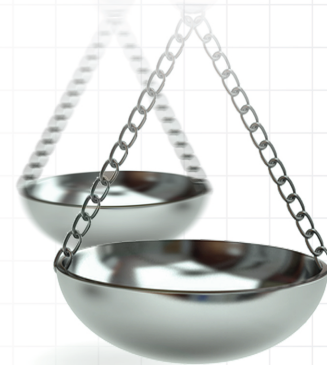




Real-world clinical outcomes of patients with localized prostate cancer treated with radical prostatectomy in SEER-Medicare

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Aim: This study examined the clinical outcomes of patients in the US with low/intermediate-risk localized prostate cancer (LIR-LPC) and high-risk localized prostate cancer (HR-LPC) who received radical prostatectomy (RP) as initial treatment. **Materials & methods:** This is a retrospective analysis of the SEER-Medicare database. Patients newly diagnosed with LPC at age of ≥ 65 years during 2012–2019 who underwent RP as initial definitive treatment and had continuous Medicare Fee-For-Service for ≥ 12 months prior to RP were included. Eligible patients were stratified into LIR-LPC and HR-LPC cohorts. Overall survival, metastatic free survival and time to advanced prostate cancer treatment (TTAT) were described and compared using the Kaplan–Meier method and Cox proportional-hazards model. **Results:** The LIR-LPC cohort ($n = 4120$) and the HR-LPC cohort ($n = 5359$) had comparable socio-demographic characteristics, with a mean age of approximately 70 years. Survival analysis showed that HR-LPC was associated with significantly shorter overall survival, metastatic free survival and TTAT than LIR-LPC (log rank $p < 0.001$). After adjusting for comprehensive socio-demographic and baseline clinical characteristics, patients with HR-LPC had an approximately 70% increased risk for all-cause death (hazard ratio [HR]: 1.72; confidence interval [CI]: 1.39–2.12), 2.5-fold increased risk for metastasis or death (HR: 2.57; CI: 2.14–3.09), and ninefold increased risk for initiating advanced treatments (HR: 9.06; CI: 6.22–13.18) compared with patients with LIR-LPC. **Conclusion:** In patients with LPC who received RP as initial definitive treatment, high risk is strongly associated with suboptimal clinical outcomes. Novel therapeutic approaches are needed to enhance the management and improve the outcomes for this patient population.

Plain language summary: Real-world clinical outcomes after radical prostatectomy for localized prostate cancer

What is this article about? Prostate cancer is the second most common cancer among men in the US. Most new cases are diagnosed at an early stage, when the cancer is still limited to the prostate, known as localized prostate cancer (LPC). Radical prostatectomy (RP) is one of the most often used initial treatments. However, the clinical outcomes are not expected to be the same depending on the risk classifications. This study examined long-term clinical outcomes among more than 9000 Medicare beneficiaries who were newly diagnosed with LPC between 2012 and 2019 and received RP as initial definitive treatment. Patients were divided into two cohorts of low/intermediate-risk (LIR-LPC) and high-risk localized prostate cancer (HR-LPC), respectively. Their clinical outcomes were compared with regards to overall survival, metastasis-free survival and time to advanced prostate cancer treatment (TTAT).

What were the results? The study found that patients with HR-LPC had significantly worse outcomes than patients with LIR-LPC even after adjusting for comprehensive socio-demographic and clinical characteristics. High risk is associated with a 70% increased risk for all-cause death, 2.5-fold increased risk for metastasis or death and ninefold increased risk for initiating advanced treatments.

What do the results mean? These findings suggest that current treatment strategies are inadequate for patients with HR-LPC. New treatments and enhanced clinical management are needed to improve care for HR patients.

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Keywords: clinical outcomes • HR-LPC • LIR-LPC • prostate cancer • radical prostatectomy • real-world evidence



Background

Prostate cancer (PC) is the second most common cancer among American men with an annual increase in incidence rate by 3% since 2014 [1,2]. The increase in PC cases has led to an increased disease burden and healthcare costs in recent years. The majority of newly diagnosed cases are localized prostate cancer (LPC) [3], and the primary treatment options include radical prostatectomy (RP), often used in conjunction with androgen deprivation therapy (ADT), external beam radiation therapy, focal therapy and active surveillance [4,5].

Clinical guidelines classify LPC into three risk levels as low, intermediate and high. The risk classification is important in determining initial treatment options and predicting clinical outcomes [4–7]. Although high risk is known to be associated with worse clinical outcomes, there are limited real-world studies quantifying the elevated risks in patients with LPC who received RP as their initial definite treatment.

