original report

Assessing Concordance With Watson for Oncology, a Cognitive Computing Decision Support System for Colon Cancer Treatment in Korea

abstract

Purpose IBM Watson for Oncology (WFO) is a clinical decision-support computing system that provides oncologists with evidence-based treatment recommendations for a variety of cancer diagnoses. The evidence-based supported treatment recommendations are presented in three categories: Recommended, representing the Memorial Sloan Kettering Cancer Center (MSKCC) preferred approach; For Consideration, evidence-based alternative treatments; and Not Recommended, alternative therapies that may be unacceptable. We examined the absolute concordance of treatment options with that of the recommendations of a multidisciplinary team of oncologists from Gachon University, Gil Medical Centre, Incheon, South Korea.

Methods We enrolled 656 patients with stage II, III, and IV colon cancer between 2009 and 2016. Cases were processed using WFO and, using retrospective clinical data, outputs were compared with the actual treatment the patient received. Absolute concordance was defined as an alignment of recommendation in the Recommended MSKCC preferred-approach category. Treatment recommendations that were represented in the For Consideration category were not the focus of this study.

Results The absolute concordance between the WFO-derived MSKCC preferred approach and Gil Medical Centre treatment recommendations was 48.9%. The percentage of cases found to be acceptable was 65.8% (432 of 656) and the stage-specific concordance rate was 32.5% for patients with stage II disease who had risk factors and 58.8% for patients with stage III disease. Patients 70 years of age and older had a concordance rate of only 20.2%, whereas younger patients had a concordance rate of 63.8% ($P = .0001$).

Conclusion The main reasons attributed to the low concordance rate were age, reimbursement plan, omitting chemotherapy after liver resection, and not recommending biologic agents (ie, cetuximab and bevacizumab).

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INTRODUCTION

Oncologists are challenged to personalize care with rapidly changing scientific evidence, treatment guidelines, and drug availability. Cognitive computing clinical decision support systems (CDSS) have the potential to help address this challenge. In this study, the absolute concordance between treatment recommendations made by the CDSS Watson for Oncology (WFO; IBM, Armonk, NY) and a multidisciplinary cancer care team (MDT) for colorectal cancer is presented.

WFO is designed to provide optimal and alternative suggestions for treatment to practicing oncologists. It is also designed to provide links to the literature for additional evidence for the suggested treatment recommendations, which physicians can use to make informed decisions about their patients' care. The cloud-based system also provides evidentiary support for its recommendations by analyzing > 300 medical journals and > 200 textbooks, which comprise > 15 million pages of medical text. The corpus of WFO includes many documents, from the Healthline Medical Taxonomy to such varied sources as ASCO, Elsevier, National Comprehensive Cancer Network, and PubMed. The need for WFO in cancer care today stems from the rate of

growth in oncology-specific knowledge. A simple PubMed search on oncology found 74,781 research papers published in medical journals in 2016 alone.[1] This amounts to > 200 new articles published daily, outpacing the ability of doctors to remain current.

In 2012, the incidence of cancers in Korea was the highest in Asia, at 308 cancer cases per 100,000 people.[2] To meet the volume demand and optimize quality of care, many Korean hospitals have created multidisciplinary cancer care teams (MDTs). There is increasing evidence that multidisciplinary care facilitates best practice by limiting numbers of adverse events, improving outcomes, and adding to overall employee and patient satisfaction.[3] However, ensuring that every patient undergoes MDT review places a significant burden on limited personnel resources.

Cognitive computing technology is novel; therefore, data on its use in oncology are lacking. Preliminary studies show high concordance rates between WFO recommendations and physician treatment plans. At Memorial Sloan Kettering Cancer Center, where WFO continues to be trained, an assessment of the accuracy of WFO's treatment plans in a training environment were found to be aligned with physician recommendations > 90% of the time in 103 patients with nonmetastatic breast cancer.[4] In a prospective concordance study in Thailand,[5] a total of 211 cases were assessed. The overall concordance rate was 83%: 89% for colorectal, 91% for lung, 76% for breast, and 78% for gastric cancer. In addition, retrospective study of data from 638 patients with breast cancer treated at Manipal Hospitals in Bangalore, India, showed 90% concordance between MDT recommendations and WFO.[6]

On December 5, 2016, Gachon University Gil Medical Center (GMC), Incheon, Republic of Korea, initiated WFO as a member of its MDT. From the founding of GMC in 1978 to the creation of the Cancer Center in 2011, GMC has had a legacy of caring and compassion. GMC has > 1,300 licensed beds and is currently ranked fifth in the nation in terms of capacity. GMC is a large medical center that cares for 50,000 cancer patients annually, an estimated 500 of whom have colorectal cancer. The purpose of this study was to evaluate, in a set of retrospective colorectal cancer cases, the absolute concordance between WFO preferred treatment recommendations suggested by Memorial Sloan Kettering Cancer Center experts and GMC oncologists.

