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Basic Original Report

Effect of Education and Standardization of Cardiac Dose Constraints on Heart Dose in Patients With Lung Cancer Receiving Definitive Radiation Therapy Across a Statewide Consortium

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Abstract

Purpose: Cardiac radiation exposure is associated with an increased rate of adverse cardiac events in patients receiving radiation therapy for locally advanced non-small cell lung carcinoma (NSCLC). Previous analysis of practice patterns within the Michigan Radiation Oncology Quality Consortium (MROQC) revealed 1 in 4 patients received a mean heart dose >20 Gy and significant heterogeneity existed among treatment centers in using cardiac dose constraints. The purpose of this study is to analyze the effect of education and initiation of standardized cardiac dose constraints on heart dose across a statewide consortium.

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The authors are not authorized to share MROQC data. The data are individually owned by the member institutions of MROQC.

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Methods and Materials: From 2012 to 2020, 1681 patients from 27 academic and community centers who received radiation therapy for locally advanced NSCLC were included in this analysis. Dosimetric endpoints including mean heart dose (MHD), mean lung dose, and mean esophagus dose were calculated using data from dose-volume histograms. These dose metrics were grouped by year of treatment initiation for all patients. Education regarding data for cardiac dose constraints first occurred in small lung cancer working group meetings and then consortium-wide starting in 2016. In 2018, a quality metric requiring mean heart dose <20 Gy while maintaining dose coverage (D95) to the target was implemented. Dose metrics were compared before (2012-2016) versus after (2017-2020) initiation of interventions targeting cardiac constraints. Statistical analysis was performed using the Wilcoxon rank sum test.

Results: After education and implementation of the heart dose performance metric, mean MHD declined from an average of 12.2 Gy preintervention to 10.4 Gy postintervention ($P < .0001$), and the percentage of patients receiving MHD >20 Gy was reduced from 21.1% to 10.3% ($P < .0001$). Mean lung dose and mean esophagus dose did not increase, and target coverage remained unchanged.

Conclusions: Education and implementation of a standardized cardiac dose quality measure across a statewide consortium was associated with a reduction of mean heart dose in patients receiving radiation therapy for locally advanced NSCLC. These dose reductions were achieved without sacrificing target coverage, increasing mean lung dose, or increasing mean esophagus dose. Analysis of the clinical ramifications of the reduction in cardiac doses is ongoing.

Introduction

Radiation therapy remains an integral component of the treatment of locally advanced non-small cell lung carcinoma (NSCLC). Recent evidence indicates that mean heart dose (MHD) is independently associated with an increase in the rate of adverse cardiac events in this population, with increased risk of grade ≥ 3 cardiac events within 24 months after therapy.[1] Subsequent analysis of practice patterns in a combination of academic and community settings revealed substantial heterogeneity in cardiac dose constraints.[2] In response to this, monthly working groups were formed within the Michigan Radiation Oncology Quality Consortium (MROQC) with the goal of educating providers about the importance of minimizing cardiac radiation dose, and a standardized cardiac dose constraint was implemented. The purpose of this study was to determine whether adoption of the heart dose education initiative and initiation of a standardized cardiac dose constraint are associated with improved mean heart dose, and to assess the effect of this constraint on target coverage and dose to other organs at risk (OARs).

Methods and Materials

In the state of Michigan, 1681 patients from 27 academic and community centers who received definitive-intent radiation therapy either alone or with concurrent chemotherapy for locally advanced NSCLC between 2012 and 2020 were included in this analysis. Dosimetric endpoints were calculated using data from dose-volume histograms. These dose metrics were grouped by year of treatment initiation for all patients.