This study investigated the clinical outcomes of elderly patients in the US with low/intermediate risk LPC (LIR-LPC) and high risk LPC (HR-LPC) after RP was received as initial definitive treatment. Overall survival (OS), metastasis-free survival (MFS) and time to initiation of advanced prostate cancer treatment (TTAT) were compared between the two cohorts. This study also described these outcomes by race and ethnicity, considering the significant racial and ethnic disparities documented in prostate cancer incidence and survival [8–10].

Materials & methods

Data source

This study used the Surveillance, Epidemiology, and End Results (SEER)-Medicare database, which was created by linking the SEER data of cancer patients eligible for Medicare with their claims for covered healthcare services under Medicare. The SEER program of the National Cancer Institute (NCI) is an authoritative source of information on cancer incidence and survival in the US from 18 population-based cancer registries covering approximately 26% of the US population [11]. The registries collect clinical and demographic information as well as data on primary tumor site, tumor morphology, stage of cancer at time of diagnosis and follow-up for vital status [11]. Use of the SEER-Medicare data for this study complied with patient requirements of the Health Insurance Portability and Accountability Act (HIPAA).

Study design

This retrospective study included Medicare beneficiaries newly diagnosed with LPC and received RP as their initial definitive treatment (Figure 1). The date of the initial LPC diagnosis was identified from the SEER CANCER data [11]. The recipient of RP was identified from the Medicare claims. Patients with LPC were stratified into two cohorts according to the National Comprehensive Cancer Network (NCCN) criteria based on tumor-node-metastasis (TNM) staging, Gleason score and prostate-specific antigen (PSA) level at diagnosis (Supplementary Table 1): LIR-LPC and HR-LPC. Patients were followed from the first Medicare claims of RP (index date) until the earliest event of death, disenrollment from Medicare Fee-For-Service (FFS) Part A/B or Part D, or the end of the study period (31 December 2020).

Study population & sample selection

The study patient sample selection is summarized in Figure 2. Patients were included in this analysis if they met the following inclusion criteria: Medicare beneficiaries newly diagnosed (at age 65 or older) with LPC between 2012 and 2019, who received RP as initial definitive treatment within 6 months of initial diagnosis and had continuously coverage of Medicare FFS Parts A, B, and prescription drug coverage (Part D) for at least 12 months prior to the index date. Exclusion criteria included a diagnosis of other primary cancers as documented in the SEER data, and indeterminate NCCN risk stratification based on TNM staging, Gleason score, and PSA level.

Patient socio-demographic & baseline clinical characteristics

Patient socio-demographic characteristics were obtained from the SEER CANCER data, including age, race/ethnicity, marital status, urban/rural residence, geographic location, household income and education level at the census tract level. TNM staging, PSA level and Gleason score were also obtained from the SEER CANCER data to derive LPC risk classification. Medicare claims were used to estimate the NCI comorbidity score, ADT use, healthcare resource utilization (HCRU), medical and pharmacy spending during the 12-month baseline period before the index date.

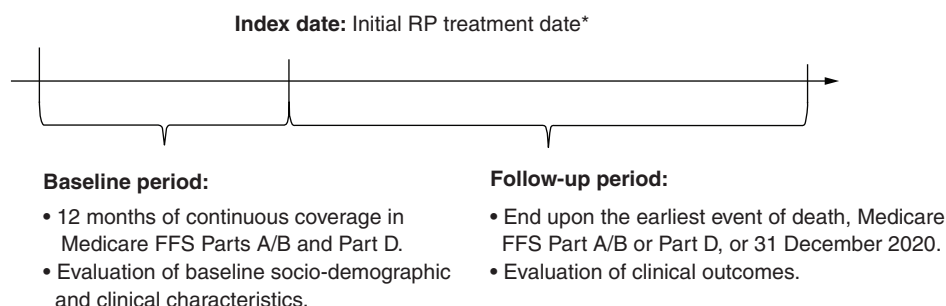


Figure 1. Study design.

*Where RP treatment was initiated within 6 months after LPC diagnosis as the patient's initial definitive therapy.
FFS: Fee-For-Service; LPC: Localized prostate cancer; RP: Radical prostatectomy.