METHODS

The study proposal was finalized and approved by the institutional review board before study initiation. This study used WFO, version 16.9. Categorical variables were analyzed with a two-sided Pearson χ^2 test, and P values < .05 were considered statistically significant.

A retrospective review at GMC identified 1,717 patients who underwent a colectomy for colon cancer between 2009 and 2016 (Fig 1). The available clinical attributes included pathology, age, sex, Eastern Cooperative Oncology Group performance status, weight, comorbid conditions, RAS mutation status, microsatellite instability status, and laboratory results. Colon cancer staging was based on the National Comprehensive Cancer Network guidelines.[7] In the WFO colon cancer cartridge, there are 85 possible patient attributes that could potentially be entered for a given case. The number of attributes needed for input to provide a recommendation changes depending on the complexity of the case. For simple cases, as few as seven attributes are needed to enter; however, a user is asked to confirm whether the patient has any relevant comorbid conditions or abnormal laboratory test values before viewing treatment recommendations; these can be six to 12 additional attributes. Once the attributes were input into the WFO system, WFO would provide treatment recommendations. When the GMC treatment decision was included in the Recommended category of the WFO treatment recommendation, then the pairwise comparison was considered concordant. However, if the GMC treatment decision was in the For Consideration or Not Recommended treatment options by WFO, then the comparison was considered discordant (Fig 2).

A single therapeutic decision, as expected, was determined by GMC physicians for each retrospective case. For each patient, a review committee at GMC considered the comparison of the WFO recommendation (WFO-Rx) and GMC treatment (GMC-Rx) decision. Then, for each patient, the committee made an assignment to one of the following categories: (A) WFO-Rx was not available at the site; (B) site treatment

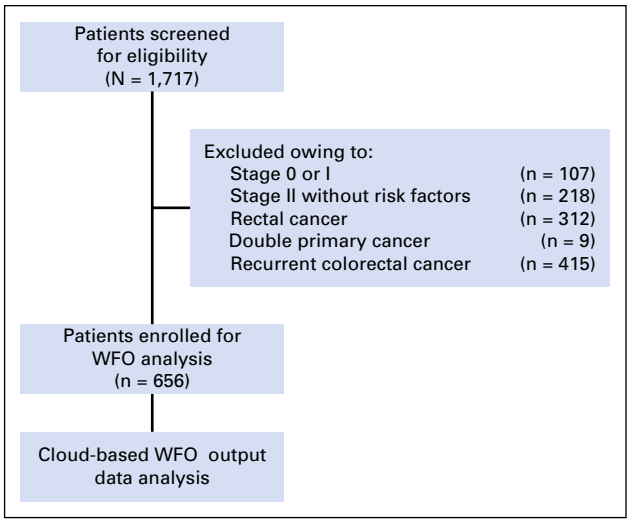

Fig 1. CONSORT diagram. WFO, Watson for Oncology.

decision was not known to WFO; (C) site treatment decision was listed as Recommended by WFO; (D) site treatment decision was listed as For Consideration by WFO; and (E) site treatment decision was listed as Not Recommended by WFO. Categories D and E contained subcategories, which are listed in Table 1.

Using "A" to refer to the number of patients assigned to category A, and "Da" to refer to the number of patients assigned to subcategory "a" in category D, the number of patients unsuitable for analysis was A + B = Q, where Q represents the number of patients for which there was no basis for comparing GMC-Rx and WFO-Rx. Thus, the number of cases available for detailed analysis was the total number of patients, Q.

RESULTS

Of the 1,717 accrued patients, 656 were eligible for WFO analysis (Fig 1). The reasons for patient exclusion were early-stage cancers (18.9%) and rectal cancer (18.2%). Of the 656 eligible patients, 73% had left-side colon tumors, 60.1% had Eastern Cooperative Oncology Group performance status 0, 2.1% had stage III cancer, and 75.5% of patients were reviewed by the MDT before starting chemotherapy (Table 2).

The percentage of patients in which the GMC-Rx was among the recommended therapies in WFO-Rx was 48.9% (Table 3). The percentage of patients in which GMC found WFO-Rx to be acceptable was 65.8% (432 of 656) and the stage-specific concordance rate was 32.5% for patients with stage II disease and with risk factors and 58.8% for patients with stage III disease.