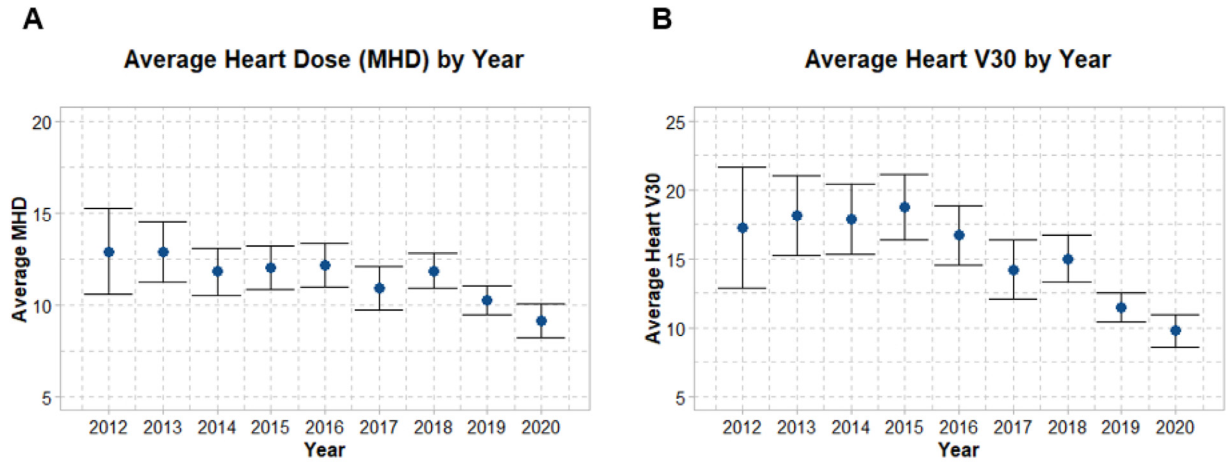
Education regarding data for cardiac dose constraints first occurred in lung cancer working group meetings designed to evaluate lung cancer specific quality measures with access to treatment Digital Imaging and Communications in Medicine to evaluate tumor and normal tissue contours. This was followed by a discussion at the annual consortium-wide meeting in 2016 highlighting the data supporting the importance of heart dose constraints. A representative from each clinical site is required to attend this consortium-wide meeting and is tasked with relaying the information discussed back to their respective clinics. In 2018, a quality metric requiring mean heart dose <20 Gy while maintaining dose coverage (D95) to the target was implemented. Planning target volumes (PTVs) were also calculated from each dose-volume histogram, and dose coverage was calculated as minimum dose to 95% PTV (D95%[Gy]).

Dose metrics were compared before (2012-2016) and after (2017-2019) initiation of interventions targeting cardiac constraints. Continuous variables including MHD were compared between periods using the Wilcoxon rank sum test, a nonparametric analog to the 2-sample t test. Binary variables such as the indicator for MHD >20 Gy were compared between periods using χ^2 tests for 2 proportions. Statistical analysis was performed using SAS V, and statistical significance was defined as 2-sided $P < .05$.

Results

Cardiac dose

MHD was calculated for each patient and averaged for all patients treated in a given year to derive average MHD. Average MHD and average heart V30 per year are represented in Figure 1. For 4 years before initiation of the MROQC education initiative (2012-2016), the average MHD was 12.2 Gy. After targeted education and initiation of a standardized cardiac dose constraint (2017-2020), average MHD in this cohort of patients fell to 10.4 Gy ($P < .0001$). Other common cardiac dosimetric parameters improved as well, with average heart V30[%] improving



C

	2012-2016	2017-2020	P value
Average Mean Heart Dose (Gy)	12.2	10.4	<0.0001
Average Heart V30 (%)	17.8	12.5	<0.0001
Average Heart V5 (%)	47.7	47.2	0.78
Percent of Patients with MHD > 20 Gy	21.1%	10.3%	<0.0001

Fig. 1 **(A)** Annual average mean heart dose (MHD) and **(B)** heart V30 for patients being treated within the statewide consortium from 2012 to 2020. **(C)** Comparison of average MHD, heart V30, heart V5, and percent of patients with MHD >20 Gy for patients treated before (2012-2016) and after (2017-2020) heart constraint initiative.

from 17.8% for the period 2012 to 2016 to 12.5% from 2017 to 2020 ($P < .0001$), and the percentage of patients receiving MHD >20 Gy improving from 21.1% to 10.3% ($P < .0001$). Average heart V5[%] remained unchanged at 47.7% from 2012 to 2016 and 47.2% from 2017 to 2020 ($P = .78$).