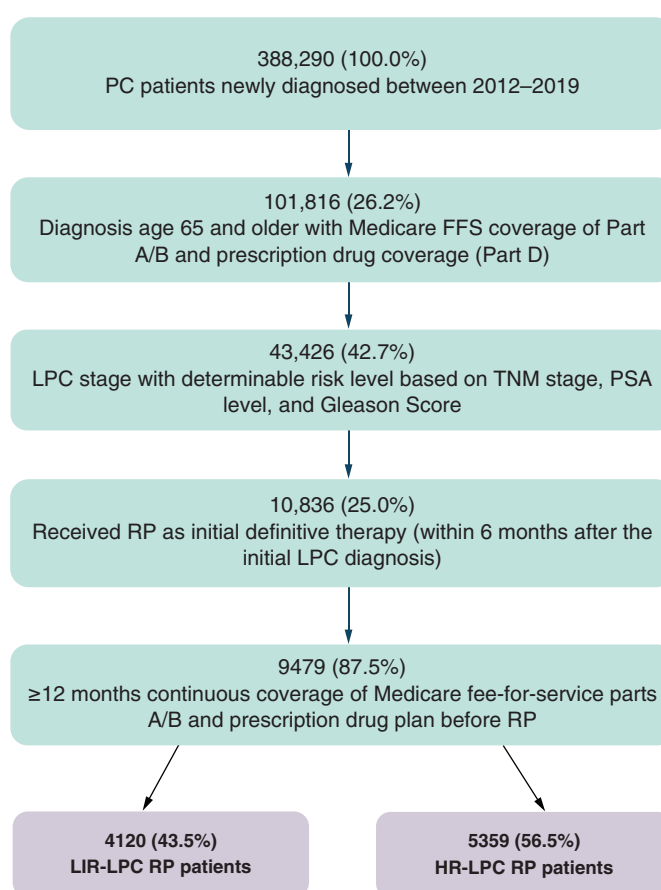


Figure 2. Patient selection criteria.

Percentages were calculated using the sample size from the preceding step as the denominator.

FFS: Fee-For-Service; HR-LPC: High-risk localized prostate cancer; LIR-LPC: Low/intermediate-risk localized prostate cancer; PC: Prostate cancer; RP: Radical prostatectomy.

Clinical outcomes

The clinical outcomes assessed in the current study include OS, MFS and TTAT. Metastasis events were defined as secondary cancer using International Classification of Diseases (ICD) diagnosis codes (ICD 9: 196x–198x; ICD10: C77x–C80x) with at least one imaging procedure code within 60 days prior. Advanced PC treatments were identified from both medical and pharmacy claims, including chemotherapy, androgen receptor signaling inhibitors, radiopharmaceuticals, PARP inhibitors and immunotherapy. All outcomes were also examined across four race/ethnicity subgroups defined as non-Hispanic (NH) White, NH Black, NH Asian and Hispanic.

Statistical analysis

Socio-demographics and baseline characteristics for the LIR-LPC and HR-LPC cohorts were summarized using descriptive statistics, including the number and proportion of patients (%) for categorical variables as well as

mean, standard deviation (SD), and/or median and interquartile range (IQR) for continuous variables. OS, MFS and TTAT were initially compared between the LIR-LPC and HR-LPC cohorts using the Kaplan–Meier (KM) method. Hazard ratios (HRs) were then obtained using Cox proportional hazard (PH) regression models, adjusting for comprehensive socio-demographic and baseline clinical characteristics, including age, race/ethnicity, marital status, urban/rural residence, region, year of initial diagnosis, household income and education level at the census-tract level, NCI comorbidity score, ADT use prior to the index date and healthcare resource utilization and costs during the 1-year baseline period.

Results

Baseline patient characteristics & treatment patterns

Among the 9479 patients who underwent RP within 6 months of LPC diagnosis, 43.5% (n = 4120) were classified as LIR-LPC and 56.5% (n = 5359) as HR-LPC (Table 1). The socio-demographic characteristics for both cohorts were comparable, with a mean age at the index date of 69.6 (SD: 3.3) years for LIR-LPC and 70.4 (SD: 3.7) years for HR-LPC. Additionally, both cohorts had nearly 88% of patients being White, 93% patients being non-Hispanic, 75% patients being married and 85% of patients resided in urban areas.

Compared with the LIR-LPC patients, the HR-LPC patients had a slightly higher mean NCI comorbidity score (1.1 vs 1.3; Table 1). The most prevalent comorbidities in both cohorts included hypertension (LIR-LPC: 71.1%, HR-LPC: 72.9%), diabetes (LIR-LPC: 24.7%, HR-LPC: 26.9%), chronic obstructive pulmonary disease (LIR-LPC: 15.2%, HR-LPC: 16.9%), obesity (LIR-LPC: 14.1%, HR-LPC: 15.9%) and peripheral vascular disease (LIR-LPC: 12.6%, HR-LPC: 15.4%). Furthermore, HR-LPC patients had a greater baseline use of ADT compared with LIR-LPC patients (1.7% vs 5.2%).