The implementation of an MDT team and insurance reimbursement changes affected the

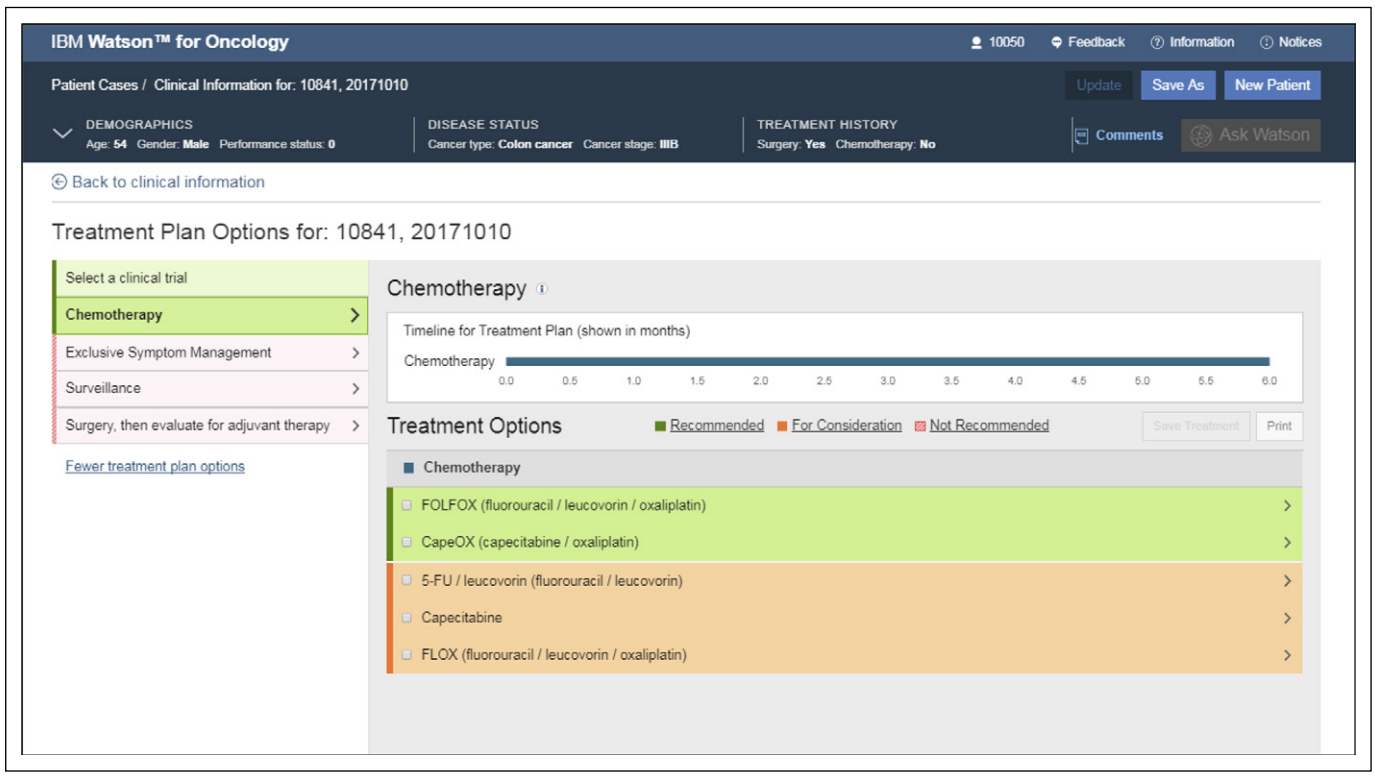

Fig 2. Watson for Oncology treatment plan option for stage III sigmoid colon cancer. Computer screen captured image courtesy of IBM Watson for Oncology.

Table 1. Patient Groupings Based on WFO Classifications

Grouping
WFO-Rx was unavailable at site.
Site-Rx was unknown to WFO (ie, not included on green, yellow, or red lists).
Site-Rx was among the green therapies in WFO-Rx.
Site-Rx was among the yellow therapies in WFO recommendation (with four subbuckets):
Site believes Site-Rx is preferred to WFO-Rx.
Site believes Site-Rx and WFO-Rx is preferred to Site-Rx.
Site believes WFO-Rx is preferred to Site-Rx.
Site believes WFO-Rx is unacceptable treatment.
Site-Rx was among the red therapies in the WFO recommendation (with four subbuckets).
Site believes Site-Rx is preferred to WFO-Rx.
Site believes Site-Rx and WFO-Rx are reasonable alternatives.
Site believes WFO-Rx is preferred to Site-Rx.
Site believes that WFO-Rx is unacceptable treatment.

