



A comparison of the survival outcomes of robotic-assisted radical prostatectomy and radiation therapy in patients over 75 years old with non-metastatic prostate cancer: A Korean multicenter study

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Purpose: To compare overall survivals (OSs) and cancer-specific survivals (CSSs) after robotic-assisted radical prostatectomy (RARP) and radiation therapy (RT), the latter of which has long been recommended primarily for elderly patients (≥ 75 years) with non-metastatic prostate cancer (PCa), given the Korean male life span of 79.7 years (2018).

Materials and Methods: Retrospective data for aged ≥ 75 years who underwent RARP or RT at seven tertiary hospitals were analyzed. To account for indication-related bias, inverse probability of treatment-weighting (IPTW) was applied before and after Cox regression.

Results: Of the 1,110 study subjects, 883 underwent RARP and 227 RT from 2007 to 2016. The differences between groups including the age (≥ 80 y; 25.4% vs. 32.8%; $p=0.034$), concomitant diabetes (14.9% vs. 22.9%; $p=0.007$), coronary heart disease (3.5% vs. 7.5%; $p=0.015$), and PCa risk stratification (high-risk; 18.2% vs. 59.7%; $p<0.001$) were balanced after IPTW. During a mean follow-up of 74.5 months, OSs (91.9% vs. 91.0%) and CSSs (97.8% vs. 98.0%) were similar. After IPTW, overall mortality was associated with diabetes (hazard ratio [HR], 2.273; $p<0.0001$) and inversely with low-risk PCa (HR, 0.314; $p<0.0001$), the last of which was solely associated with cancer-specific mortality (HR, 0.245; $p=0.0005$). The implementation of local treatment between RARP and RT demonstrated no impact on survival, for whole and high-risk populations.

Conclusions: Even aged over 75 years, patients who underwent RARP for non-metastatic PCa had similar survival with RT regardless of risk stratification. However, the survival needs to be weighed with the morbidity of local treatment in a future study.

Keywords: Mortality; Prostatectomy; Radiotherapy; Robotic surgical procedures

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Received: 20 February, 2021 • **Revised:** 21 April, 2021 • **Accepted:** 1 June, 2021 • **Published online:** 5 August, 2021

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INTRODUCTION

Radical prostatectomy (RP) and radiation therapy (RT) combined with androgen deprivation therapy (ADT) are currently the approved standards of care for localized/locally advanced prostate cancer (PCa). Even after debates on the over-treatment triggered by prostate-specific antigen (PSA) based screening strategy for the general population, increasing evidence over the past decade supports the oncologic efficacy of RP even in high-risk disease [1,2]. However, there is a paucity of data concerning the role of radical surgery in elderly patients (≥ 75 y), mainly because contemporary guidelines limit the application of RP in men with a life expectancy of < 10 years [3,4]. Despite several comparative studies, elderly subjects have been excluded from the majority of them, thus questions about the clinical relevance of RP versus RT in the aged population remain unanswered. However, given the unfavorable nature of PCa development in the elderly as compared with younger counterparts [5-8], radical removal of the entire gland might be justified in this age group.

Given the longer survival of PCa than other malignant conditions, studies on the aged appear to have the advantage that they enable direct comparisons of survival outcomes as compared with those based on the use of PSA as a surrogate marker. The purpose of this study, therefore, was to document and compare overall survivals (OSs) and cancer-specific survivals (CSSs) after robotic-assisted radical prostatectomy (RARP), the contemporary way of RP, and RT that has long been the recommended modality for the patients with non-metastatic PCa and limited life expectancy. To account for indication bias between two different modalities, inverse probability of treatment-weighting (IPTW) was applied, and then IPTW unadjusted and adjusted modeling was performed.

MATERIALS AND METHODS

1. Study population and variables investigated

Retrospective data of the patients managed by RARP or external-beam RT for localized/locally advanced PCa at seven South Korean tertiary hospitals from 2007 to 2016 were analyzed. The study inclusion criteria were: 1) aged ≥ 75 years at the time of treatment; 2) a minimum follow-up of 3 years after treatment to achieve survival result; and 3) a non-metastatic disease status as determined by bone scan, and abdominopelvic computerized tomography (CT) prior to treatment commencement. Exclusion criteria were: 1) the presence of lymphatic spread on baseline CT image;

2) non-robotic RP, including laparoscopic or open RP; and 3) receipt of ADT > 6 months before the initiation of RT. Data collected included initial PSA, clinical stage, Gleason score, date of death, and cause of death. American Society of Anesthesiologists' physical status scores (ASA scores), as rated by an anesthesiologist, were recorded for patients that underwent RARP. For the patients who underwent RT, total radiation dose, and adjuvant ADT duration (if applied) were also recorded. As is required by the privacy guidelines of the Health Insurance Portability and Accountability Act, all personal identification numbers were encrypted before data processing. The responsible Institutional Review Board of the Yeungnam University Hospital approved all procedural and ethical aspects of the study beforehand (approval number: YUMC 201909044). The board exempted the requirement for informed consent because of the retrospective nature of the study.