Target coverage

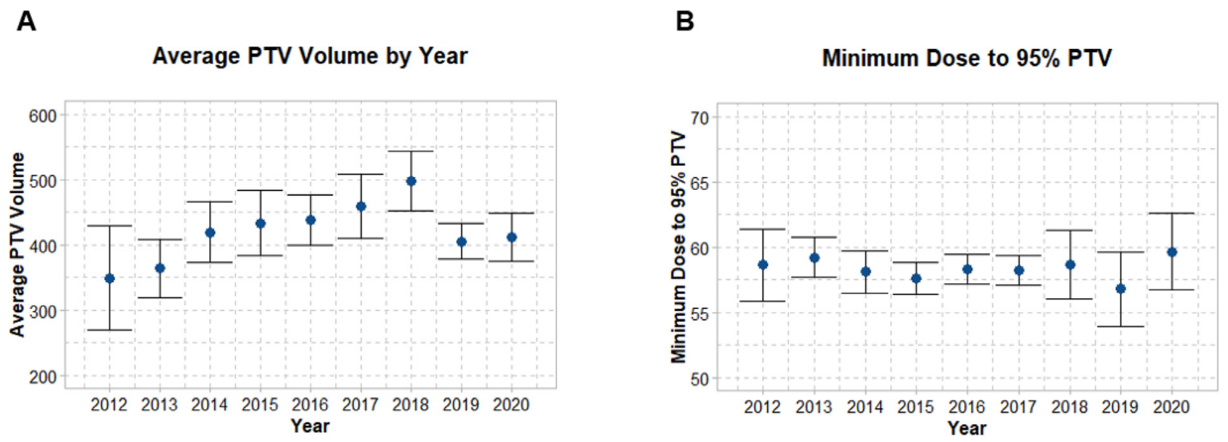
Trends involving the average volume of PTV and PTV coverage were analyzed (Fig. 2). Average PTV volume did not change significantly over time, with PTV averaging 414 cc from 2012 to 2016 and 441 cc from 2017 to 2020 ($P = .10$). PTV coverage was assessed by calculating minimum dose to 95% PTV for each case, then averaging by year as previously discussed. From 2012 to 2016, the average minimum dose to 95% PTV was 58.2 Gy, which remained unchanged at 58.2 Gy for patients treated 2017 to 2020 ($P = .99$).

Exposure of OARs

Established dosimetric constraints for other thoracic OARs were analyzed, including mean lung dose (MLD), lung V20[%], average esophageal dose, and esophagus $D2_{cc}$ [Gy] (Fig. 3). For patients treated 2012 to 2016, average MLD and lung V20[%] were 14.7 Gy and 24.9%, respectively, compared with 14.3 Gy and 24.6%, respectively, for patients treated 2017 to 2020 ($P = .08$ for MLD, $P = .74$ for lung V20[%]). Average lung V5[%] increased slightly from 52.3% from 2012 to 2016 to 56% from 2017 to 2020. In the 2012 to 2016 cohort, 94.1% of patients met the lung V20[%] constraint of 35%, compared with 91.8% of patients treated from 2017 to 2020 ($P = .11$). The average esophagus dose for patients treated 2012 to 2016 was 22.1 Gy, compared with 20 Gy for those treated 2017 to 2020 ($P < .0001$). Point dose to the esophagus, as measured by D2cc [Gy] did not significantly differ, averaging 52.2 Gy in those treated 2012 to 2016 compared with 52.4 Gy in those treated 2017 to 2020 ($P = .71$).

Treatment modality

The proportion of treatment plans using intensity modulated radiation therapy (IMRT) was analyzed (Fig. 4). The rate of IMRT use increased over time, from 61.4% in the 2012 to 2016 cohort to 84.8% in the 2017 to 2020 cohort ($P < .0001$). MHD in the 2012 to 2016 and 2017 to 2020 cohorts were analyzed adjusting for treatment modality. Among 3-dimensional (3D) conformal treatment plans, MHD decreased from 12.2 Gy in the



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	2012-2016	2017-2020	P value
Average PTV Volume (cc)	414	441	0.10
Minimum Dose to 95% PTV (Gy)	58.2	58.2	0.99

Fig. 2 **(A)** Annual average planning target volume (PTV) and **(B)** minimum dose to 95% PTV for patients being treated within the statewide consortium from 2012 to 2020. **(C)** Comparison of average PTV and minimum dose to 95% PTV for patients treated before (2012-2016) and after (2017-2020) heart constraint initiative **(C)**.

pre-2017 cohort to 9 Gy in the 2017 to 2020 cohort (*P* = .003). Similarly, among IMRT treatment plans, MHD decreased from 12.1 Gy in the pre-2017 cohort to 10.6 Gy in the 2017 to 2020 cohort (*P* = .002)