HR-LPC patients had slightly greater baseline HCRU and healthcare spending compared with LIR-LPC patients. Approximately 20% of both LIR-LPC and HR-LPC patients visited the emergency room, with hospital admission rates of 8.2% and 9.1%, respectively. The median number of physician office visits and outpatient encounters were 10 versus 11 and 5 versus 6 for LIR-LPC and HR-LPC patients, respectively. Median baseline medical spending and pharmacy spending were \$5601 versus \$5848 and \$185 versus \$228 for LIR-LPC and HR-LPC patients, respectively.

Clinical outcomes during follow-up period

Although the HR-LPC cohort had a shorter follow-up time than the LIR-LPC cohort (43.8 vs 47.7 months), they experienced more deaths and metastasis events. KM analyses (Figures 3A–C) showed significantly shorter OS, MFS and TTAT in HR-LPC patients compared with the LIR-LPC patients (log rank $p < 0.001$). After adjusting for comprehensive socio-demographic and baseline clinical characteristics by using Cox PH models, the elevated risks in HR-LPC patients remained substantial. HR-LPC patients had an approximately 2.5-fold increased risk for metastasis or death (HR: 2.57; CI: 2.14–3.09), a 70% increased risk for death (HR: 1.72; CI: 1.39–2.12), and ninefold increased risk for initiating advanced treatments (HR: 9.06; CI: 6.22–13.18) compared with LIR-LPC patients (Table 2).

Clinical outcomes stratified by race & ethnicity

Clinical outcomes and survival probabilities over a 5-year period were stratified by racial/ethnic groups and summarized in Table 3. The proportion of patients who died or had metastatic PC ranged from 4% to 7% for LIR-LPC patients and 8% to 14% for HR-LPC patients across race and ethnic groups. The 5-year MFS analysis indicated a lower probability of survival for patients with HR-LPC relative to LIR-LPC across all racial and ethnic groups, with the largest difference for NH Black patients (87% vs 94%). NH Black patients also exhibited the highest all-cause mortality rate (11.2% among the HR-LPC cohort).

Discussion

In this real-world study of Medicare beneficiaries diagnosed with LPC who received RP as their initial definitive treatment, patients with HR-LPC experienced significantly worse clinical outcomes than patients with LIR-LPC. The KM analyses showed that HR-LPC patients were much more likely to progress to metastasis and/or death and were much more likely to receive advanced therapy than LIR-LPC patients. Furthermore, the Cox PH models indicated that the elevated risks associated with HR-LPC persisted after adjusting for comprehensive socio-

Table 1. Demographic and clinical characteristics of patients with low/intermediate-risk localized prostate cancer and high-risk localized prostate cancer.

	LIR-LPC (n = 4120)	HR-LPC (n = 5359)
Age at diagnosis, mean (SD)	69.6 (3.3)	70.4 (3.7)
Age categories (years)		
65–69	2305 (56.0%)	2550 (47.6%)
70–74	1460 (35.4%)	2117 (39.5%)
75–79	314 (7.6%)	593 (11.1%)
80+	41 (1.0%)	99 (1.9%)
Race		
White	3633 (88.2%)	4700 (87.7%)
Black	243 (5.9%)	282 (5.3%)
Asian/Pacific Islander/American-Indian/Alaskan Native	206 (5.0%)	333 (6.2%)
Unknown	38 (0.9%)	44 (0.8%)
Ethnicity		
Non-Hispanic	3853 (93.5%)	4995 (93.2%)
Hispanic	267 (6.5%)	364 (6.8%)
Geographic location		
Northeast	660 (16.0%)	811 (15.1%)
North Central	591 (14.3%)	666 (12.4%)
South	932 (22.6%)	1058 (19.7%)
West	1937 (47.0%)	2824 (52.7%)
T stage		
T0/T1/Tx/unknown	161 (3.9%)	91 (1.70%)
T2	3959 (96.1%)	1408 (26.3%)
T3	0 (0%)	3788 (70.7%)
T4	0 (0%)	72 (1.34%)
N stage		
N0	4120 (100%)	4814 (89.8%)
N1	0 (0%)	545 (10.2%)
PSA level at diagnosis		
<10 ng/ml	3543 (86.0%)	3369 (62.9%)
10–20 ng/ml	577 (14%)	1074 (20.0%)
>20 ng/ml	0 (0%)	595 (11.1%)
Unknown	0 (0%)	321 (5.99%)
Gleason score at diagnosis		
2–6	596 (14.5%)	56 (1.0%)
7	3524 (85.5%)	2023 (37.8%)
8–10	0 (0%)	3266 (60.9%)
Missing	0 (0%)	14 (0.3%)
NCI comorbidity score [†] , mean (SD)	1.1 (1.4)	1.3 (1.5)
Selected individual comorbidities [‡]		
Hypertension	2930 (71.1%)	3907 (72.9%)
Diabetes	1019 (24.7%)	1442 (26.9%)
Chronic Obstructive Pulmonary Disease	627 (15.2%)	904 (16.9%)
Peripheral Vascular Disease	518 (12.6%)	823 (15.4%)
Obesity	580 (14.1%)	850 (15.9%)
Liver Disease	362 (8.8%)	636 (11.9%)
Baseline ADT use	71 (1.7%)	276 (5.2%)