2. Study design and outcome measurements

The study endpoints were OSs and CSSs in the two study groups. Given the influence of tumor aggressiveness and age on survival, both outcome variables were investigated after risk stratification and age. Multivariable analysis was used to adjust for intergroup differences between epidemiologic characteristics and tumor biologies, and then the impacts of RARP and RT on OSs and CSSs were calculated.

3. Statistical analysis

The impacts of variables on the study endpoints were investigated using a multivariate Cox proportional hazards model. The covariate balance for IPTW modeling was evaluated using the standardized mean difference (SMD) approach. The variables included in the IPTW model were age, concomitant diabetes, coronary heart disease, and PCa risk stratification. Unbalanced covariates included in the IPTW model had an SMD > 0.1 .

The Student's t-test was used to compare continuous variables, and the chi-square test was used to compare binary and categorical variables. Kaplan–Meier analysis with the log-rank method was used to assess the impacts of patient characteristics on survival outcomes. Given a relatively large sample size after IPTW adjustment ($n=1,927$), two-sided p-values of < 0.01 were considered to be statistically significant. The analysis was performed using SAS software (SAS Institute, Cary, NC, USA).

RESULTS

1. IPTW-based group adjustment

The data of 1,110 patients over 75 years were finally sub-

jected to analysis; 883 underwent RARP and 227 RT. For the RT group, the mean±standard deviation radiation dose was 71.0±13.1 Gy, and 84.3% of them used adjuvant ADT with a mean duration of 24.9±17.7 months. After RARP, only 14

Table 1. Characteristics of the study subjects

Variable	Unadjusted				IPTW-adjusted			
	Total	RARP (n=883)	RT (n=227)	p-value (SMD)	Total	RARP	RT	p-value (SMD)
Age (y)	78.15	78.03	78.61	0.018 (-0.188)	78.09	78.15	78.04	0.583 (0.025)
75–79	705 (73.1)	570 (74.6)	135 (67.2)	0.034	1,429 (74.2)	709 (73.4)	720 (74.9)	0.450
≥80	260 (26.9)	194 (25.4)	66 (32.8)		498 (25.8)	257 (26.6)	241 (25.1)	
Diabetes								
No	805 (83.4)	650 (85.1)	155 (77.1)	0.007	1,599 (83.0)	804 (83.2)	796 (82.8)	0.836
Yes	160 (16.6)	114 (14.9)	46 (22.9)		327 (17.0)	163 (16.8)	165 (17.2)	
Coronary heart disease								
No	923 (95.6)	737 (96.5)	186 (92.5)	0.015	1,836 (95.3)	922 (95.4)	914 (95.2)	0.810
Yes	42 (4.4)	27 (3.5)	15 (7.5)		91 (4.7)	44 (4.6)	46 (4.8)	
Risk stratification								
High risk	259 (26.8)	139 (18.2)	120 (59.7)	<0.001	521 (27.0)	261 (27.0)	260 (27.1)	0.909
Intermediate risk	118 (12.2)	95 (12.4)	23 (11.4)		241 (12.5)	118 (12.2)	123 (12.8)	
Low risk	588 (60.9)	530 (69.4)	58 (28.9)		1,165 (60.5)	588 (60.8)	577 (60.1)	
Initial PSA (ng/dL)	18.72	10.93	48.43	0.004 (-0.455)	18.84	12.19	25.58	0.092 (-0.120)
<10	545 (56.6)	484 (63.4)	61 (30.5)	<0.001	1,053 (54.9)	550 (57.0)	503 (52.7)	0.057
≥10	418 (43.4)	279 (36.6)	139 (69.5)		866 (45.1)	415 (43.0)	451 (47.3)	
Gleason score								
6	343 (36.0)	286 (38.0)	57 (28.4)	<0.001	670 (35.0)	319 (33.4)	351 (36.6)	0.055
7	374 (39.2)	314 (41.7)	60 (29.9)		745 (38.9)	396 (41.6)	348 (36.2)	
≥8	237 (24.8)	153 (20.3)	84 (41.8)		499 (26.1)	238 (25.0)	261 (27.2)	
ASA score (only for RARP)								
1	209 (27.4)	209 (27.4)	-		257 (26.6)	257 (26.6)	-	
2	520 (68.1)	520 (68.1)	-		660 (68.3)	660 (68.3)	-	
≥3	35 (4.6)	35 (4.6)	-		50 (5.1)	50 (5.1)	-	
Nervesparing (only for RARP)								
Full	396 (52.1)	396 (52.1)	-		477 (49.7)	477 (49.7)	-	
Partial	88 (11.6)	88 (11.6)	-		110 (11.5)	110 (11.5)	-	
None	276 (36.3)	276 (36.3)	-		372 (38.8)	372 (38.8)	-	
Adjuvant RT (only for RARP)								
None	582 (97.8)	582 (97.8)	-		723 (97.1)	723 (97.1)	-	
Radiation	13 (2.2)	13 (2.2)	-		21 (2.9)	21 (2.9)	-	
Total radiation dose (only for RT)	70.97		70.97		70.79		70.79	
Adjuvant hormone (only for RT)								
No	31 (15.7)	-	31 (15.7)		196 (20.9)	-	196 (20.9)	
Yes	166 (84.3)	-	166 (84.3)		740 (79.1)	-	740 (79.1)	
Adjuvant hormone period (only for RT)	24.47		24.47		22.49		22.49	
Follow-up after each management (mo)	74.45	78.24	60.08	<0.001 (0.601)	68.71	76.58	60.79	<0.001 (0.414)

