Impact of Decision-Support on Clinicians' Assessment of Febrile Neutropenia Risk

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Background

Febrile neutropenia (FN) remains one of the most clinically significant adverse events associated with chemotherapy administration. The introduction of myeloid growth factors in 1989 changed the management of this complication and allowed for prevention through primary prophylaxis. ASCO, NCCN, and EORTC have all issued guidelines on the administration of myeloid growth factors that primarily rely on the myelosuppressive risk of the planned regimen to determine the need for primary prophylaxis.[1-3] Currently, the guidelines recommend that primary prophylaxis be used for any regimen with a risk of FN greater than 20%, although certain other factors may necessitate the need for prophylaxis in lower risk regimens. Several studies conducted during the 1990s reported good provider compliance with the guidelines for primary CSF prophylaxis. However, these studies were limited in that they only examined the compliance in prescribed drugs; most failed to determine whether providers who did not prescribe growth factor did so in accordance with the guidelines.[4-7] It is unclear from the recent published literature how guideline compliance has changed in the 21st century, but it is clear that use of CSFs is increasing dramatically.[8,9] Here, we investigate the role that an electronic clinical decision support system (CDSS) based on a validated predictive model can play in standardizing administration of myeloid growth factor for primary prophylaxis of FN.

Methods

Medical oncology clinicians (physicians, physician's assistants, nurse practitioners) were recruited from the Atlanta, GA and Research Triangle Park, NC areas, according to the primary cancer type they treated. After Institutional Review Board approval, a total of 39 clinicians were recruited, 22 of whom were medical oncologists, 2 were medical oncology fellows, 3 were physician assistants, and 12 were oncology nurse practitioners. Each clinician was presented with a series of eight simulated patient cases (in randomized order) relevant to the cancer type they primarily treat in practice. Each simulated patient case contained FN risk factor information for the patient, including demographics, baseline labs, medical history, planned regimen and other treatment information. Clinicians were asked to provide their estimation of the risk of febrile neutropenia as high, intermediate or low probability using their typical heuristic decision-making process. The patient's risk for FN as determined by a validated logistic regression model was then presented to the participant through the CDSS. Afterwards, the clinicians were again asked their assessment of the patient's risk. Kappa (κ) and Kendall's correlation coefficient (τ) were used to determine the concordance between the participants' assessments both before and after the CDSS intervention.

Table 1. Provider Type and Cases Reviewed by Cancer

Cancer Type	Number of Clinicians				Cases Reviewed
	MD	Fellow	PA	NP	
Breast	4	0	0	2	46 of 48
NSCLC	3	0	1	2	46 of 48
SCLC	4	1	1	2	64 of 64
Ovarian	3	0	1	1	38 of 40
Lymphoma	5	1	0	2	64 of 64
Colorectal	3	0	0	3	46 of 48