[†] <https://healthcareelivery.cancer.gov/seermedicare/considerations/comorbidity.html>.[‡] Included comorbidities that were present at >10%.[§] All spending amounts were inflated to 2022 values based on Consumer Price Index.

ADT: Androgen deprivation therapy; HR-LPC: High-risk localized prostate cancer; IQR: Interquartile range; LIR-LPC: Low/intermediate-risk localized prostate cancer; NCI: National Cancer Institute; PSA: Prostate-specific antigen; RP: Radical prostatectomy; SD: Standard deviation.

Table 1. Demographic and clinical characteristics of patients with low/intermediate-risk localized prostate cancer and high-risk localized prostate cancer (cont.).

	LIR-LPC (n = 4120)	HR-LPC (n = 5359)
Baseline emergency room visit		
Yes	828 (20.1%)	1071 (20.0%)
No	3292 (79.9%)	4288 (80.0%)
Baseline hospital admission		
Yes	338 (8.2%)	488 (9.1%)
No	3782 (91.8%)	4871 (90.9%)
Baseline physician office visit		
Mean (SD)	11.6 (6)	11.8 (6.4)
Median (IQR)	10 (7, 15)	11 (7, 15)
Baseline outpatient encounter		
Mean (SD)	5.4 (5.4)	6.1 (5.5)
Median (IQR)	4 (2, 7)	5 (2, 8)
Baseline medical spending [§]		
Mean (SD)	\$8566 (\$11,489)	\$9338 (\$12,817)
Median (IQR)	\$5601 (\$3,702, \$8,863)	\$5848 (\$4021, \$9366)
Baseline pharmacy spending [§]		
Mean (SD)	\$1230 (\$4,652)	\$1395 (\$5078)
Median (IQR)	\$185 (\$0, \$1441)	\$228 (\$0, \$1588)

[†] <https://healthcaredelivery.cancer.gov/seermedicare/considerations/comorbidity.html>.

[‡] Included comorbidities that were present at >10%.

[§] All spending amounts were inflated to 2022 values based on Consumer Price Index.

ADT: Androgen deprivation therapy; HR-LPC: High-risk localized prostate cancer; IQR: Interquartile range; LIR-LPC: Low/intermediate-risk localized prostate cancer; NCI: National Cancer Institute; PSA: Prostate-specific antigen; RP: Radical prostatectomy; SD: Standard deviation.

demographic and clinical characteristics. In the subgroup analysis, HR-LPC patients consistently appeared to have worse post-RP clinical outcomes than LIR-LPC patients across all the race/ethnic subgroups.

RP has been demonstrated to improve survival rates and reduce the risk of disease progression in LPC patients relative to deferred treatment [12]. Consistent with our findings, several real-world studies show that the effectiveness of RP is reduced in patients with HR-LPC. In a study by Carver *et al.* assessing long-term outcomes following RP in 176 patients with high-risk PC, 48% of patients exhibited disease recurrence during the mean follow-up period of 6.4 years [13]. In a study by Ward *et al.*, 5652 patients with LPC who underwent RP at a single institution were included [14]. Patients with locally advanced stage of clinical T3 had worse long-term clinical outcomes than those with clinical T2 disease. The 5-year and 10-year death rates were 10% versus 5% and 25% versus 16%, respectively. The biochemical recurrence rates were 42% versus 26% and 57% versus 39%, respectively. Our study provides additional insights by quantifying the elevated risks in real-world clinical outcomes among Medicare beneficiaries. Despite receiving the same initial definite treatment of RP, patients with HR-LPC experienced a substantially worse clinical outcomes compared with patients with LIR-LPC, with a 2.5-fold increased risk for metastasis or death and a ninefold increased risk for initiating advanced treatments. Another key observation of our study is the low utilization of advanced treatment. During a mean follow-up time of nearly 5 years, 6.3% of patients with HR-LPC received advanced treatment after RP. This rate is relatively low considering that more than 30% of high-risk patients are expected to receive post-RP salvage therapies [15–17]. Potential contributing factors to the under use of advanced treatment include evolving clinical evidence and guidelines, a preference for observation with early salvage to avoid overtreatment, variations in physician referral patterns, as well as patient- and access-related factors [15,18]. These findings together suggest room to improve the current management for patients with HR-LPC and highlight the need for novel treatment approaches.

