurance ($p < 0.0001$), living without a life partner ($p < 0.0001$), and stage II at diagnosis ($p < 0.0001$) (Table 1).

Predictors of refusal at multivariate analysis included older patients (50–64 years: $OR_{\text{adj}} 1.38$, 95% CI 1.15–1.64; 65–79 years $OR_{\text{adj}} 2.56$, 2.14–3.05; 80+ years $OR_{\text{adj}} 1.99$, 1.57–2.52 vs. < 50 years), non-White race/ethnicity (non-Hispanic Black: $OR_{\text{adj}} 2.02$, 95% CI 1.86–2.20; Hispanic: $OR_{\text{adj}} 1.26$, 1.12–1.41; non-Hispanic other race: $OR_{\text{adj}} 1.72$, 1.51–1.96 vs non-Hispanic White), lack of insurance ($OR_{\text{adj}} 2.10$, 95% CI 1.72–2.56), and lack of a life partner ($OR_{\text{adj}} 1.94$, 95% CI 1.81–2.09) (Table 2).

Impact of surgical refusal on survival

Patients refusing surgery and not undergoing any chemotherapy or radiotherapy experienced significantly increased risk of death ($HR_{\text{adjBREAST}} 5.78$, 4.78–7.00; $HR_{\text{adjCOLON}} 12.44$, 10.06–15.40; $HR_{\text{adjLUNG}} 4.50$, 95% CI 3.69–5.49; $HR_{\text{adjPROSTATE}} 1.60$, 1.06–2.43). Patients who refused surgical intervention but received chemotherapy or radiotherapy also had statistically significant increased risk of death compared to those who received surgery ($HR_{\text{adjBREAST}} 6.58$, 5.25–8.24; $HR_{\text{adjCOLON}} 15.29$, 10.30–22.70; $HR_{\text{adjLUNG}} 2.84$, 95% CI 2.47–3.26; $HR_{\text{adjPROSTATE}} 1.27$, 0.93–1.73) (Fig. 1).

Table 1 General characteristics of the sample: surgical refusal according to sociodemographic, clinical, and treatment variables