Discussion

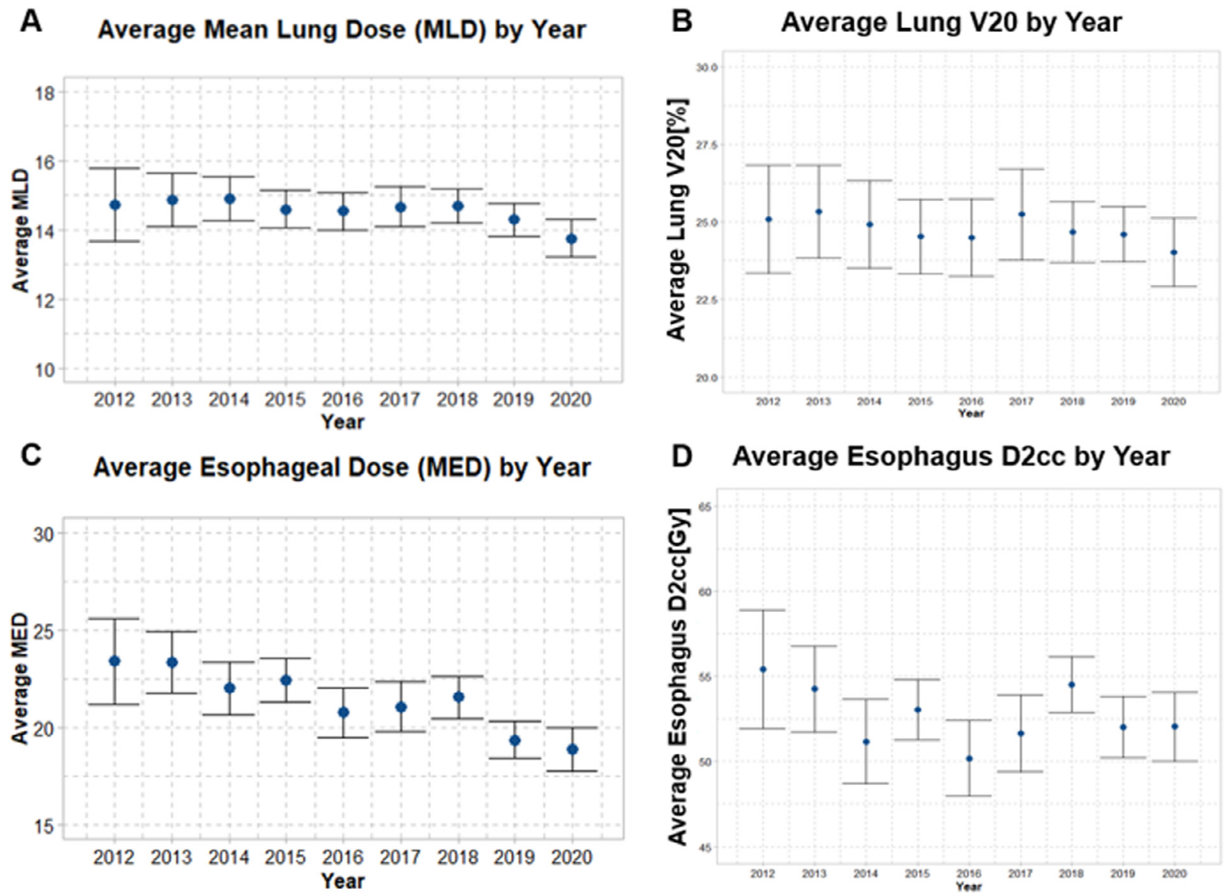
In this analysis of patients treated across a statewide consortium, MHD, heart V30 Gy, and the proportion of patients receiving >20 Gy MHD all decreased in the years after directed education and standardized heart dose constraint implementation. This was achieved without sacrificing target coverage, with the average minimum dose to 95% PTV being 58.2 Gy both before and after constraint standardization. Average mean lung dose, lung V20, and esophageal D2cc were unchanged, with modest improvement in mean esophageal dose. The proportion of patients meeting lung constraints did not significantly change, though a slight increase in average lung V5 was observed.

