

Palliative Radiotherapy During the Last Month of Life: Have COVID-19 Recommendations Led to Reduced Utilization?

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Abstract. *Background/Aim:* The study aimed to evaluate practice changes in the time period of the early wave of the COVID-19 pandemic. *Patients and Methods:* This was a retrospective single institution study. We defined palliative radiotherapy (PRT) initiated before Saturday, March 14th as pre-COVID and PRT initiated later as during-COVID (through June 30th). *Results:* National COVID-19 recommendations led to a significant decrease in PRT with 10 or more fractions, while re-irradiation and radiotherapy during the final 30 days of life were equally common before and after these recommendations had been issued in March 2020. *Conclusion:* Rapid adoption of modified PRT regimens was feasible. However, the challenge of overtreatment in the final phase of the disease, due to inaccurate survival prediction, persisted.

Palliative radiotherapy (PRT) is among the cornerstones of oncological approaches in patients with incurable cancer (1). In our institution, which has a dedicated PRT program that serves a small and scattered population of less than 200,000 inhabitants in rural North-Norway (large parts of Nordland County with a total of population of 243,000), overtreatment and 30-day mortality (30DM) has long been a topic of research (2-6). The first comprehensive analysis related to the time period 2007-2009 (7). In 9% of patients, PRT was administered during the final 30 days of life. We were able to develop and validate a predictive model [presence of 6 parameters: lung or bladder cancer, Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 3-4, low serum hemoglobin, opioid analgesic use, steroid use, progressive disease outside the PRT volume], which correctly identified 75% of PRT courses administered during the final 30 days of life. Given that our

further research focused on PRT and survival prediction, and that only three clinical oncologists assessed patients and prescribed PRT, we hypothesized that increased awareness and knowledge about factors predicting 30DM might have led to decreased 30DM in a later time period. Consequently, we evaluated our data obtained between 01.09.2013 and 31.08.2014 (8). We were disappointed to learn that even in our small facility, 30DM did not improve compared to the first study (17% in patients with metastatic cancer, 5% in those with non-metastatic cancer).

In March 2020, the global COVID-19 pandemic also arrived in Norway. On March 10th, the Norwegian Institute of Public Health had registered 277 people with confirmed infection. Based on national recommendations distributed to all oncology departments, we encouraged the utilization of altered fractionation regimens with a focus on short overall treatment time, as well as a thorough assessment of the potential benefit of PRT, as also suggested by international groups (9, 10). The aim of the present analysis was to evaluate the impact of COVID-19-related changes, primarily regarding PRT during the final 30 days of life and secondarily regarding PRT with 10 or more fractions.

Patients and Methods

We analyzed the treatment administered in the time period between 01.01.and 30.06.2020 and defined PRT initiated before Saturday, March 14th as pre-COVID and PRT initiated later as during-COVID. The analysis was performed on September 13th and survival data were available for all patients. The statistical evaluation employed the 2-tailed Fisher exact probability test (IBM SPSS v.25, significance was defined as $p \leq 0.05$ in two-sided tests).

Results

Forty-seven patients were treated in the pre-COVID phase (0.9 started PRT each business day; 25 received PRT for bone metastases, 53%), including 5 re-irradiations (11%). The largest group consisted of patients with non-small cell lung cancer (n=15, 32%). Twenty-eight patients (60%) received 10 or more fractions. Only 3 patients (6%), all with metastatic cancer, were treated during the final 30 days of life.

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Table I. Rate of palliative radiotherapy during the last month of life stratified by cancer types (stereotactic radiotherapy and radical treatment of oligometastases not included, all patients were older than 20 years).