Variables	Breast cancer <i>n</i> = 274,346			Colon cancer <i>n</i> = 69,490			Lung cancer <i>n</i> = 36,763			Prostate cancer <i>n</i> = 118,328						
	Surgery %	Refused %	<i>p</i> (χ^2)	Surgery %	Refused %	<i>p</i> (χ^2)	Surgery %	Refused %	<i>p</i> (χ^2)	Surgery %	Refused %	<i>p</i> (χ^2)				
Age (years)			<0.0001			<0.0001			<0.0001			<0.0001				
<50	61,873	0.23	135	0.14	5450	0.08	2	0.01	1344	0.04	6	0.01	6347	0.06	138	0.04
50–64	108,156	0.40	216	0.23	20,931	0.30	25	0.11	11,127	0.31	123	0.16	63,961	0.56	1686	0.44
65–79	80,947	0.30	211	0.22	27,443	0.40	53	0.23	19,733	0.55	353	0.47	40,352	0.35	1849	0.48
80+	22,423	0.08	385	0.41	15,431	0.22	155	0.66	3805	0.11	272	0.36	3847	0.03	148	0.04
Sex								0.341								0.907
Male	–	–	–	–	34,571	0.50	110	0.47	17,318	0.48	361	0.48	–	–	–	–
Female	–	–	–	–	34,684	0.50	125	0.53	18,691	0.52	393	0.52	–	–	–	–
Race/Ethnicity								<0.0001								<0.0001
NH-White	193,964	0.71	597	0.63	48,525	0.70	149	0.63	28,590	0.79	541	0.72	83,517	0.73	2306	0.60
NH-Black	26,606	0.10	172	0.18	8023	0.12	49	0.21	3115	0.09	114	0.15	14,999	0.13	872	0.23
Hispanic	28,609	0.11	84	0.09	7099	0.10	18	0.08	1774	0.05	35	0.05	10,555	0.09	379	0.10
NH-other	24,220	0.09	94	0.10	5608	0.08	19	0.08	2530	0.07	64	0.08	5436	0.05	264	0.07
Insurance								<.0001								0.262
Insured	269,574	0.99	917	0.97	67,363	0.97	231	0.98	35,386	0.98	745	0.99	112,983	0.99	3708	0.97
Uninsured	3825	0.01	30	0.03	1892	0.03	4	0.02	623	0.02	9	0.01	1524	0.01	113	0.03
Urban proximity								0.055								0.569
In metro	246,795	0.90	874	0.92	60,474	0.87	206	0.87	31,118	0.86	654	0.85	102,742	0.90	3446	0.90
Suburban	15,525	0.06	37	0.04	4996	0.07	14	0.06	2750	0.08	51	0.07	6967	0.06	230	0.06
Rural	11,079	0.04	36	0.04	3785	0.06	15	0.07	2141	0.06	49	0.07	4798	0.04	145	0.04
Home partner								<0.0001								<0.0001
Married/home partner	158,726	0.58	269	0.28	37,450	0.54	84	0.36	20,455	0.57	280	0.36	86,534	0.76	2274	0.60
Single	103,856	0.38	607	0.64	28,460	0.41	131	0.56	14,235	0.39	452	0.61	21,726	0.19	1196	0.31
Unknown	10,817	0.04	71	0.08	3345	0.05	20	0.08	1319	0.04	22	0.03	6247	0.05	351	0.09
Stage								<0.0001								<0.0001
Stage 1	157,863	0.58	378	0.40	32,606	0.47	199	0.85	29,991	0.83	649	0.86	759	0.01	0	0.00
Stage 2	115,536	0.42	569	0.60	36,649	0.53	36	0.15	6018	0.17	105	0.14	113,748	0.99	3821	1.00
Chemo								<0.0001								<0.0001
No/unknown	172,808	0.63	879	0.93	62,724	0.91	228	0.97	29,615	0.82	668	0.89	114,358	1.00	3808	1.00
Yes	100,591	0.38	68	0.07	6531	0.09	7	0.03	6394	0.18	86	0.11	149	0.00	13	0.00
Radiation								<0.0001								<0.0001
No/unknown	117,728	0.43	655	0.69	68,395	0.99	201	0.86	33,508	0.93	210	0.28	109,499	0.96	1191	0.31
Yes	155,671	0.57	292	0.31	860	0.01	34	0.14	2501	0.07	544	0.72	5008	0.04	2630	0.69
Treatment								<0.0001								<0.0001

Table 1 (continued)

Variables	Breast cancer n = 274,346			Colon cancer n = 69,490			Lung cancer n = 36,763			Prostate cancer n = 118,328						
	Surgery	%	Refused	%	Refused	%	Surgery	%	Refused	%	Surgery	%	Refused	%	p (χ^2)	
Surgery	273,399	1.00	0	0.00	69,255	1.00	0	0.00	36,009	1.00	0	0.00	114,507	1.00	0	0.00
Non-surgical	0	0.00	334	0.36	0	0.00	38	0.16	0	0.00	555	0.74	0	0.00	2635	0.69
No surgery, chemo, or radiation	0	0.00	613	0.65	0	0.00	197	0.84	0	0.00	199	0.26	0	0.00	1186	0.31
Histology																
Ductal	230,200	0.84	777	0.82												
Lobular	40,496	0.15	166	0.18												
Tubular	2703	0.01	4	0.00												

NH non-Hispanics. “Non-Surgical” indicates a patient who refused surgery but underwent either chemotherapy or radiation

Older age, non-Hispanic Black race/ethnicity, stage II disease, living outside of a metropolitan county, and marital status were significantly associated with increased risk of mortality across all cancer types (Table 3; Supplementary Figure).