Abbreviations: Site-Rx, site recommendation; WFO, Watson for Oncology; WFO-Rx, Watson for Oncology recommendation.

Table 2. Patient Characteristics (n = 656)

Characteristic	No.	%
Age, years, median (range)	63 (25-89)	
Sex ratio, female:male	390:266	
Body weight, mean kg	60.9	
ECOG performance status		
0	394	60.1
1	237	36.1
2	25	3.8
Cancer stage		
II with risk factors	169	25.8
III	342	52.1
IV	145	22.1
Right colon	176	26.8
Left colon	480	73.2
Year first treated		
2009	76	11.6
2010	85	12.9
2011	75	11.4
2012	44	6.8
2013	69	10.5
2014	101	15.4
2015	105	16.0
2016	101	15.4
Before MDT (2009-2010)	161	24.5
After MDT (2011-)	495	75.5

Abbreviations: ECOG, Eastern Cooperative Oncology Group; MDT, multidisciplinary team.

absolute concordance. A total of 495 patients (75.5%) were treated after the implementation of MDT meetings in 2011, and the absolute concordance rate increased from 38.9% to 47.4%, though this was not statistically significant (P = .402). Additionally, after implementation of biologic agent reimbursement in 2013, concordance rates dropped from 64.2% to 20.3%, with statistical significance (P = .003), in patients undergoing palliative chemotherapy (Table 3).

Patients receiving the FOLFIRI regimen, which includes folinic acid (leucovorin), fluorouracil, and irinotecan (camptosar), had the highest concordance rate, at 94.4%. A total of 30 patients received either cetuximab or bevacizumab per GMC physician recommendation, which was not included in the Recommended category of WFO but was included in the For Consideration category (Table 4).

The proportion of cases in which GMC found WFO's advice to be unacceptable was 34.1%. Of note, 39 patients with curatively resected liver metastasis or localized peritoneal metastasis were recommended to undergo regular surveillance as opposed to chemotherapy. These patients were categorized for analytic purposes in the "rejected by site" subcategory.

Patients 70 years of age and older had a concordance rate of only 20.2%, whereas younger

Table 3. Assessing Concordance Rate: Absolute Agreement Between the Site-Treatment and Watson for Oncology Treatment Recommendations (n = 656)

Parameter	No. or Fraction	Concordance Rate, %	*P*
Absolute concordance rate	321	48.9	—
Stage-specific concordance rate			—
II with risk factors	55	32.5	
III	201	58.8	
IV	52	35.9	
Before MDT (2009-2010)	161	38.9	.402
After MDT (2011-)	363	47.4	
Before biologic agent reimbursement (2013)	43/67	64.2	.003
After biologic agent reimbursement (2013)	22/108	20.3	
ECOG performance status 0			
0	214/394	54.3	
1	99/263	37.6	
2	25/25	100.0	

Abbreviations: —, not available; ECOG, Eastern Cooperative Oncology Group; MDT, multidisciplinary team.

patients had a concordance rate of 63.8% ($P < .001$; Table 5).

DISCUSSION

Given the growing reliance on cognitive computing CDSS to support physician decision making, this study analyzed retrospective data to assess absolute concordance rates between GMC physician treatment plans and WFO. Key findings include an increase in the absolute concordance rate after the implementation of an MDT, a decrease in the absolute concordance rate after payer approval for biologic agent therapies, a low absolute concordance rate in elderly patient cases, and a high absolute concordance rate for patients treated with FOLFIRI.

Before the implementation of an MDT at GMC, the absolute concordance rate was 38.9%. However, with the start of MDT meetings, the concordance rate increased to 47.4%, and the general acceptance rate was 65.8%. These findings suggest that WFO may be useful in simulating the effect of an MDT in situations where an MDT is otherwise unavailable or impractical The use of WFO could then potentially reduce unexplained variation between providers and sites of care. There is increasing evidence that multidisciplinary care leads to the provision of best practice through the adoption of evidence-based guidelines, improved patient outcomes, and streamlined treatment pathways.[3,7-9]

Prior studies have assessed concordance before and after an MDT conference for a variety of cancers. A retrospective study of 1,516 patient cases discussed at a brain tumor multidisciplinary board reported that 91% of meeting recommendations were followed.[10] A smaller lung cancer MDT study reported a 72% concordance rate,[11] and an Australian study with 160 patients demonstrated that 95% of upper GI and colorectal MDT meeting recommendations were implemented.[12] GMC is conducting a study to assess how often WFO-Rx are followed and the reasons why.

