Anticoagulant Use is Associated With Improved Biochemical Control of High-Risk Prostate Cancer Patients Treated With Radiation Therapy

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INTRODUCTION

The coagulation system modulates multiple cancer pathways, including tumor proliferation, angiogenesis, host immunologic defense, and metastasis. Prior studies have reported improved survival and freedom from biochemical failure (FFBF) in prostate cancer (PCa) patients taking aspirin and other anticoagulants (ACs).[1,2] We reviewed the outcomes of patients with high-risk PCa who received ACs and definitive radiation therapy (RT).

MATERIALS AND METHODS

Patients with nonmetastatic high-risk adenocarinoma of the prostate (stage ≥ T3a, or Gleason score (GS) ≥ 8, or prostate-specific antigen (PSA) ≥ 20) treated with definitive RT between 2005-2008 at UTSW were identified. The AC group consisted of patients who had warfarin, clopidogrel, or aspirin recorded on the medication list at any clinical visit. FFBF of patients was determined using the Phoenix definition. Log-rank test was used to correlate FFBF with the ACs. Univariate and multivariate analysis (MVA) of FFBF to pretreatment PSA, GS, stage, hormone use, total RT dose, and ACs was performed.

RESULTS

Among the 76 patients identified, 45 (59.2%) comprised the AC group. Within the AC group, 43 were taking aspirin, 8 were taking warfarin, 8 were taking clopidogrel, and 13 were taking multiple ACs. Median follow up was 61.2 months (range 3.1-89.4) for the AC group and 55.1 months (range 6.5-88.9) for the non-AC group. Patients receiving ACs exhibited significantly improved FFBF compared to the control group (p=0.0018; log-rank test). The estimated 4-year FFBF was 83.7% and 63.2% for the AC and non-AC groups, respectively. Among the patients taking a single AC, only aspirin showed significantly improved FFBF (p=0.0037). The hazard ratio for T-stage was 1.18 (95% CI 0.75, 1.85; p=0.4672) in the AC group and 1.67 (95% CI 1.09, 2.58; p=0.0196) in the non-AC group, implying a benefit from taking the AC. Aspirin use, T-stage, and N-stage remained significantly correlated to FFBF (p=0.0002, p=0.0056, and p=0.0040, respectively). The early and late grade 2 toxicity rates for rectal bleeding were 7.7% in patients on multiple ACs and 0% for patients on a single AC or no AC. No patients experienced grade 3 rectal toxicity.

CONCLUSION

Use of ACs in high-risk PCa patients improved the FFBF after definitive RT without increasing rates of rectal bleeding. This suggests that daily use of a single anticoagulant, especially aspirin, in high-risk PCa patients treated with definitive RT decreases biochemical failure and may improve outcome. Large prospective data are needed to validate the findings of this study.

REFERENCES

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2. Choe KS, Cowan JE, Chan JM, Carroll PR, D'Amico AV, Liauw SL. Aspirin Use and the Risk of Prostate Cancer Mortality in Men Treated With Prostatectomy or Radiotherapy. Journal of Clinical Oncology. 2012 Oct 1;30(28):3540-4.

TABLE 1. PATIENT CHARACTERISTICS

Category		Number	Percent
Median Age (Range)		69 (49-86)	
T-stage	T1c	17	22.4
	T2a-b	22	28.9
	T2c	14	18.4
	T3a	9	11.8
	T3b	11	14.5
	Unknown	3	3.9
N-stage	N0	60	78.9
	N1	7	9.2
	Unknown	9	11.8
Prostate-Specific Antigen (PSA)	PSA <10	17	22.4
	PSA 10-20	12	15.8
	PSA >20 (range 20.02-332.7)	47	61.8
Gleason Score (GS)	GS 6	6	7.9
	GS 7	18	23.7
	GS 8	25	32.9
	GS 9	24	31.6
	GS 10	3	3.9
Hormone Therapy	Yes	64	84.2
	No	8	10.5
	Unknown	4	5.3
Duration of Hormone Therapy	0 months	8	10.5
	1-6 months	4	5.3
	8-20 months	14	18.4
	≥24 months	34	44.7
	Unknown	16	21.1