Values are presented as mean or number (%).

IPTW, inverse probability of treatment-weighting; RARP, robotic-assisted radical prostatectomy; RT, radiation therapy; SMD, standardized mean difference; PSA, prostate-specific antigen; ASA score, American Society of Anesthesiologists' physical status score; -, not available.

men (2%) had adjuvant RT. Patient characteristics are summarized in Table 1, which reveal differences in terms of mean age (78.03 y vs. 78.61 y; $p=0.018$), age distribution (≥ 80 y; 25.4% vs. 32.8%; $p=0.034$), and proportions with diabetes (14.9% vs. 22.9%; $p=0.007$) or coronary heart disease (3.5% vs. 7.5%) between RARP and RT groups. PCa risk stratification was distinctively unfavorable in the RT group, as evidenced by significantly higher proportions with an elevated PSA and higher Gleason grade. Consequently, the proportion of high-

risk PCa stratification was significantly skewed toward the RT group than the RARP group (59.7% vs. 18.2%). These differences were balanced by IPTW adjustment (Fig. 1), which demonstrated a decrease in SMD of <0.1 for all variables. After IPTW, age and risk-based subgroup distributions between groups became similar (Fig. 2).

2. Survival outcomes before and after IPTW adjustment

OSs and CSSs at 1, 3, and 5 years after treatment in the two groups are summarized in Table 2. During a mean follow-up of 74.5 months, OS (91.9% vs. 91.0%) and CSS (97.8% vs. 98.0%) were similar between groups. After IPTW adjustment, the RT group had higher OS (97.8% vs. 91.8%) and CSS (100% vs. 96.0%) than the RARP group in 5 years for patients aged over 80 years without adjusting other covariates (Table 3). Similarly, a low PCa risk population demonstrated numerically higher OS (98.9 vs. 96.4%) and CSS (100% vs. 98.5%) in the RT group. When considered all variables, the multivariate analysis showed overall mortality was positively associated with concomitant diabetes (hazard ratio [HR], 2.273; $p<0.0001$), and inversely associated with low PCa risk (HR, 0.314; $p<0.0001$). Similarly, PCa specific mortality was only found to be inversely associated with low PCa risk (HR,

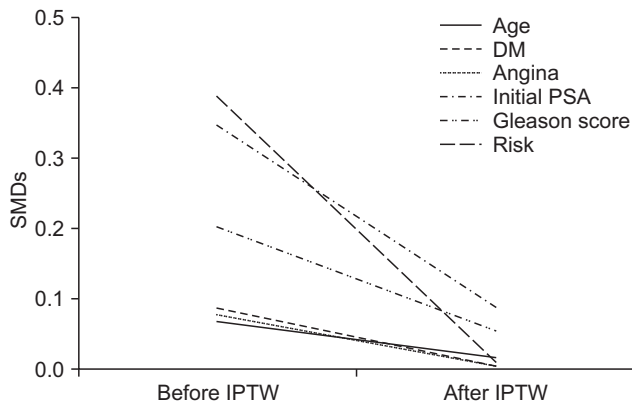


Fig. 1. Standardized mean differences (SMDs) before and after inverse probability of treatment-weighting (IPTW) adjustment. DM, diabetes mellitus; PSA, prostate specific antigen.

