Assessment of the Use of Preoperative CT Scan Image for Predicting Lymph Nodes for Resection of Colorectal Cancer: A Retrospective Study

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Keywords
Preoperative CT scan · Lymph nodes · Predictive value · Diagnostic accuracy · Colorectal cancer

Abstract
Introduction: Colorectal cancer (CRC) is the most common cancer that accounts for nearly 10% of the cancers, with 1.36 million people worldwide. Nodal status (N-stage) evaluation was inferior between observers, which considered CT scanning a good N-stage. We hypothesized that CRC patients’ preoperative CT scan imaging predicts the nodal and metastatic stage. Methods: This noninterventional retrospective study was carried out using patients’ medical records, including medical history and results of diagnostic tests, and preoperative clinical and pathological stages. All direct identifiers have been removed from all patient data. This study included 96 patients who underwent resection curative surgery for CRC at the Tertiary Hospital, Sudan, between March 2009 and December 2020. Results: The median age was 69 years (47–74 years), and 49 (51.04%) were female. The tumor stage of the patients was 4, 11, 74, and 7 as T1, T2, T3, and T4, respectively. A total of 38 patients with a malignant spread in lymph nodes were observed, and the median lymph node count was 11 (range 4–52). Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value (PPV), negative predictive value (NPV), and accuracy calculated for the malignant lymph nodes were 75.56% (95% CI: 60.46–87.12%), 45.10% (95% CI: 31.13–59.66%), 1.38 (95% CI: 1.02–1.86), 0.54 (95% CI: 0.30–0.98), 54.84% (95% CI: 47.38–62.09%), 67.65% (95% CI: 53.53–79.15%), and 59.38% (95% CI: 48.87–69.29%), respectively. Conclusion: The preoperative CT scan images were used to predict lymph nodes with a diagnostic accuracy of 59.38% for N-stage in patients with CRC.
bowel habits, anemia, occult blood, and rectal bleeding [5–7]. CRC's pathology begins from the aberrant crypt, evolving into a neoplastic precursor lesion called polyp and exacerbated into advanced CRC [5–7]. During surgery of colorectal resection, to localize and ensure the colorectal tumor were used many techniques (colono-
scopic metallic clips, intraoperative ultrasound, preoperative CT colonography) recently [8–11]. There are many risk factors of CRC, published in many recent literatures, and some of them are obesity, lack of physical activity, tobacco and alcohol consumption, aging, and recurrent bowel inflammatory [1, 2].

The computed tomography (CT) scan is the imaging method used to detect polyps and CRC [12]. It is used for locoregional and distant staging accuracy and helps guide the treatment decision [12–14]. However, an MRI scan is used routinely to identify the locoregional stage of CRC [15]. Locoregional staging for CRC using CT scans is crit-
ical because neoadjuvant systemic therapy can downsize locally advanced tumors [12–15]. Recent studies indicate that the preoperative examination of patients with CRC using CT scanning is essential to diagnose the primary tumor and distant metastases [16]. However, the preoperative CT scan is theoretically applicable for the prediction of lymph node involvement. Besides that, the classification of tumor-node-metastasis TNM staging, histo-
logical subtyping, grading, perineural, venous invasion, and tumor-based markers is increasingly being recognized. Moreover, many pathologists and radiologists have commonly used the TNM classification for the staging of CRC [17–19].

Recent reports indicate that the accuracy of CT scans for preoperative CRC staging ranges from 48% to 77% [20–22]. However, many reports suggest limitations of CT staging such as failure to distinguish conclusive meta-
static nodes, nodes overlap with tumor and unreliability of the depth of tumor invasion via colonic wall. Notably, clinical studies indicate excellent outcomes for evaluating tumor invasion grade with poor sensitivity, specificity, and diagnostic odds ratios to evaluate nodal status (N-stage). In particular, nodal status (N-stage) evaluation was very poor between observers, which considered CT scanning reasonable N-stage [20–22].

We hypothesized that CRC patients’ preoperative CT scan imaging predicts the nodal and metastatic stage re-
lating to the accuracy, sensitivity, specificity, positive predict-
dictive value (PVV), and negative predictive value (NPV). The primary aim of our study was to assess the reliability of CT scan imaging predicting the histological N- and M-stage.

Materials and Methods

This non-interventional retrospective study was carried out using patients’ medical records, including medical history and results of diagnostic tests, and preoperative clinical and pathological stages. All direct identifiers have been removed from all patient data. This study included 96 patients who underwent resection curative surgery for CRC at the Tertiary Hospital, Sudan between March 2009 and December 2020.