Propensity matched analysis showed patients who refused surgery more likely to experience mortality in comparison to those who received surgery. (HR_{adjBREAST} 5.82, 3.90–8.69; HR_{adjCOLON} 7.92, 4.34–14.43; HR_{adjLUNG} 2.67, 95% CI 2.09–3.40; HR_{adjPROSTATE} 1.81, 1.18–2.80) (Fig. 2).

Discussion

Our results suggest that several identifiable factors exist that predict the likelihood of refusal of recommended surgery in early-stage breast, colon, lung, and prostate cancers; these include both sociodemographic and clinical predictors. Non-White race, male sex, increasing age, lack of health insurance, and unmarried status were all predictive of an increased likelihood of early-stage cancer surgery refusal. Patients with stage II diagnoses in lung and colon were less likely to refuse surgery, but stage II breast cancer patients were more likely to refuse intervention. This is particularly relevant in view of the fact that surgery is considered curative in early-stage cancers. Although we don’t have an explanation for the higher surgery refusal in stage II breast cancer, we can speculate that the cosmetic element plays a role, and that women tend to refuse the more extensive mastectomies that are necessary in advanced stages of the disease.

In breast, colon, and lung cancers, those who underwent surgical intervention had improved survival rates than those who refused surgical intervention but underwent either chemotherapy or radiation treatment. Across all cancers, those who received surgery had better survival than those who did not undergo surgery, chemotherapy, or radiation treatment. After completing a propensity matched analysis, refusal of breast, colon, lung, and prostate breast cancer surgery put patients at an increased risk of death regardless of whether they received alternative treatment.

Understanding why these disparities in early-stage cancer surgery refusal exist will require further research. The retrospective nature of the data used makes it difficult to parse out the nuances of treatment decision making. Some potential explanations include compromised healthcare literacy [11] and distrust of both individual medical providers and the overall US healthcare system reported by minority patients [12]. Older patients, especially patients above the age of 80 years, may be more likely to refuse surgical intervention due to a fear in decrease of quality of life, as they may be affected by other comorbidities that make them frail [13], while those without a life partner might be more inclined to refuse surgery because of a perceived lack of social support

Table 2 Relative odds of surgical refusal

Variable	Breast cancer <i>n</i> = 274,346		Colon cancer <i>n</i> = 69,490		Lung cancer <i>n</i> = 36,763		Prostate cancer <i>n</i> = 118,328		
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	
Age (years)									
<50	1	ref	1	ref	1	ref	1	ref	
50–64	0.99	0.79 1.22	2.67	0.63	11.27	2.42	1.06	5.51	1.38 1.15 1.64
65–79	1.32	1.05 1.64	5.26	1.28	21.71	4.21	1.87	9.48	2.56 2.14 3.05
80+	7.51	6.10 9.24	35.28	8.68	143.48	16.60	7.34	37.56	1.99 1.57 2.52
Sex									
Female/male		–	0.75	0.57	0.99	0.81	0.69	0.94	–
Race/Ethnicity									
NH-White	1	ref	1	ref	1	ref	1	ref	
NH-Black	2.00	1.68 2.39	3.04	2.17	4.26	2.19	1.77	2.71	2.02 1.86 2.20
Hispanic	1.05	0.83 1.33	1.19	0.72	1.95	1.03	0.73	1.46	1.26 1.12 1.41
NH-other	1.56	1.25 1.95	1.39	0.86	2.26	1.43	1.10	1.88	1.72 1.51 1.96
Insurance status									
Uninsured/insured	2.75	1.89 3.99	1.60	0.58	4.44	1.05	0.54	2.08	2.10 1.72 2.56
Marital status									
Married/union	1	ref	1	ref	1	ref	1	ref	
Single	2.16	1.85 2.51	1.56	1.16	2.10	2.11	1.80	2.47	1.94 1.81 2.09
Unknown	2.82	2.16 3.68	2.23	1.36	3.66	1.24	0.80	1.93	2.14 1.90 2.40
Metro proximity									
Metro area	1	ref	1	ref	1	ref	1	ref	
Suburbs	0.68	0.49 0.95	0.91	0.53	1.57	1.06	0.79	1.42	1.04 0.90 1.19
Rural	0.91	0.65 1.27	1.41	0.83	2.41	1.37	1.01	1.84	0.97 0.82 1.15
Stage									
Stage 2/1	1.94	1.70 2.22	0.13	0.09	0.18	0.71	0.52	0.96	–
Histology									
Ductal	1	ref		–		–		–	
Lobular	1.11	0.94 1.32							
Tubular	0.63	0.24 1.69							