Strengths

One highlight of the current study is the inclusion of a large sample size of more than 9000 patients and a long follow-up time of approximately 7 years on average. The target population of Medicare beneficiaries is relevant for PC research given that the median PC onset age is 67 years old in the US [1]. The SEER-Medicare linkage is another

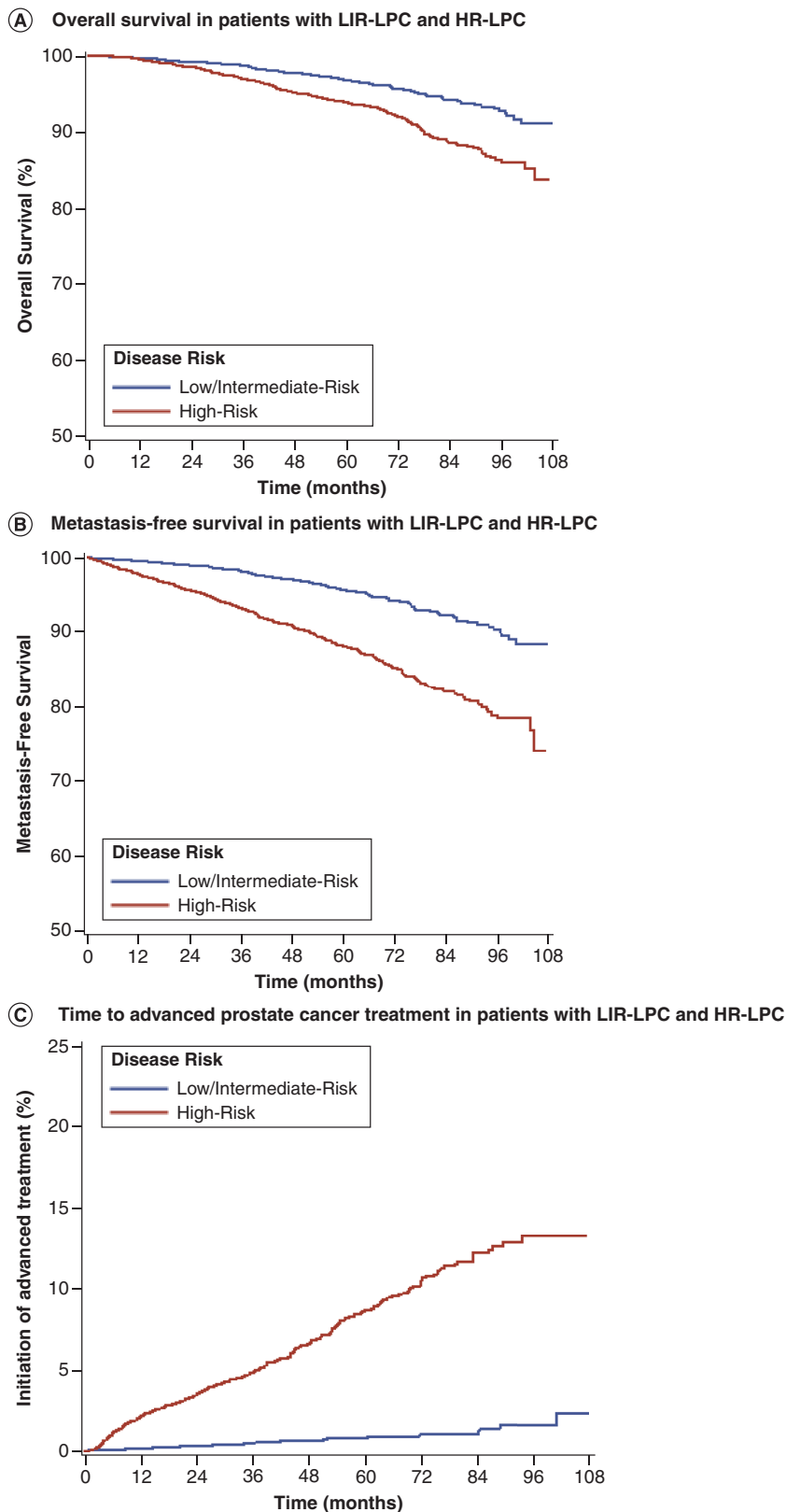


Figure 3. Kaplan-Meier analyses. (A) Overall survival in patients with LIR-LPC and HR-LPC. **(B)** Metastasis-free survival in patients with LIR-LPC and HR-LPC. **(C)** Time to advanced prostate cancer treatment in patients with LIR-LPC and HR-LPC.

HR-LPC: High-risk localized prostate cancer; LIR-LPC: Low/intermediate-risk localized prostate cancer.

Table 2. Cox proportional hazard analysis of clinical outcomes in patients with low/intermediate-risk localized prostate cancer and high-risk localized prostate cancer.

Outcomes	LIR-LPC patients with events (n = 4120), n (%)	HR-LPC patients with events (n = 5358), n (%)	Adjusted hazard ratio [‡] (95% CI) HR-LPC vs LIR-LPC patients	p-value
Metastasis or death	154 (3.7%)	489 (9.1%)	2.57 (2.14, 3.09)	<0.0001
Death	131 (3.2%)	289 (5.4%)	1.72 (1.39, 2.12)	<0.0001
Advanced prostate cancer treatment [†]	30 (0.7%)	339 (6.3%)	9.06 (6.22, 13.18)	<0.0001

[†]Initiation of the earliest treatments such as chemotherapy, PARP inhibitors, radiopharmaceuticals, related immunotherapies or advanced androgen signaling inhibitors.