Table 2. Summary of Simulated Patient Case Data

Cancer Type	Case Number	Age	Prior Chemo	Baseline WBC	Abnormal Liver Function	Regimen	NCCN Regimen Risk	Model Risk
Breast	1	56	No	9.1	No	AC	Intermediate	High
	2	56	No	7.5	No	CT	*Low*	High
	3	66	No	4.5	No	CMF	Intermediate	High
	4	50	No	8.5	No	TCH	*Unknown*	Intermediate
	5	65	Yes	5.0	No	Capecitabine+H	*Low*	Intermediate
	6	65	Yes	9.0	No	Paclitaxel+H	Intermediate	Low
	7	75	No	10.1	No	Vinorelbine+H	*Low*	Low
	8	51	No	8.1	No	CMF	Intermediate	Low
Colorectal	1	76	Yes	4.0	Yes	Irinotecan+Cetuximab	*Low*	High
	2	62	No	9.0	No	Irinotecan (Weekly)	*Low*	High
	3	52	No	6.0	Yes	FolFoxIri	*Low*	High
	4	76	Yes	5.0	No	Roswell Park	*Low*	Intermediate
	5	56	No	9.0	No	Folfiri	*Low*	Intermediate
	6	69	No	6.8	Yes	CapeOx	*Low*	Low
	7	59	No	9.5	No	Irinotecan+Cetuximab	*Low*	Low
	8	55	No	4.0	No	FolFox 4	Intermediate	Low
Lymphoma	1	67	No	9.2	No	CHOP	Intermediate	High
	2	50	No	10.1	Yes	ABVD	Intermediate	High
	3	70	No	8.9	No	ABVD	Intermediate	High
	4	70	No	5.2	No	FCR	*Low*	Intermediate
	5	43	No	9.6	No	FCR	*Low*	Intermediate
	6	69	No	9.1	No	R-CVP	*Unknown*	Low
	7	56	No	9.1	No	FCR	*Low*	Low
	8	52	No	9.1	No	FR	*Low*	Low
Non-Small Cell Lung	1	73	Yes	7.4	No	Vinorelbine/Cisplatin	Intermediate	High
	2	59	Yes	6.1	No	Carboplatin/Paclitaxel	Intermediate	High
	3	58	Yes	7.4	Yes	Gemcitabine/Paclitaxel	*Low*	High
	4	70	Yes	7.5	No	Gemcitabine/Cisplatin	*Low*	Intermediate
	5	45	No	9.4	No	EP (80/80)	Intermediate	Intermediate
	6	51	Yes	8.8	No	Carboplatin/Paclitaxel	Intermediate	Low
	7	57	No	6.8	Yes	Docetaxel	Intermediate	Low
	8	51	No	8.1	No	Vinorelbine/Cisplatin	Intermediate	Low
Small Cell Lung	1	69	No	6.8	Yes	Carboplatin/Etoposide	Intermediate	High
	2	57	Yes	6.8	Yes	EP (80/80)	*Intermediate*	High
	3	45	No	10.0	No	Irinotecan/Cisplatin	*Low*	High
	4	55	No	9.0	No	EP (25/100)	*High*	Intermediate
	5	75	Yes	10.0	No	Topotecan	High	Intermediate
	6	35	No	7.0	No	Paclitaxel	*Intermediate*	Low
	7	41	Yes	8.0	Yes	Gemcitabine	*Low*	Low
	8	43	No	10.2	No	EP (25/100)	*High*	Low
Ovarian	1	66	Yes	4.7	Yes	Carboplatin/Paclitaxel	*Low*	High
	2	68	No	6.2	No	BEP	*Low*	High
	3	47	Yes	5.3	Yes	Gemcitabine	*Low*	High
	4	48	Yes	9.2	Yes	Doxorubicin liposomal	*Low*	Intermediate
	5	53	No	7.3	No	Cisplatin/Paclitaxel	*Low*	Intermediate
	6	67	Yes	8.3	No	Doxorubicin liposomal	*Low*	Low
	7	64	No	9.1	No	Carboplatin/Paclitaxel	*Low*	Low
	8	68	Yes	10.0	Yes	Gemcitabine/Cisplatin	*Low*	Low

Table 3. Pre-Intervention Risk Assessment

Cancer Type		Case 1 (High Risk)	Case 2 (High Risk)	Case 3 (High Risk)	Case 4 (Inter. Risk)	Case 5 (Inter. Risk)	Case 6 (Low Risk)	Case 7 (Low Risk)	Case 8 (Low Risk)	κ	KCC
Breast	Low	1	1	1	0	5	4	2	2	0.089	0.520
	Intermediate	2	2	4	4	1	2	4	3		
	High	3	3	0	1	0	0	0	1		
	Concordance	50.0%	50.0%	0.0%	80.0%	16.7%	66.7%	33.3%	33.3%		
Ovarian	Low	0	2	3	3	0	4	3	1	0.097	0.606
	Intermediate	3	1	1	0	2	1	2	2		
	High	2	1	1	1	3	0	0	2		
	Concordance	40.0%	25.0%	20.0%	0.0%	40.0%	80.0%	60.0%	20.0%		
Colorectal	Low	0	3	3	4	1	0	0	3	0.173	0.408
	Intermediate	4	0	3	0	4	4	3	2		
	High	2	3	0	1	0	2	3	1		
	Concordance	33.3%	50.0%	0.0%	0.0%	80.0%	0.0%	0.0%	50.0%		
Lymphoma	Low	0	0	0	1	0	4	1	4	0.155	0.446
	Intermediate	2	5	2	4	5	3	7	4		
	High	6	3	6	3	3	1	0	0		
	Concordance	75.0%	37.5%	75.0%	50.0%	62.5%	50.0%	12.5%	50.0%		
NSCLC	Low	1	0	3	1	1	0	2	3	0.002	0.191
	Intermediate	3	4	1	2	2	5	4	3		
	High	1	2	2	2	3	1	0	0		
	Concordance	20.0%	33.3%	33.3%	40.0%	33.3%	0.0%	33.3%	50.0%		
SCLC	Low	0	1	0	2	3	5	5	2	0.111	0.384
	Intermediate	3	3	3	3	0	3	3	5		
	High	5	4	5	3	5	0	0	1		
	Concordance	62.5%	50.0%	62.5%	37.5%	0.0%	62.5%	62.5%	25.0%		
ALL CANCERS										**0.105**	**0.426**