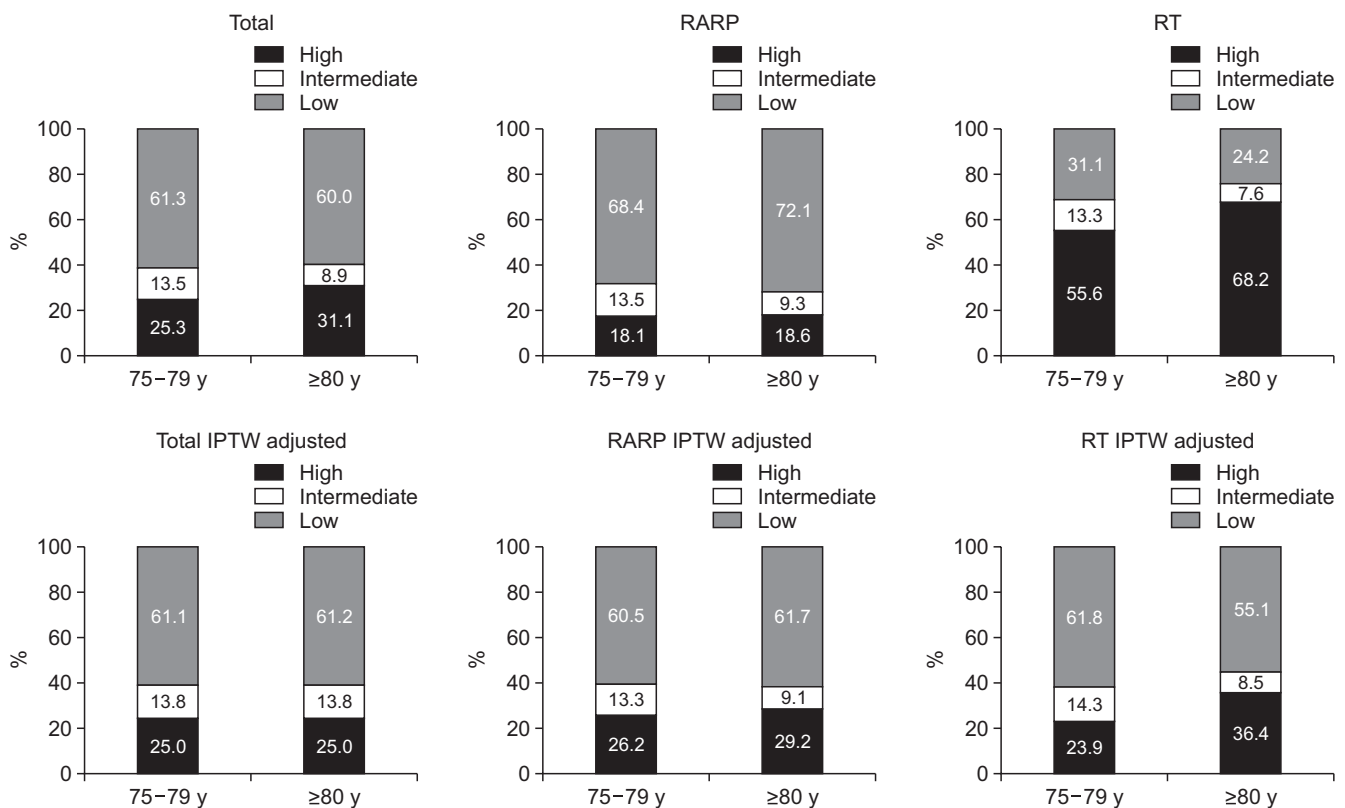


Fig. 2. Risk and age stratification of the RARP and RT groups before and after IPTW adjustment. RARP, robotic-assisted radical prostatectomy; RT, radiation therapy; IPTW, inverse probability of treatment-weighting.

Table 2. Summary of group OS and CSS outcomes

Variable	Unadjusted			IPTW-adjusted		
	1 y	3 y	5 y	1 y	3 y	5 y
OS						
Total						
Survive	956 (99.1)	934 (96.8)	913 (94.6)	1,914 (99.3)	1,870 (97.0)	1,833 (95.1)
Death	9 (0.9)	31 (3.2)	52 (5.4)	13 (0.7)	57 (3.0)	94 (4.9)
RARP						
Survive	758 (99.2)	744 (96.9)	724 (94.8)	959 (99.3)	932 (96.5)	910 (94.1)
Death	6 (0.8)	24 (3.1)	40 (5.2)	7 (0.7)	34 (3.5)	57 (5.9)
RT						
Survive	198 (98.5)	194 (96.5)	189 (94.0)	955 (99.4)	937 (97.6)	923 (96.1)
Death	3 (1.5)	7 (3.5)	12 (6.0)	6 (0.6)	23 (2.4)	37 (3.9)
p-value (RARP vs. RT)	0.353	0.807	0.682	0.755	0.159	0.044
CSS						
Total						
Survive	962 (99.7)	955 (99.0)	948 (98.2)	1,923 (99.8)	1,907 (99.0)	1,897 (98.5)
Death	3 (0.3)	10 (1.0)	17 (1.8)	4 (0.2)	20 (1.0)	30 (1.6)
RARP						
Survive	761 (99.6)	756 (99.0)	750 (98.2)	963 (99.6)	956 (98.9)	948 (98.0)
Death	3 (0.4)	8 (1.0)	14 (1.8)	4 (0.4)	11 (1.1)	19 (2.0)
RT						
Survive	201 (100.0)	199 (99.0)	198 (98.5)	961 (100.0)	951 (99.1)	949 (98.9)
Death	0 (0.0)	2 (1.0)	3 (1.5)	0 (0.0)	9 (0.9)	11 (1.1)
p-value (RARP vs. RT)	0.374	0.948	0.745	0.062	0.778	0.187