[‡]After adjusting for age, race/ethnicity, marital status, urban/rural residence, region, year of initial diagnosis, household income and education level at census tract level, National Cancer Institute comorbidity score, ADT use prior to index date, HRU and cost during the 1-year baseline period.
HR-LPC: High-risk localized prostate cancer; LIR-LPC: Low/intermediate-risk localized prostate cancer.

Table 3. Clinical outcomes and survival probability for 5 years in patients with low/intermediate-risk localized prostate cancer and high-risk localized prostate cancer stratified by race and ethnicity.

Clinical outcomes	Non-Hispanic White (n = 7739)		Non-Hispanic Black (n = 517)		Non-Hispanic Asian (n = 514)		Hispanic (n = 631)	
	LIR-LPC (n = 3382)	HR-LPC (n = 4357)	LIR-LPC (n = 239)	HR-LPC (n = 278)	LIR-LPC (n = 198)	HR-LPC (n = 316)	LIR-LPC (n = 267)	HR-LPC (n = 364)
Metastasis or death, n (%)	120 (3.6%)	390 (9.0%)	16 (6.7%)	39 (14.0%)	†	24 (7.6%)	14 (5.2%)	30 (8.2%)
Death, n (%)	102 (3.0%)	222 (5.1%)	14 (5.9%)	31 (11.2%)	†	13 (4.1%)	13 (4.9%)	19 (5.2%)
Use of advanced PC treatment, n (%)	24 (0.7%)	286 (6.6%)	†	13 (4.7%)	†	18 (5.7%)	†	19 (5.2%)
5-year survival probability (95% CI)[‡]								
Metastasis free survival	96.0% (95.0%, 96.8%)	88.4% (87.1%, 89.6%)	89.7% (81.7%, 94.3%)	77.7% (69.3%, 84.1%)	96.7% (88.4%, 99.1%)	91.2% (86.2%, 94.4%)	91.5% (84.5%, 95.4%)	89.8% (84.3%, 93.4%)
Overall survival	96.9% (96.1%, 97.5%)	94.1% (93.1%, 95%)	93.9% (88.7%, 96.8%)	86.7% (80.8%, 90.9%)	98.5% (89.9%, 99.8%)	96.3% (92.9%, 98.1%)	94.4% (89.3%, 97.1%)	94.6% (90.5%, 96.9%)
No advanced PC treatment	99.2% (98.7%, 99.5%)	91.1% (89.9%, 92.2%)	97.4% (90.5%, 99.3%)	92.3% (86.3%, 95.7%)	0% (–, –)	91.2% (85.5%, 94.7%)	98.5% (95.2%, 99.5%)	93.3% (89.2%, 95.9%)

