SECONDARY MALIGNANCIES AFTER RADIOTHERAPY FOR PROSTATE CANCER: A POPULATION-BASED STUDY

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Background

- Survival of prostate cancer (PCa) patients has improved over time thanks to improvement of surgical and radiation therapy (RT) technics.
- Recent evidence[1,2] has shown that receiving RT may predispose to secondary malignancies.

Objective

To assess the risk of secondary malignancies in men treated with RT and radical prostatectomy (RP).

Methods

A cohort study was constructed using Quebec administrative databases (Med-Echo and RAMQ).

- **Included:** men being diagnosed and treated with radical prostatectomy (RP) or radiotherapy (RT) for PCa patients between 2000-2016.
- **Outcomes of interest**: incidence of bladder cancer (BCa) and colorectal cancer (CRCa). End of follow-up: incidence of BCa or of CRCa, death, or Dec 31, 2016.
- **Excluded**: Patients with evidence of BCa or CRCa prior to PCa diagnosis

Statistical analyses

Inverse probability of treatment weighting (IPTW) based on a propensity score was used to control for potential confounding.

IPTW-Cox proportional hazards models were used to evaluate the associations between the initial PCa treatment (radiotherapy- EBRT, brachytherapy or RP) and the incidence of BCa, and CRCa, respectively.

Results

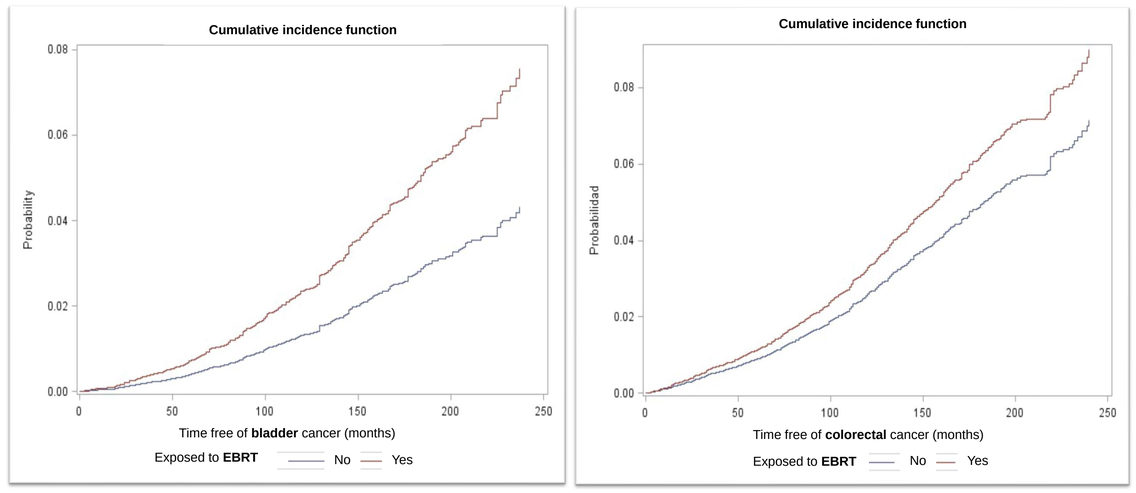
Table 1. Cohort baseline characteristics for prostate cancer patients with secondary colorectal and bladder cancer

Variable	Secondary bladder cancer						Secondary colorectal cancer					
	Crude/Unweighted Study Cohort			IPT-weighted Study Cohort			Crude/Unweighted Study Cohort			IPT-weighted Study Cohort		
	EBRT (n= 15481)	RP (n= 27783)	ASMD Before IPTW*	EBRT (n= 15481)	RP (n= 27783)	ASMD After IPTW*	EBRT (n= 15499)	RP (n= 27788)	ASMD Before IPTW*	EBRT (n= 15499)	RP (n= 27788)	ASMD After IPTW*
Age >75 years (yes/no)	27.7	1.9	0.776	11.3	11.8	0.013	27.8	2.0	0.777	11.3	11.7	0.013
Prior cardiovascular disease	38.9	27.2	0.251	31.5	31.9	0.008	38.9	27.2	0.251	31.6	31.9	0.008
Prior cancer (yes/no)	17.2	48.7	0.710	36.5	37.1	0.013	17.3	48.7	0.707	36.6	37.1	0.013
Prior hypertension (yes/no)	62.9	49.2	0.279	54.4	54.6	0.004	62.9	49.2	0.279	54.4	54.6	0.004
Prior dyslipidemia (yes/no)	43.2	37.9	0.105	39.8	40.4	0.011	43.2	38.0	0.105	39.8	40.4	0.011
Prior diabetes (yes/no)	20.0	13.6	0.171	16.2	15.9	0.010	20.0	13.7	0.170	16.3	15.9	0.010
Charlson comorbidities score	49.0	28.1	0.440	36.7	36.5	0.003	49.0	28.1	0.441	36.7	36.6	0.003

Table 2. Risk of secondary malignancies (bladder or colorectal cancer) for patients exposed to different treatments

		Events	PYs	Incidence rate (IR)/100 PYs	Hazard ratio (HR) 95%CI		12-month risk (IPTW)
					Crude	IPTW adjusted	
Bladder cancer	RP	344	261194.67	0.18	Ref.		0.22
	EBRT	368	127889	0.41	**2.27 (1.96;2.63)**	**1.78 (1.54;2.07)**	0.38
	Brachytherapy	11	5647.75	0.37	**2.03 (1.11;3.72)**	1.09 (0.55;2.15)	0.20
Colorectal cancer	RP	709	260030.08	0.35	Ref.		0.36
	EBRT	487	127441.91	0.49	**1.44 (1.29;1.62)**	**1.27 (1.13;1.43)**	0.45
	Brachytherapy	27	5576.5	0.78	**2.36 (1.59;3.47)**	**1.77 (1.22;2.57)**	0.60

Figure 1. Cumulative incidence functions for secondary bladder cancer and colorectal cancer.



Strengths and Limitations

- The use of provincial administrative databases provides the effects of these treatments in real life without participants being under strict protocols.
- Patients were followed up for up to 20 years, which provided a sufficient latency period to establish an association between the date of exposure to radiation and the development of a secondary cancer.
- Lastly, the use of IPTW method minimize the presence of bias by balancing groups in terms of baseline variables.
- Due to the use of administrative healthcare claims data, we lacked important information on confounders which might bias the risk attributed to radiotherapy. For instance, smoking and obesity, are known factors predisposing patients to bladder cancer, and to colon and prostate cancer, respectively.
- Even if confounding variables were taken in count through appropriate statistical methods using propensity score, it is possible that other unknown or unmeasured factors linking secondary malignancies to initial treatments might have been missed.

Conclusion

This study confirmed that men undergoing EBRT for prostate cancer had an increased risk of secondary bladder and colorectal cancer compared to patients undergoing RP. Patients undergoing brachytherapy showed an increased significant risk of colorectal cancer but not of bladder cancer.

References

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