Values are presented as number (%).

OS, overall survival; CSS, cancer-specific survival; IPTW, inverse probability of treatment-weighting; RARP, robotic-assisted radical prostatectomy; RT, radiation therapy.

0.245; $p=0.0005$), but the implementation of local treatment between RARP and RT demonstrated no impact on survival (Table 4). For high-risk PCa populations, overall mortality was reversely affected by age (>80 y; HR, 2.037; $p=0.004$), concomitant diabetes (HR, 3.453; $p=0.001$), and higher Gleason score (≥ 7 ; HR, 2.458; $p=0.002$), not by the local treatment modalities. PCa specific mortality for this particular group was not influenced by the implementation of RARP or RT (Fig. 3).

DISCUSSION

Characteristically, PCa affects the elderly and exhibits age-related increases in incidence rates in the Western and Asian populations [9], the last of which has allegedly lower incidence rates. A western research study showed that the prevalence of incidental PCa was 30% among men between 30 and 69 years of age, but increased to 75% for those >70 years old [10]. In Japan, where PCa became the most common male cancer in 2016, about 70% of the population aged over 75 contracted the disease [11]. In Korea, PCa was the

tenth most common malignant disease among men a decade ago but became the third most common in 2017 [12]. Furthermore, the incidence of PCa is projected to increase significantly in parallel with societal aging and to become an increasingly important health care issue among elderly men [13].

Another unique characteristic of PCa is that it is more aggressive in the elderly. Published data indicate that men >70 years old develop higher grade and stage disease and present larger tumors [14,15]. In the same context, studies suggest that older patients have higher risks of biochemical recurrence, distant metastasis, and disease-specific death [14-16]. Therefore, given the remaining limited life span of these patients and the unfavorable characteristics of PCa, proper management plans need to be determined. In cases of localized and locally advanced PCa, two evidence-based standard interventions, namely RP and RT, could reduce PCa-related mortality. In comparison with active monitoring, local treatment by RP or RT significantly reduced both metastatic disease and clinical progression while similar CSSs was reported in a randomized clinical trial with a median of 10

Table 3. Summary of OS and CSS by PCa risk and age stratification before and after IPTW