The increasing availability of highly conformal treatment techniques is likely to influence the ability to meet both target and OAR dosimetric priorities during treatment planning. Accordingly, analysis of IMRT utilization revealed an increase from 61.4% to 84.8% in the 2012 to 2016 and 2017 to 2020 cohorts, respectively. To account for this, average MHD for the preintervention and postintervention cohorts were assessed adjusting for treatment modality, revealing a decrease in average MHD postintervention in both patients treated with 3D and IMRT. The magnitude of average MHD decease was larger in the cohort treated with 3D conformal radiation therapy, possibly reflecting progressive limitation of this technique to targets distant from the heart.

Recent studies have demonstrated an association between radiation dose to the heart and future risk of major adverse cardiac events (MACE) in patients being treated with radiation therapy as part of definitive-intent treatment for locally advanced NSCLC[1,3] and a strong correlation between heart dose and overall survival in the setting of postoperative radiation.[4] This occurs despite the competing risk of cancer-associated mortality, and therefore bears consideration when performing radiation planning for NSCLC. The data herein suggest that, on average, careful consideration of cardiac dose constraints can facilitate meaningful dose reduction without sacrificing tumor coverage in this population.

The findings from this cohort analysis emphasize the importance of leveraging data from a large statewide consortium to standardize quality of treatment. Multiple recent studies from this consortium have contributed to quality improvement through the analysis of practice patterns,[2,5-7] racial disparities,[8] and patient-reported outcomes[9] of patients receiving radiation therapy in the state of Michigan for a wide variety of disease sites. These findings are propagated throughout the involved treatment centers and continually refine the quality of radiation treatment delivered to patients in the state of Michigan.

One limitation to this study is the unknown clinical effect of reducing mean heart dose in this cohort of patients. Although previous studies have indicated a correlation between MHD and 24-month risk of MACE,[1] ongoing analyses of this patient cohort are required to assess whether the reduction in MHD in this study



E

	2012-2016	2017-2020	P value
Mean Lung Dose (Gy)	14.7	14.3	0.08
Average Lung V20 (%)	24.9	24.6	0.74
Average Lung V5 (%)	52.3	56	<0.0001
% patients with lung V20 <35%	94.1	91.8	0.11
Average Esophagus Dose (Gy)	22.1	20	<0.0001
Average Esophagus D2cc (Gy)	52.2	52.4	0.71

Fig. 3 **(A)** Annual average mean lung dose, **(B)** average lung V20, **(C)** average esophageal dose, and **(D)** average esophagus dose for patients being treated within the statewide consortium from 2012 to 2020. **(E)** Comparison of annual average mean lung dose, average lung V20, average lung V5, percentage of patients receiving lung V20 <35%, average esophageal dose, and average esophagus D2cc for patients treated before (2012-2016) and after (2017-2020) heart constraint initiative.

population is associated with a corresponding reduction in cardiac events.

There also remains uncertainty within the field as to which dosimetric constraint best predicts future risk of MACE. Multiple studies have demonstrated the importance of mean heart dose in this setting,[1,3,10,11] but recent efforts to identify the cardiac substructures most at risk have identified left anterior descending artery (LAD) V15 Gy and left ventricle V15 Gy as independent predictors of MACE.[12] Further, subsequent analysis of the previously mentioned cohort revealed discordance between MHD and LAD V15 Gy,[13] indicating that MHD is not an adequate surrogate of dose to cardiac substructures. Further advances in standardization of radiographic cardiac substructure definition offer a common basis for comparison and should lead to better understanding of how radiation

A

Year	IMRT	3D	Unknown	P-value
2012-2016	61.4%	37.4%	1.2%	
2017-2020	84.8%	11.6%	3.6%	<0.0001

B

Year	Modality	N Obs	MHD	P-value
2012-2016	3D	289	12.2	
2017-2020	3D	105	9	0.003
2012-2016	IMRT	474	12.1	
2017-2020	IMRT	771	10.6	0.002

Fig. 4 **(A)** Utilization rates of 3-dimensional conformal radiation therapy (3D-CRT) and intensity modulated radiation therapy (IMRT) before (2012-2016) and after (2017-2020) targeted interventions aimed at reducing cardiac dose. **(B)** Mean heart dose (MHD) analyzed by treatment modality in each temporal cohort. *Abbreviation:* N Obs = number observed.

to individual substructures affects the risk of future cardiac events.[14]

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