Primary cancer type	Time period	Target volume	Number of fractions	Treatment in the final		
				2 wk	3 wk	month
Prostate cancer	Pre	2 (prostate), 6 (oss)	2 (1), 1 (8), 5 (10)		1	
	During	5 (oss)	3 (1), 2 (5)			
Breast cancer	Pre	2 (oss), 2 (bra)				
	During	4 (oss), 1 (other)	3 (10), 1 (20)		1	
Thyroid cancer	Pre	1 (oss)	2 (1), 1 (5), 1 (10), 1 (12)			
	During	1 (oss)	1 (10)			
Non-small cell lung cancer	Pre	6 (oss), 8 (lung), 1 (bra)	3 (2), 3 (5), 6 (10), 1 (13), 2 (15)	1		
	During	11 (oss), 7 (lung), 3 (bra)	4 (1), 5 (2), 3 (5), 1 (6), 2 (8), 6 (10)		2	1
Small cell lung cancer	Pre	1 (bra)	1 (10)			
	During	2 (bra), 1 (other), 1 (lung)	3 (10), 1 (15)			
Colorectal cancer	Pre	1 (oss), 1 (rectum), 2 (other)	1 (2), 2 (5), 1 (12)			
	During	3 (rectum), 5 (other), 1 (bra)	2 (1), 5 (5), 1 (7), 1 (12)		1	
Gastric cancer	Pre	1 (oss)	1 (5)			
	During					
Esophageal cancer	Pre	1 (esophagus), 1 (oss)	1 (6), 1 (13)			
	During	1 (esophagus), 1 (bra)	1 (10), 1 (13)	1		
Bladder cancer	Pre	1 (oss), 2 (other)				
	During	1 (1), 2 (13)				
Kidney cancer	Pre	3 (oss)	1 (7), 1 (8), 1 (10)			
	During	2 (oss), 1 (bra), 1 (other)	1 (1), 1 (5), 1 (10), 1 (13)			
Sarcoma	Pre	2 (oss)	1 (9), 1 (10)			
	During	1 (oss)	1 (5)	1		
Hepatocellular cancer	Pre	1 (oss)	1 (10)			
	During	1 (other)	1 (13)			
Malignant melanoma	Pre					
	During	2 (other), 1 (bra), 1 (oss)	1 (3), 3 (5)			
Gynecological cancers	Pre	1 (oss)	1 (13)			
	During	1 (other)	1 (10)			
Pancreatic cancer	Pre	1 (pancreas)	1 (12)			
	During					
Multiple myeloma	Pre	3	1 (5), 1 (6), 1 (10)			
	During	5	1 (4), 4 (5)			
Lymphoma	Pre					
	During	3	1 (5), 1 (8), 1 (10)	1		
Others	Pre					
	During	1 (other), 1 (lung)	1 (5), 1 (10)			

oss: Bone metastases; bra: brain metastases; other: lymph nodes and soft tissue.

Seventy-one patients were treated in the during-COVID phase (1.0 started PRT each business day; 29 received PRT for bone metastases, 41%), including 7 re-irradiations (10%). The largest group consisted of patients with non-small cell lung cancer (n=21, 30%). Twenty-four patients (34%) received 10 or more fractions. Eight patients (11%; 7 with metastatic cancer and 1 with lymphoma) were treated during the final 30 days of life (Table I).

For both time periods combined, *i.e.* the first half of 2020, 9% of all patients received PRT during the final 30 days of life. Non-small cell lung cancer was a common diagnosis in these patients. None of the deaths was related to COVID-19.

The only statistically significant difference regarding the data reported in the Results section relates to a reduced utilization of PRT with 10 or more fractions ($p=0.008$, 2-tailed Fisher exact probability test).

Discussion

The COVID-related fractionation recommendations issued in March 2020 resulted in a significant change in PRT fractionation in this single-institution study. In contrast, the number of new patients who started PRT each business day, re-irradiation utilization, and the number of patients who received

PRT during the final 30 days of life remained stable. Overall, 9% of all patients who received PRT did so during the final 30 days of life in the first 6 months of 2020. In our first analysis (2007-2009), an identical rate of 9% was reported (7). A recent study from Australia found that deaths within 14 and 30 days of treatment with radiotherapy were 3.8 and 8.0%, respectively (11). Wu *et al.* analyzed 518 patients treated with external beam radiotherapy to a site of metastatic disease between 2012 and 2016 (12). Median time from radiotherapy to death was 74 days. One hundred and twenty-five patients (24%) died within 30 days of irradiation. A systematic review by Park *et al.* found PRT utilization rates during the last month of life in the range of 5-10% among patients who died of cancer, and in 9-15% of patients who received PRT (13). The most commonly used regimen was 30 Gy in 10 fractions (36-90%). Single fraction RT utilization ranged from 0% to 59%. ECOG PS 3-4 was significantly associated with patients receiving RT in the last 30 days of life and a shorter survival. In line with our current results, previous experience (14) also suggested that PRT utilization during the final 30 days of life has remained relatively stable over time, despite the publication of predictive models that aimed at the identification of patients with a very short survival (15, 16).

It would be interesting to compare our results with those obtained in other regions of the world, especially regions where the pandemic has had a greater impact on the healthcare system and death rates (17, 18). Our healthcare region (Nordland county) with 243,000 inhabitants (some served by other hospitals) has seen a relatively low number of people with COVID-19 infections (110 cases until August 31st, no reported death due to the infection, sufficient intensive care resources to handle all hospitalized patients). Consequently, oncology care has largely continued as planned (under certain precautions such as procedures for testing and quarantine). Other regions might have seen lower rates of PRT during the final 30 days of life than under pre-COVID operations, if patient selection and prioritization was changed. However, higher rates might also occur if patients who otherwise would have survived have died from COVID-19. It will also be interesting to learn whether the observed change in PRT fractionation simply reflects a desirable development (19-21), accelerated by the pandemic, or if some patients experience harm due to undertreatment.

Conflicts of Interest

The Authors declare that they have no conflicts of interest in relation to this study.

Authors' Contributions

CN, BM and RY collected and analyzed the patient data. CN and EH drafted the manuscript. All Authors read and approved the final manuscript.

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