Variable	Unadjusted						IPTW-adjusted											
	1 y		3 y		5 y		1 y		3 y		5 y							
	RARP	RT	p-value	RARP	RT	p-value	RARP	RT	p-value	RARP	RT	p-value						
OS																		
Age (y)																		
Whole	758 (99.2)	198 (98.5)	0.353	740 (96.9)	194 (96.5)	0.807	724 (94.8)	189 (94.0)	0.682	959 (99.3)	955 (99.4)	0.755	932 (96.5)	937 (97.6)	0.159	910 (94.2)	923 (96.1)	0.044
75-79	565 (99.1)	134 (99.3)	0.877	554 (97.2)	131 (97.0)	0.922	543 (95.3)	126 (93.3)	0.360	704 (99.2)	718 (99.7)	0.169	689 (97.2)	702 (97.5)	0.699	674 (95.0)	688 (95.6)	0.626
≥80	193 (99.5)	64 (97.0)	0.098	186 (95.9)	63 (95.5)	0.883	181 (93.3)	63 (95.5)	0.529	256 (99.6)	237 (98.4)	0.202	243 (94.6)	236 (97.8)	0.062	236 (91.8)	236 (97.8)	0.003
Risk																		
High	139 (100.0)	117 (97.5)	0.061	133 (95.7)	115 (95.8)	0.952	127 (91.4)	111 (92.5)	0.739	261 (100.0)	254 (97.8)	0.015	248 (95.0)	250 (96.2)	0.525	236 (90.7)	241 (92.5)	0.444
Intermediate	93 (97.9)	23 (100.0)	0.483	88 (92.6)	22 (95.7)	0.605	86 (90.5)	21 (91.3)	0.908	115 (97.9)	123 (100.0)	0.101	109 (92.7)	117 (94.6)	0.540	107 (90.6)	112 (90.9)	0.941
Low	526 (99.3)	58 (100.0)	0.507	519 (97.9)	57 (98.3)	0.857	511 (96.4)	57 (98.3)	0.458	583 (99.2)	577 (100.0)	0.036	575 (97.9)	571 (98.9)	0.202	566 (96.4)	571 (98.9)	0.006
CSS																		
Age (y)																		
Whole	761 (99.6)	201 (100.0)	0.374	756 (99.0)	199 (99.0)	0.948	750 (98.2)	198 (98.5)	0.745	963 (99.6)	961 (100.0)	0.062	956 (98.9)	951 (99.0)	0.778	948 (98.1)	949 (98.8)	0.187
75-79	568 (99.7)	135 (100.0)	0.491	567 (99.5)	133 (98.5)	0.234	563 (98.8)	132 (97.8)	0.380	707 (99.7)	720 (100.0)	0.120	706 (99.5)	711 (98.7)	0.114	701 (98.8)	709 (98.4)	0.532
≥80	193 (99.5)	66 (100.0)	0.559	189 (97.4)	66 (100.0)	0.188	187 (96.4)	66 (100.0)	0.118	256 (99.6)	241 (100.0)	0.305	250 (97.3)	241 (100.0)	0.010	247 (96.0)	241 (100.0)	0.002
Risk																		
High	139 (100.0)	120 (100.0)	-	138 (99.3)	119 (99.2)	0.917	136 (97.8)	118 (98.3)	0.774	261 (100.0)	260 (100.0)	-	258 (99.1)	257 (99.0)	0.906	255 (97.7)	255 (98.2)	0.705
Intermediate	94 (99.0)	23 (100.0)	0.621	92 (96.8)	22 (95.7)	0.777	92 (96.8)	22 (95.7)	0.777	117 (98.9)	123 (100.0)	0.250	114 (96.9)	117 (94.6)	0.393	114 (96.9)	117 (94.6)	0.393
Low	528 (99.6)	58 (100.0)	0.639	526 (99.3)	58 (100.0)	0.507	522 (98.5)	58 (100.0)	0.346	585 (99.6)	577 (100.0)	0.137	583 (99.2)	577 (100.0)	0.036	579 (98.5)	577 (100.0)	0.003

Values are presented as number (%).

OS, overall survival; CSS, cancer-specific survival; PCa, prostate cancer; IPTW, inverse probability of treatment-weighting; RARP, robotic-assisted radical prostatectomy; RT, radiation therapy.

Table 4. Summary of Cox regression for OS and CSS

	Unadjusted			IPTW-adjusted		
	p-value	Hazard ratio	95% confidence interval	p-value	Hazard ratio	95% confidence interval
Overall mortality, variable (reference)						
RARP (RT)	0.7207	0.899	0.501–1.613	0.8870	1.025	0.726–1.448
Age ≥80 y (<80 y)	0.0204	1.698	1.085–2.658	0.1431	1.291	0.917–1.816
Diabetes (none)	0.0151	1.867	1.128–3.089	<0.0001	2.273	1.590–3.250
Angina (none)	0.7270	0.777	0.189–3.198	0.2361	0.483	0.145–1.610
Intermediate risk (high)	0.2457	0.658	0.325–1.333	0.1257	0.685	0.422–1.112
Low risk (high)	0.0001	0.357	0.211–0.601	<0.0001	0.314	0.219–0.449
Cancer-specific mortality, parameter						
RARP (RT)	0.5167	0.676	0.207–2.205	0.1422	0.603	0.307–1.185
Age ≥80 y (<80 y)	0.1316	1.953	0.818–4.662	0.1049	1.740	0.891–3.401
Diabetes (none)	0.7909	0.847	0.248–2.891	0.5553	0.749	0.286–1.960
Intermediate risk (high)	0.9536	0.964	0.278–3.340	0.5186	1.295	0.591–2.840
Low risk (high)	0.0638	0.377	0.135–1.058	0.0005	0.245	0.111–0.538

OS, overall survival; CSS, cancer-specific survival; IPTW, inverse probability of treatment-weighting; RARP, robotic-assisted radical prostatectomy; RT, radiation therapy.