Patients with unknown race/ethnicity were excluded from this analysis.
[†]Counts less than 11 were suppressed in compliance with CMS cell suppression policies for the SEER-Medicare data.
[‡]The survival probabilities were based on KM methods.
CI: Confidence interval; HR-LPC: High-risk localized prostate cancer; KM: Kaplan-Meier; LIR-LPC: Low/intermediate-risk localized prostate cancer; PC: Prostate cancer.

highlight of the current study, as it is a population-based, high-quality database for real-world cancer research. SEER provides validated tumor-level data, which improves case ascertainment and clinical risk classification. The included vital status makes SEER one of the most often used databases for cancer survival studies. The availability of race/ethnicity and census tract level family income and education data help mitigate the potential confounding due to socio-economic disparities. Medicare FFS and Part D data record comprehensive inpatient and outpatient encounters, procedures, and pharmaceutical treatments, enabling analyses of broad comorbid conditions, treatment history and outcomes. Lastly, concerns over confounding are mitigated in our study by using Cox PH models that account for comprehensive socio-demographic and clinical characteristics.

Limitations

The findings from the current study should be interpreted within the context of several limitations. First, there are inherent biases associated with claims data, such as miscoding and misclassification errors, which may have led to misclassifications. Particularly, it may not be accurate to determine metastatic progression by using a Medicare claims-based algorithm consisting of diagnosis and procedure codes. Second, we cannot exclude the possibility that the observed association between LPC risk classification and clinical outcomes were due to any unmeasured confounding factors, such as patients' lifestyle and genetic testing information, which may impact the clinical outcomes. Nevertheless, we do not expect any unmeasured confounding factors to be strong enough to change the overall conclusion given the substantial elevated risks found in the HR-LPC cohort after accounting for comprehensive socio-demographics and clinical characteristics. Third, the current study did not explore the pattern and impact of post-RP adjuvant or salvage therapies of either radiation or ADT. It is unclear how post-RP clinical management contributed to the differential outcomes associated with risk classifications. However, the

main purpose of the study is to illustrate the independent association between LPC risk classification at diagnosis and post-RP clinical outcomes. Although post-RP clinical management is important, it falls outside of the scope of this study. Lastly, the current study population is restricted to US Medicare FFS beneficiaries. The findings may not be generalizable to patients with LPC in other countries, or US patients primarily covered by other types of health insurance, such as Medicare Advantage, Commercial or Medicaid.

Conclusion

Despite receiving RP as initial definitive treatment, patients with HR-LPC were substantially more likely to experience disease progression and death than those with LIR-LPC. The elevated risks were independent of sociodemographic factors and pre-existing comorbidities, and were consistent across race/ethnicity groups. Together these findings underscore the need for novel therapeutic approaches and enhanced clinical management to improve long-term clinical outcomes in patients with HR-LPC.

Summary points

- This study used Surveillance, Epidemiology, and End Results (SEER)-Medicare data, a population-based high-quality database for real-world cancer research among Medicare patients in the US.
- The study included patients aged 65 and older, diagnosed between 2012 and 2019, with continuous Medicare coverage for a year before surgery.
- All selected patients were stratified into low/intermediate-risk localized prostate cancer (LPC) and high-risk LPC cohorts and compared regarding overall survival, metastasis-free survival and time to advanced prostate cancer treatment (TTAT) using the Kaplan–Meier method and Cox proportional hazard models.
- Among the 9479 patients who underwent radical prostatectomy within 6 months of LPC diagnosis, 43.5% (n = 4120) were classified as low/intermediate risk LPC and 56.5% (n = 5359) as high-risk LPC, with similar baseline medical and pharmacy spending.
- Patients with high-risk LPC exhibited a statistically significant 70% increased risk for all-cause death, a 2.5-fold increased risk for metastasis or death, and a ninefold increased risk for initiating advanced treatments.
- These trends were also reflected across race/ethnicity subgroups, with non-Hispanic Black patients with high-risk LPC exhibited the highest mortality rate among all race/ethnicity subgroups.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: <https://becarispublishing.com/doi/pdf/10.57264/cer-2025-0004>

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Competing interests disclosure

L Karsh is an employee of The Urology Center of Colorado and has received consulting fees from Johnson & Johnson. S Du and J He are employees of Johnson & Johnson and stockholders of Johnson & Johnson. N Shore is an employee of Carolina Urologic Research Center and has received consulting fees from Johnson & Johnson. The authors have no other competing interests or

relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

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Ethical conduct of research

Use of the SEER-Medicare data for this study complies with patient requirements of the Health Insurance Portability and Accountability Act (HIPAA).

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