Odds ratios adjusted for all variables listed in table above and year of diagnosis
CI confidence interval, *OR* Odds Ratio, *NH* non-Hispanic

[14]. Patients without healthcare coverage may find surgery and surgery-related costs prohibitively high, and thus be more likely to refuse such intervention [6].

Females with colon and lung cancer were less likely to refuse surgery in our study. It is known that females tend to utilize health care at higher rates than males [15, 16], however specific data on refusal of curative cancer surgery with sex is lacking. Prior studies confirm our findings that females are less likely to refuse surgical intervention [8, 17], but other studies show the opposite [18, 19]. Unfortunately, bias in sex on refusal in prostate and breast cancer cannot be tested, although this would add valuable information to the field.

Better understanding of these sociodemographic predictors will require analysis beyond the capability of existing survey databases such as SEER, such as prospective qualitative or mixed-methods approaches. Our results suggest that

undergoing recommended surgical treatment improves cancer-specific survival and understanding the reasons behind the refusal could be a first step in improving disparities in cancer outcomes.

In addition to the limitations inherent in this retrospective analysis, i.e., unmeasured confounding, our study was limited by the inability to adjust for comorbidities given the lack of such information in SEER. Sicker patients may be less willing to undergo treatments that may carry risk of exasperating their ill-being, even when recommended by a physician. We attempted to mitigate this limitation by conducting a propensity matched analysis. Also, while insurance was considered in the analysis, we were unable to investigate how patient's income and their ability to afford treatment affects surgery refusal.

Reasons for refusal may differ across cancer sites, and could be associated with the patients' perceived gravity

Table 3 Predictors of survival according to cancer type

Variable	Breast cancer <i>n</i> =268,774			Colon cancer <i>n</i> =67,337			Lung cancer <i>n</i> =36,219			Prostate Cancer <i>n</i> =111,954		
	HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
Treatment												
Surgery	1	ref		1	ref		1	ref		1	ref	
Non-surgical	6.58	5.25	8.24	15.29	10.30	22.69	2.84	2.47	3.26	1.27	0.93	1.73
No surgery, chemo, or radiation	5.78	4.78	7.00	12.44	10.06	15.40	4.50	3.69	5.49	1.60	1.06	2.43
Age (years)												
< 50	1	ref		1	ref		1	ref		1	ref	
50–64	0.99	0.93	1.05	1.20	1.04	1.38	1.22	1.06	1.40	2.99	1.41	6.37
65–79	1.38	1.30	1.48	1.99	1.74	2.27	1.64	1.43	1.88	10.95	5.18	23.12
80+	3.08	2.86	3.32	4.08	3.56	4.67	2.21	1.91	2.56	103.32	48.76	218.94
Sex												
Female/male		–		0.81	0.76	0.85	0.67	0.64	0.70		–	
Race/Ethnicity												
NH-White	1	ref		1	ref		1	ref		1	ref	
NH-Black	1.62	1.52	1.73	1.32	1.22	1.43	1.07	0.99	1.16	1.22	1.01	1.49
Hispanic	1.14	1.05	1.23	1.07	0.98	1.18	1.03	0.93	1.15	1.10	0.88	1.39
NH-other	0.74	0.67	0.82	0.88	0.79	0.98	0.76	0.69	0.85	1.04	0.78	1.39
Insurance status												
Uninsured/insured	1.52	1.30	1.78	1.28	1.08	1.52	1.13	0.94	1.34	1.90	1.11	3.24
Marital status												
Married/union	1	ref		1	ref		1	ref		1	ref	
Single	1.23	1.17	1.29	1.41	1.33	1.49	1.23	1.17	1.29	1.60	1.39	1.85
Unknown	1.19	1.06	1.34	1.22	1.07	1.39	0.89	0.77	1.03	1.18	0.89	1.56
Metro proximity												
Metro area	1	ref		1	ref		1	ref		1	ref	
Suburbs	1.20	1.10	1.31	1.15	1.05	1.27	1.18	1.09	1.28	1.00	0.78	1.28
Rural	1.24	1.12	1.38	1.14	1.02	1.28	1.25	1.15	1.37	1.35	1.04	1.75
Stage												
Stage 2/1	3.93	3.73	4.13	3.08	2.89	3.29	2.41	2.29	2.54		–	
Histology												
Ductal	1	ref										
Lobular	0.60	0.56	0.65		–			–			–	
Tubular	0.24	0.14	0.42									