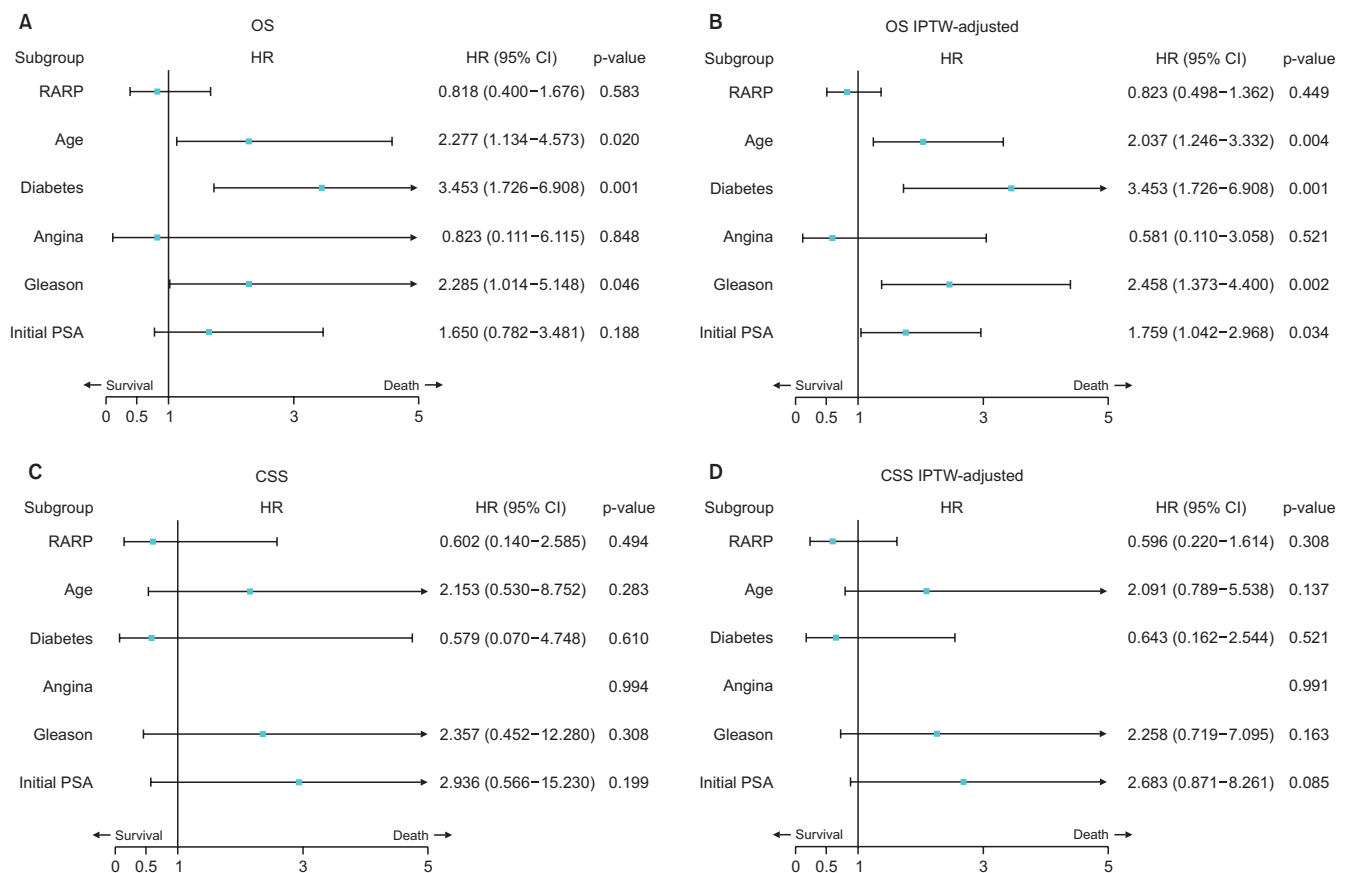


Fig. 3. Summary of OSs and CSSs before and after IPTW adjustment for high-risk population. (A) OS unadjusted, (B) OS adjusted by IPTW, (C) CSS unadjusted, (D) CSS adjusted by IPTW. OS, overall survival; CSS, cancer-specific survival; IPTW, inverse probability of treatment-weighting; RARP, robotic-assisted radical prostatectomy; PSA, prostate-specific antigen; HR, hazard ratio; CI, confidence interval.

years follow-up [5]. However, because of the poorer physical status, more advanced disease, and the higher pathological grades presented by older patients [17], it might be expected that outcomes of RP for elderly people may also be poorer, and this expectation regarding treatment outcomes is the main reason why RT is recommended over RP, especially for men over 75 years old.

