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Original article

Adjuvant radiation with hormonal therapy is associated with improved survival in men with pathologically involved lymph nodes after radical surgery for prostate cancer

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Abstract

Purpose: Recent studies have suggested that the addition of adjuvant radiation therapy (aRT) may improve outcomes in men with pathologically involved lymph nodes (pN+). The objective of this study was to assess the treatment patterns and the overall survival (OS) outcomes in men with pN+ prostate cancer using the National Cancer Data Base.

Methods: Men diagnosed with nonmetastatic prostate cancer between 2004 and 2011, who underwent radical prostatectomy for pN+ were identified in the National Cancer Data Base. Patients were stratified into subgroups of those receiving no adjuvant therapy and those receiving adjuvant hormonal therapy (aHT) alone, aRT alone, and aRT + aHT. OS was analyzed using Kaplan-Meier method and compared between the groups using the log-rank test. Multivariable Cox regression was used to identify covariates that affected OS.

Results: A total of 7,225 patients were included in this analysis, of whom 3,636 (50.3%) received no adjuvant therapy, 2,041 (28.2%) received aHT alone, 350 (4.8%) received aRT alone, and 1,198 (16.5%) received aRT + aHT. The 5-year OS rates were 85.2% for no adjuvant therapy, 82.9% for aHT alone, 88.3% for aRT alone, and 88.8% for combination hormonal therapy, i.e., aRT + aHT ($P < 0.001$). On multivariable analysis, aRT + aHT was associated with a significantly decreased risk of death (hazard ratio [HR] = 0.67; 95% CI: 0.54–0.83; $P < 0.001$) compared with no adjuvant therapy, whereas aHT alone (HR = 0.99; 95% CI: 0.85–1.15; $P = 0.90$) and aRT alone (HR = 1.02; 95% CI: 0.74–1.40; $P = 0.92$) were not.

Conclusion: Patients treated with multimodal aRT + aHT had significantly higher OS rate than patients treated without adjuvant therapy or with aHT/aRT alone.

Keywords: Prostate cancer; Prostatectomy; Radiotherapy; Combined modality therapy; Outcomes

1. Introduction

Radical prostatectomy is accepted as one of the various treatment options for men with localized disease [1,2]. However, up to 15% of men undergoing prostatectomy would be found to have lymph node metastasis at the time of surgery [3,4], which has been associated with worse cancer-specific survival and a higher rate of distant metastasis [5]. As such, these patients may benefit from adjunctive therapy to improve outcomes.

National guidelines suggest various adjunctive treatment options for these patients including observation or hormonal therapy (HT) with or without radiation therapy (RT). Unfortunately, there is little high-level evidence to guide clinical decisions. HT is considered a standard therapeutic option based on a small phase III trial that demonstrated a significant prostate cancer and overall survival (OS) benefit to early adjuvant HT (aHT) over delayed salvage HT [6]. This survival advantage for early aHT over delayed salvage HT was confirmed by a subsequent meta-analysis [7]. There are even fewer data addressing the role of adjuvant RT (aRT) in these patients. Several retrospective series have suggested that aRT may improve survival [8–10], but these

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findings have yet to be confirmed in a prospective randomized controlled trial.

As the optimal management for pathologic node-positive patients has yet to be established, we analyzed the National Cancer Data Base (NCDB) to determine contemporary patterns of care regarding the use of aHT and aRT and to compare survival outcomes between treatment groups.

2. Materials and methods

2.1. Data source

The NCDB is a joint project of the American Cancer Society and the Commission on Cancer of the American College of Surgeons. It is estimated that 70% of all diagnosed malignancies in the United States are captured by facilities participating in this registry and reported to the NCDB. The Commission on Cancer's NCDB and the hospitals participating in the NCDB are the source of the de-identified data used in this study. However, they have not verified and are not responsible for the statistical validity or conclusions derived by the authors of this study. Exemption was obtained from the New York Harbor Veterans Affairs Committee for Research and Development before the initiation of this study.

2.2. Patient selection

The NCDB was queried to identify men who were diagnosed with prostate adenocarcinoma between 2004 and 2011 and who underwent radical prostatectomy. To be included, patients must have had ≥ 1 pathologically positive lymph node. Data regarding the receipt of postoperative RT and HT were collected. Data regarding the preradiation prostate-specific antigen (PSA) values were not available in the NCDB.

2.3. Statistical analysis

Descriptive statistics were used to identify details regarding the postoperative management of these patients, including the use of aRT or HT or both and temporal changes in use over the course of this study. In addition, the RT dose and its changes over time were measured, as well as the effect of margin status or pathologic stage on the selection of RT, the use of 3-dimensional conformal radiotherapy or intensity-modulated RT (IMRT), and the RT

Table 1
Patient characteristics by treatment group

	No adjuvant therapy	RT alone	Hormonal therapy alone	RT + hormonal therapy	*P* value
Age (median, interquartile range)	63 (57–67)	60 (55–65.3)	62 (57–67)	60 (55–65)	
≤60	1,445 (46.9%)	175 (5.7%)	846 (27.4%)	618 (20.0%)	<0.001
61–70	1,718 (51.9%)	145 (4.4%)	943 (28.5%)	504 (15.2%)	
>70	473 (56.9%)	30 (3.6%)	252 (30.3%)	76 (9.1%)	
Race					<0.001
White	2,984 (49.4%)	293 (4.8%)	1,722 (28.5%)	1,044 (17.3%)	
Black	485 (58.8%)	40 (4.8%)	197 (23.9%)	103 (12.5%)	
Other	167 (46.8%)	17 (4.8%)	122 (34.2%)	51 (14.3%)	
Gleason					<0.001
≤6	129 (81.1%)	7 (4.4%)	18 (11.3%)	5 (3.1%)	
7 (3 + 4)	838 (61.1%)	70 (5.1%)	287 (20.9%)	176 (12.8%)	
7 (4 + 3)	927 (56.1%)	100 (6.0%)	388 (23.5%)	238 (14.4%)	
8	561 (48.0%)	47 (4.0%)	361 (30.9%)	200 (17.1%)	
9–10	1,092 (41.6%)	100 (3.8%)	900 (34.3%)	530 (20.2%)	
pT					<0.001
pT2	913 (65.9%)	53 (3.8%)	299 (21.6%)	121 (8.7%)	
pT3a	852 (57.3%)	79 (5.3%)	386 (26.0%)	169 (11.4%)	
pT3b	1,467 (44.0%)	167 (5.0%)	1,025 (30.8%)	673 (20.2%)	
pT3NOS	256 (42.1%)	32 (5.3%)	185 (30.4%)	135 (22.2%)	
pT4	148 (35.8%)	19 (4.6%)	146 (35.4%)	100 (24.2%)	
Margins					<0.001
Negative	2,212 (58.2%)	150 (3.9%)	1,019 (26.8%)	419 (11.0%)	
Positive	1,424 (41.6%)	200 (5.8%)	1,022 (29.8%)	779 (22.7%)	
Number of nodes					<0.001
1	2,505 (54.6%)	266 (5.8%)	1,069 (23.3%)	748 (16.3%)	
>1	1,094 (42.7%)	81 (3.2%)	949 (37.0%)	438 (17.1%)	
Unknown	37 (49.3%)	3 (4.0%)	23 (30.7%)	12 (16.0%)	

NOS = not otherwise specified.