Table 4. Assessment of Concordance Rate of Chemotherapeutic Regimen: Absolute Agreement Between Site Treatment and Watson for Oncology Treatment Recommendation

Treatment	Fraction	Concordance Rate, %
FOLFIRI	17/18	94.4
Capecitabine plus oxaliplatin	21/27	77.8
FU/leucovorin	23/31	74.2
FOLFOX	218/383	56.9
Capecitabine	21/68	30.9
FOLFOX + biologic agent*	0/13	0
FOLFIRI + biologic agent*	0/68	0
Capecitabine + biologic agent*	0/1	0
Tegafur/uracil	0/6	0
No chemotherapy	5/10	50.0

Abbreviations: FU, fluorouracil; FOLFIRI, folinic acid, fluorouracil, and irinotecan hydrochloride; FOLFOX, folinic acid, fluorouracil, and oxaliplatin.
*Biologic agent: cetuximab or bevacizumab.

Table 5. Age-Specific Concordance Rate

Age, years (total No.)	No.	Concordance Rate (%)	*P*
< 70 (n = 434)	277	63.8	< .001
≥ 70 (n = 222)	45	20.2	

Before 2013, there was no reimbursement for biologic agents in Korea; the high economic cost and financial strain for patients were why these agents rarely were prescribed. After the determination that there would be reimbursement of biologic agents in 2013, there was a dramatic shift toward use of systemic chemotherapy for stage IV colon cancer, which caused the absolute concordance rate to drop from 64.2% to 20.3% between WFO and GMC physicians. It is well documented that adding biologic agents to cancer treatment regimens increases survival [13,14]; however, in the Recommended category, WFO recommended combination chemotherapy without biologic agents. This was the main reason behind discordance in this subgroup. It is important to note that biologic agents were present in the For Consideration category of the WFO treatment options.

Patients 70 years of age and older were a subgroup in which discordance between GMC physicians and WFO was high. The finding was unexpected and warrants further exploration. According to Korean clinical practice guidelines for colon and rectal cancer, adjuvant chemotherapy for stage II high-risk and stage III colon cancer is recommended after surgery.[15] According to these guideline, there is no age limit for providing adjuvant chemotherapy for advanced colon cancer.

Undertreatment, as defined by the Asian practice guidelines, is well documented in older patients with cancer and has the potential to compromise survival.[12,16] There is strong evidence that older patients, especially those with breast cancer, have lower odds of receiving standard-of-care therapy and treatment that are consistent with international breast cancer treatment guidelines.[17,18] Potential reasons for undertreatment in the elderly population include limited life expectancy, pre-existing comorbid conditions, and concern about an increased frequency of adverse events during chemotherapy.[19,20] In addition, there may be a misconception among physicians that older patients have less-aggressive cancers.[21] In this age group, WFO generally recommends fluorouracil and leucovorin[18] rather than oxaliplatin-based FOLFOX or FLOX (folinic acid, fluorouracil, and oxaliplatin)[22-24] chemotherapy. In our study, among the 89 patients who received FOLFOX as adjuvant therapy, WFO did not recommend oxaliplatin-based therapy in the Recommended category, but it was present in the For Consideration category. Thus, following such recommendation, per the Asian cancer guidelines, may have contributed to undertreatment in this group. The main determinants of treatment options should be based on tumor characteristics and comorbid conditions, not age in and of itself. Furthermore, otherwise healthy older patients can and should be treated with the same standard adjuvant chemotherapy as the younger population. However, it is worthwhile to note that these patient groups are under-represented in clinical trials and there are not enough data to support the safety and efficacy of adding or not adding oxaliplatin.

During the analysis, it was observed that WFO recommended surveillance for patients with colon cancer and a solitary liver metastasis. Physician users were aware that these patients can be cured with resection of the metastatic lesion followed by chemotherapy.[25] This ultimately proved to be an error in the system, which has since been rectified in a subsequent WFO release version.

WFO provides good references and literature for clinicians, especially those who are medical students and residents, or those who are unfamiliar with the disease entity and are seeking options for chemotherapy. Visually, it provides a clear first-choice recommendation in green and other options for consideration are in yellow.

Applying cognitive computing in oncology is an important step forward with great potential to improve the quality of physician treatment decisions. In this study of 656 patients with colon cancer, the absolute concordance between WFO-Rx and GMC-Rx was 48.9%. Key factors that contributed to low concordance rates include age, insurance reimbursement, omitting chemotherapy after liver resection, and not recommending biologic agents (ie, cetuximab and bevacizumab). Although concordance data

provide information about how often WFO or other cognitive computing systems agree with physicians' treatment plans, they do not provide evidence of clinical benefit or utility. As new prospective data are gathered, a better understanding of the effect of WFO on clinical decisions and patient outcomes will emerge.

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