Table 4. Post-Intervention Risk Assessment

Cancer Type		Case 1 (High Risk)	Case 2 (High Risk)	Case 3 (High Risk)	Case 4 (Inter. Risk)	Case 5 (Inter. Risk)	Case 6 (Low Risk)	Case 7 (Low Risk)	Case 8 (Low Risk)	κ	KCC
Breast	Low	0	0	0	0	1	6	5	5	0.699	0.877
	Intermediate	0	0	1	5	5	0	1	1		
	High	6	6	4	0	0	0	0	0		
	Concordance	100.0%	100.0%	80.0%	100.0%	83.3%	100.0%	83.3%	83.3%		
Ovarian	Low	0	0	0	0	1	5	5	5	0.903	0.975
	Intermediate	1	0	1	4	4	0	0	0		
	High	4	4	4	0	0	0	0	0		
	Concordance	80.0%	100.0%	80.0%	100.0%	80.0%	100.0%	100.0%	100.0%		
Colorectal	Low	0	0	0	0	0	6	6	4	0.850	0.956
	Intermediate	0	0	1	5	5	0	0	2		
	High	6	6	5	0	0	0	0	0		
	Concordance	100.0%	100.0%	83.3%	100.0%	100.0%	100.0%	100.0%	66.7%		
Lymphoma	Low	0	0	0	0	0	8	8	8	1.000	1.000
	Intermediate	0	0	0	8	8	0	0	0		
	High	8	8	8	0	0	0	0	0		
	Concordance	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%		
NSCLC	Low	0	0	0	0	0	5	5	5	0.924	0.979
	Intermediate	0	0	1	5	5	1	0	1		
	High	5	6	5	0	1	0	1	0		
	Concordance	100.0%	100.0%	83.3%	100.0%	83.3%	83.3%	83.3%	83.3%		
SCLC	Low	0	0	0	0	0	8	8	8	0.953	0.985
	Intermediate	0	1	0	8	8	0	0	0		
	High	8	7	8	0	0	0	0	0		
	Concordance	100.0%	87.5%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%		
ALL CANCERS										0.888	0.962

Results

304 of the 312 (97.4%) case reviews were completed with 8 participants failing to complete the final case review in the time allotted. These data, along with the distribution of providers by cancer type, are presented in Table 1. Table 2 presents the abstract of the case data reviewed by the participant as well as the corresponding regimen risk and CDSS risk score. The case assessments, interobserver agreement as expressed by kappa, and Kendall's coefficient of concordance are shown before and after the participant was exposed to the CDSS risk score in Tables 3 and 4, respectively. Interobserver agreement as expressed by kappa improved significantly across all cancer types and the overall inter-observer agreement improved from 0.105 (slight agreement) to 0.888 (almost perfect agreement) after use of the CDSS ($p < 0.001$). Similarly, the strength of relationship as expressed by the overall Kendall's coefficient of concordance also significantly improved following use of the CDSS from 0.426 to 0.962 ($p < 0.001$). The significant improvements in interobserver agreement and Kendall's coefficient of concordance between pre and post-intervention risk assessments persisted when only the subgroup of physicians was analyzed. The clinicians changed their assessment of risk in 174 of the 304 (57.2%) cases after using the CDSS.

Discussion

Use of the clinical decision support system dramatically influenced clinicians' assessment of FN risk and resulted in a significant increase in the concordance between the risk assessments of medical oncology clinicians. This effect was observed across several cancer types.

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CONFLICT OF INTEREST DISCLOSURE—INVESTIGATORS WEBB, HEAD, LEITHE, WU AND SINGH ARE EMPLOYEES AND EQUITY HOLDERS IN THE COMPANY THAT MANUFACTURES THE CDSS SYSTEM USED IN THIS STUDY. INVESTIGATOR LYMAN CONSULTS, HOLDS EQUITY AND SITS ON AN ADVISORY BOARD FOR THE COMPANY THAT MANUFACTURES THE CDSS SYSTEM USED IN THIS STUDY.