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abstract

Receiver Operating Characteristic (ROC) Analysis to Identify Bone Marrow Dose Constraint Cut-Offs for Predicting Hematological Toxicities in High-Risk Endometrial Cancer

Raouia Ben Amor, Ines Mlayeh, Amal Riahi, Zeineb Naimi, Rihab Hadded, Ghada Bouguerra, Awatef Hamdoun, Lotfi Kochbati

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Receiver Operating Characteristic (ROC) Analysis to Identify Bone Marrow Dose Constraint Cut-Offs for Predicting Hematological Toxicities in High-Risk Endometrial Cancer

Author: Raouia Ben Amor^{1,2}, Ines Mlayeh^{1,2}, Amal Riahi^{1,2}, Zeineb Naimi^{1,2}, Rihab Hadded¹, Ghada Bouguerra¹, Awatef Hamdoun¹, Lotfi Kochbati^{1,2}

Affiliation: ¹Radiation Oncology Department, Abderrahmen Mami Hospital, Ariana, Tunisia

²Faculty of Medicine of Tunis, Tunis El Manar University, Tunis, Tunisia

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Introduction: The new standard of adjuvant treatment (chemotherapy and whole pelvis radiotherapy) in patients with high risk endometrial cancer (EC) was associated to more hematological toxicity. We aimed to identify the predictive bone marrow (BM) dose constraints values for hematological toxicities (HT) ≥ 2 .

Methodology: Patients with high risk EC treated with adjuvant chemotherapy and VMAT chemoradiation were analysed. Pelvic bones (PB) were delineated from the inferior border of the ischial tuberosities up to 25 mm superior to the PTV. We used the following consensual bone marrow (BM) doses constraints for plan acceptance : V10 Gy $\leq 90\%$, V20 Gy $\leq 75\%$ and V40 Gy $\leq 37\%$. HT were assessed according to the consensus Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Receiver operating characteristic (ROC) curve was

applied to evaluate the significance of V10 Gy, V20Gy, V30Gy, and V40 Gy on grade 2 or more HT. We displayed the precision, the sensitivity and the specificity. We also visualized the roc curve, and measured the optimal cut-off value and the area under the curve (AUC) then we used a logistic regression model for the z-test in combined detection comparison (P < 0.05 was considered as statistically significant).

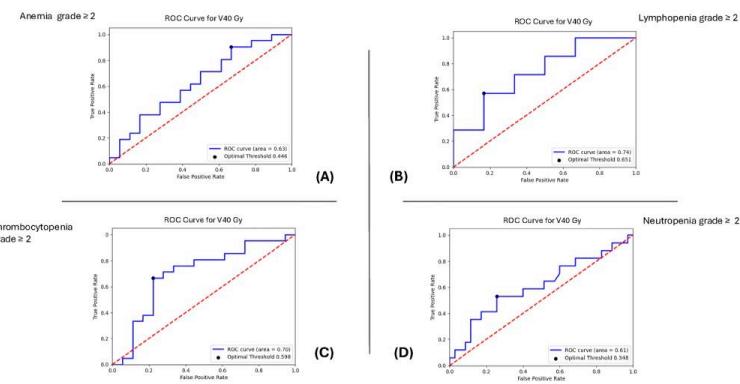
Results: Fifty patients were included. Hematological toxicity occurred in 40 patients. Anemia, lymphopenia, neutropenia and thrombocytopenia grades > 2 were observed in 14, 32, 17 and 13 patients, respectively. Selected cut-off values for V20Gy ($\geq 78.7\%$, p = 0.057), V30Gy ($(\geq 36.16\%, p = 0.011)$ and V40Gy ($(\geq 22.78\%, p=0.009)$ appear to have good discriminating power to predict lymphopenia grade ≥ 2 (Table 1).

BM dose constraint values predicting Anemia grade ≥ 2 were V20Gy ($\geq 83.1\%$, $p = 0.019$), V30Gy ($\geq 40.6\%$, $p = 0.03$) and V40Gy ($\geq 31.27\%$, $p=0.002$). (Table 1).

Cut-off values for V30Gy ($\geq 44.4\%$, $p = 0.036$), and V40Gy ($\geq 34.64\%$, $p = 0.025$) demonstrate strong discriminatory power in predicting grade 22 neutropenia (Table 1). Only the cut-off value for V40Gy ($\geq 20.35\%$, $p = 0.03$) demonstrates strong discriminative ability in predicting grade ≥ 2 thrombocytopenia (Table 1).

Conclusion: Adjuvant CT in high-risk EC patients is associated with increased HT of grade ≥ 2 . We suggest that the current V40Gy threshold of $<35\%$ should be lowered to 20-25%. Additionally, we suggest a new V30Gy constraint, recommending that it be kept below 40-45%.

Table 1: Comparison of detection of V10 Gy, V30Gy, V20Gy, and V40 Gy on grade \geq hematological toxicities.



Anemia Grade ≥ 2

mov10gy	83.684	0.696	0.444	0.857	0.437	0.012
mov20gy	83.1	0.596	0.444	0.857	0.54	0.019
mov30gy	40.62	0.609	0.667	0.771	0.571	0.03
mov40gy	31.27	0.652	0.444	0.786	0.63	0.002

Lymphopenia Grade ≥ 2

mov10gy	87.68	0.568	0.667	0.5	0.701	0.132
mov20gy	78.7	0.667	0.571	0.778	0.646	0.057
mov30gy	36.166	0.59	0.81	0.633	0.705	0.011
mov40gy	22.784	0.718	0.667	0.778	0.743	0.009

Neutropenia Grade ≥ 2

mov10gy	82.558	0.547	0.4	1	0.557	0.062
mov20gy	70.321	0.588	0.7	0.714	0.6	0.047
mov30gy	44.4	0.647	0.5	0.857	0.571	0.036
mov40gy	34.64	0.706	0.3	1	0.617	0.025

Thrombocytopenia Grade ≥ 2

mov10gy	83.684	0.442	1	0.667	0.581	0.289
mov20gy	88.66	0.492	0.429	1	0.438	0.114
mov30gy	40.912	0.669	0.857	0.667	0.514	0.088
mov40gy	20.35	0.846	0.857	0.822	0.701	0.03

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