Hazard ratios adjusted for all variables listed in table above and year of diagnosis

CI confidence interval, HR hazard ratio. NH non-Hispanic. “Non-Surgical” indicates patients who refused surgery but underwent either chemotherapy or radiation

of the cancer and of the side effects of surgery. Surgical intervention in tumors that are more indolent and carry a good long term prognosis, such as prostate, could be seen less favorable by patients, considering the risk of surgery-associated complications such as incontinence and sexual dysfunction. Concerns for cosmesis may be a prevalent factor contributing to refusal among later stages breast cancer patients, where breast conserving lumpectomies are less likely to be offered. Unfortunately, SEER does not collect information on the types of surgery offered to patients and

does not collect specific information regarding patient’s reasons for refusal.

This study, however, has several strengths. The SEER database is a nationally representative registry. To our knowledge, this study is the first to examine the impact of refusal on specifically stage I and stage II cancers in lung, breast, colon, and prostate, in which surgical intervention is recommended with curative intent. This was also the first to use propensity matched analysis to assess the impact of surgical refusal on cancer outcome specifically by cancer type.

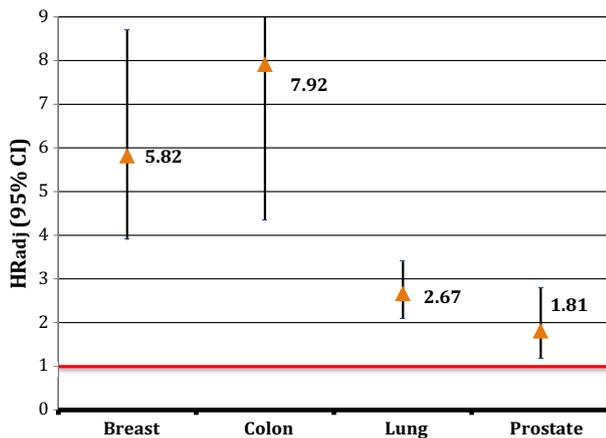


Fig. 2 Risk of death with surgery refusal versus undergoing recommended surgery—propensity matched analysis. Hazard of death among those who refuse surgery versus those who underwent recommended surgery (reference category) in a propensity matched analysis. Measures propensity matched with a 1:1 score to create a balanced cohort

In conclusion, our study identified several sociodemographic risk factors of surgery refusal in patients with early-stage cancers. Troublingly, more vulnerable patients seem to be at higher risk of refusing recommended surgery, and this decision negatively impacts their survival. Cancer outcome disparities are well established for African Americans [2–5], the uninsured [6], and unmarried patients [7], and our results suggest that refusal of recommended surgeries may be contributing to these disparities. Physicians should be aware of these sociodemographic predictors of surgery refusal, while interventions should be implemented that target these at-risk groups.

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