The introduction and widespread use of RARP has been driven by its minimally invasive nature and shorter period of functional loss after RP without compromising oncologic control, and these benefits may lower barriers to its use, especially among elderly patients. Based on this background, we included patients who underwent RP only using a robotic approach. With regard to the age limitation for RP, contemporary guidelines recommend that it be considered in patients with low-intermediate risk disease and a life expectancy of >10 years or patients with high-risk disease and a life expectancy of >5 years [18]. Thus, given a current average life span of 79.7 years for Korean men [19], we carried out a multicenter study, which involved representative tertiary Korean hospitals located across the nation to investigate the benefit of different local treatments in men older than 75 years with non-metastatic disease.

This study revealed a distinctive difference between the RARP and RT groups, namely that patients in the RT group presented with more unfavorable tumor characteristics and were older, thus reflecting the conventional favoring of RT for patients aged >75 years. To adjust for this difference in the survival analysis, we adopted IPTW, which provides a means of creating balanced groups for comparison purposes. After this adjustment, OSs and CSSs were generally similar in the RARP and RT groups. Though the IPTW-adjusted 5 years OSs and CSSs look higher in RT groups in some subgroup population, the other co-variables which could strongly affect the mortality in the elderly should be taken into account, and it was hard for us to find a substantial clinical implication from 2% to 6% of the difference between them with 91.8% to 100% of range. Also, it should be considered that the follow-up periods were significantly shorter in the RT group than the RARP group before and even after IPTW adjustment. Given three times higher proportion of high-risk PCa population in RT group and RARP population (18% vs. 60%), the multivariable analysis adjusted for age, the presence of concomitant disease (e.g., diabetes and coronary heart disease), and PCa risk stratification demonstrated no difference between the survivals achieved using the two local treatment modalities.

Based on these findings, we believe that considerations of age alone should not be used to exclude RARP as a treat-

ment modality. Rather, exclusively from the perspective of oncologic controllability, we believe that for healthy elderly with aggressive disease, RARP could be performed primarily given it allows a radical removal of the entire organ. Indeed, there may also be indirect disadvantages associated with RT, as 84% of these patients received ADT in this series, the prolonged administration of which is associated with increased risks of myocardial infarction and stroke [20].

Although elderly men are generally excluded from the majority of observational studies, some registry-based studies have focused on this population. Rice et al. [13] evaluated the outcomes of RP, RT, and watchful waiting (WW) in a 770 cohort of low-risk PCa patients over 70 years old treated between 1989 and 2009. Over a median follow-up of 6.4 years, the poorest OS and progression-free survival rates were observed in the WW group. Furthermore, the multivariate analysis failed to detect a significant difference between RP and RT in terms of OS or biochemical recurrence. Sheng et al. [8] focused on patients with T3 disease aged over 75 years registered in the Surveillance, Epidemiology, and End Results (SEER) database. Some of these patients received local treatment and some did not. RP and RT groups of 482 patients each were constructed by propensity matching, and group CSSs and OSs were found to be similar at 5 and 10 years. The present study was performed on a larger cohort with more detailed treatment information and produced similar results. Moreover, it should be noted this is the first report on RARP to exclude laparoscopic and open RP data.

The present study is limited by reliance on retrospective data, and despite our efforts to compensate for differences in patient characteristics, our results might be confounded by the indications used for RARP and RT, which is an inherent shortcoming of observational studies. By nature of multicenter series, detailed policies and treatment strategies adopted at each institution may have differed. For instance, though active surveillance has become a choice especially for the elderly, its indication has not been generalized yet. It is also notable that all the RARP procedures in this study were performed by experienced surgeons of the representative tertiary hospital across the nation because RP over 75 years old could not be generalized in currently available guidelines. Most importantly, given that each treatment modality has unique side effects including aggravation of low urinary tract symptoms especially in RT, and development of incontinence following RARP, the quality of life after treatment could not be properly assessed by the retrospective nature of the study. Thus, we hope the presented results will be considered hypothesis-generating and spur further investigations on the proper local management of PCa in el-

derly patients. Given the obvious trend toward increased life spans globally and in Asia, there is an increasing need for optimal management of non-metastatic PCa in the elderly. The present study that focused on the aged thereby allows direct comparisons of OSs and CSSs suggests considerations of age alone should not be used to determine whether RARP could or could not be adopted. However, these survival outcomes should be weighed balanced with the functional outcomes and the morbidity generated by a local treatment modality in a future study.

CONCLUSIONS

With the limitation of retrospective study design performed by experienced surgeons, even the patient over 75 years old who underwent RARP for non-metastatic PCa had a similar survival in comparison with RT regardless of risk stratification, reflecting age alone should not be used to exclude patients for RARP. However, these survival outcomes need to be weighed with the morbidity generated by each local treatment modality in a future study.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

ACKNOWLEDGMENTS

This work was supported by a Yeungnam University Research Grant (2019).

AUTHORS' CONTRIBUTIONS

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