TABLE 2. MEDICATIONS VS. BIOCHEMICAL FAILURE

Medication	Number of Patients Taking Medication	Number with Biochemical Failure (%)	P-value
Aspirin	43	6 (14.0)	0.0037
Warfarin	8	1 (12.5)	0.4884
Clopidogrel	8	1 (12.5)	0.4870
Multiple Anticoagulants	13	2 (15.4)	0.4710
Any Anticoagulant	45	6 (13.3)	0.0018
No Anticoagulant	31	12 (38.7)	

TABLE 3. UNIVARIATE ANALYSIS

Category		HR (95% CI)	P-value
T-stage	Continuous	1.26 (0.96-1.67)	0.1021
N-stage	N0 vs. N1		<0.0001
Highest Gleason Score	Continuous	1.32 (0.83-2.10)	0.2426
Pretreatment PSA	Continuous	1.00 (1.00-1.01)	0.1835
% Core Positivity	Continuous	2.64 (0.49-14.17)	0.2577
Total Radiation Dose	Continuous	0.99 (0.73-1.36)	0.9619

TABLE 4. MULTIVARIATE ANALYSIS

Category		HR (95% CI)	P-value
Aspirin	No vs. Yes	11.99 (3.29-43.71)	0.0002
T-stage	Continuous	1.77 (1.18-2.65)	0.0056
N-stage	N1 vs. N0	6.25 (1.79-21.78)	0.0040

FIGURE 1. FREEDOM FROM BIOCHEMICAL FAILURE BY ANTICOAGULANT USE

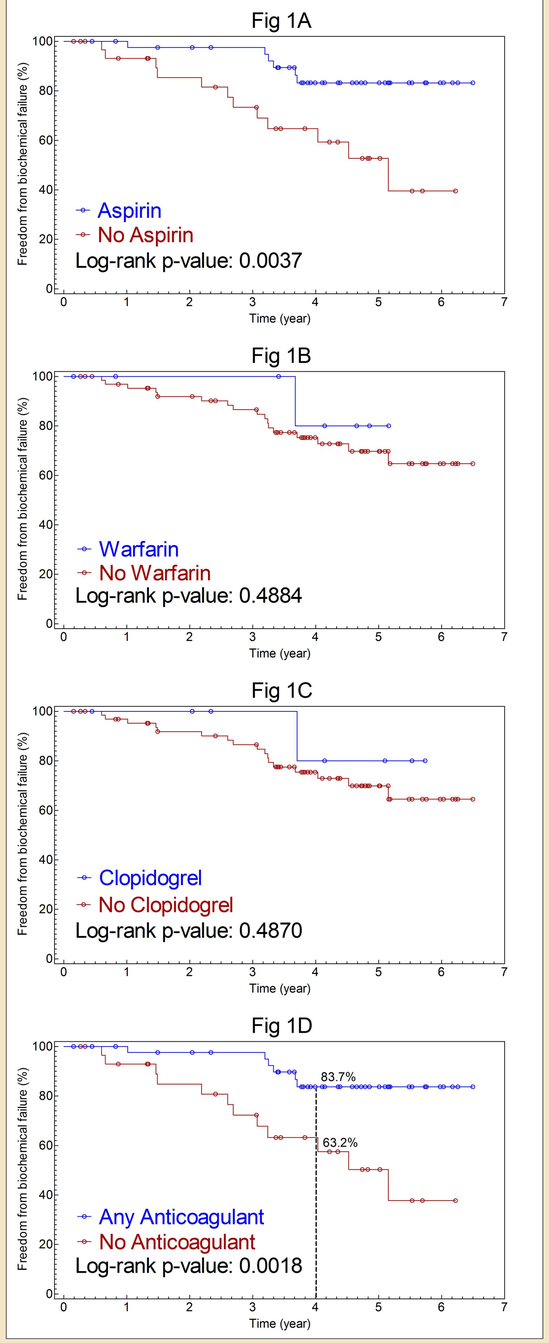

Figure 1. Although aspirin (Fig 1A), warfarin (Fig 1B), and clopidogrel (Fig 1C) all appear to improve biochemical control, only aspirin was statistically significant. Patients taking one or more of these anticoagulants also had improved FFBF (Fig 1D), but the vast majority (95.6%) of patients in this group took aspirin.