Patients with rectal cancer, chemotherapy, neoadjuvant radio-
therapy, distant metastases, and not scanned preoperatively were excluded from this study. The radiologist received data only the endoscopic location of the primary tumor and no other information about the patients. The radiologist has reviewed all the preoperative CT scans independently and was filled out the case record form. Based on the radiological positive nodal status from the ear-
lier studies, the regional lymph nodes of >1 cm and clusters of ≥3 cm lymph nodes were scored as N+. In contrast, the nonappear-
ance of clustered or enlarged lymph nodes was scored as N0 [23–
25]. Moreover, the radiologist has recorded the information on the use of either oral or intravenous contrast. We ensured that all the participants were filled out their case recorded form and confirmed any disagreement with the radiologist prior to statistical analysis.

The lymph nodes were examined carefully with dissection of the specimen without any fat-clearing techniques and palpation, and findings for each variable were recorded on a standard pro-
forma. Based on the original Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria, lymph nodes were classified preoperatively. A metastatic tumor with one or more lymph nodes was considered as N+. Moreover, the significant variables such as the number of large lymph nodes, the total number of lymph nodes, and enhancing lymph nodes were also recorded. The distinction between subgroup analysis was performed and confirmed with the TNM classification system (tumor [T] stage, nodal [N] stage, and metastases [M]). The histology of the re-
sected colonic specimen was used as the standard. Patients with T1 or T2 tumors on CT scans were classified as good radiological cancer, and T3 or T4 tumors were classified as poor radiological cancer.

CT Scanning

The preoperative CT scanning was performed for all the participants using a CT scanner with slice thickness 5, 3, and 2 mm, pixel size 0.47, and reconstruction matrix 512. The CT scan image was taken with sufficient quality to analyze, and impaired images with motion or metal prostheses were repeated, and the repetition of the sequence was a part of the scanning protocol. Radiologists examined all CT scans on 3 mm axial sliced images, and the maximum short axis in the axial plane was measured.

Statistical Analysis

All the data were statistically analyzed using the SPSS 22.0 (SPSS Inc., Chicago, III, DE, USA). All the variables such as sensi-
tivity, specificity, accuracy, true positive (TP), false positive (FP), true negative (TN), false negative (FN), interobserver agreement, PVV, and NPV were calculated on all cases.
Results

Baseline Characteristics of the Study Population

The baseline characteristics of the patients are shown in Table 1. A total of 127 patients have undergone resection of CRC between March 2009 and December 2020 in our hospital. Out of these 127 patients, there were 96 patients included based on the inclusion criteria. The median age was 69 years (ranges 47–74 years), and 49 (51.04%) were female.

Based on the histological confirmation of the colonic section, the tumor stage of the patients was 2, 11, 74, and 7 as T1, T2, T3, and T4, respectively. Notably, a higher percentage of tumors (39.58%) were located in the sigmoid colon region, and a minor percentage of the tumors (8.33%) were found in the descending colon region. Similarly, the nodal stage of the patients was 53, 25, and 18 as N0, N1, and N2, respectively. Remarkably, a higher percentage of tumors without metastases stages (83.33%) were observed.

Lymph Nodes in Preoperative Imaging

A total of 38 patients with a malignant spread in lymph nodes were observed, and the median lymph node count was 11 (range 4–52).

CT Scan Accuracy for Lymph Node Metastasis

The predicted and actual abnormal and normal rates of the CT scan are shown in Table 2. The predicted and actual abnormal and normal rates of the CT scan were found as 34 TPs, 28 FPs, 23 TNs, and 11 FNs. Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, PPV, NPV, and accuracy calculated for the malignant lymph nodes were 75.56% (95% CI: 60.46–87.12%), 45.10% (95% CI: 31.13–59.66%), 1.38 (95% CI: 1.02–1.86), 0.54 (95% CI: 0.30–0.98), 54.84% (95% CI: 47.38–62.09%), 67.65% (95% CI: 53.53–79.15%), and 59.38% (95% CI: 48.87–69.29%), respectively.

Subgroup analysis of the predicted and actual abnormal and normal differences between the combined samples N1 + N0 and N2 + N0 disease is shown in Table 3. Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, PPV, NPV, and accuracy calculated for the distinction between N1-N0 disease were 72.97% (95% CI: 55.88–86.21%), 48.78% (95% CI: 32.88–64.87%), 1.42 (95% CI: 1.00–2.04), 0.55 (95% CI: 0.30–1.03), 47.44% (95% CI: 36.01–59.07%), 56.25% (95% CI: 47.35–64.76%), and 66.67% (95% CI: 51.94–78.73%), respectively. Similarly, for N2 versus N0 disease, we observed that sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, PPV, NPV, and accuracy of the subgroup analysis of the predicted and actual abnormal and normal differences between combined samples M1 + M0 were 75.68% (95% CI: 58.80–88.23%), 41.18% (95% CI: 24.65–59.30%), 1.29 (95% CI: 0.92–1.80), 0.59 (95% CI: 0.29–1.18), 58.33% (95% CI: 50.03–66.19%), 60.87% (95% CI: 43.68–75.73%), and 59.15% (95% CI: 46.84–70.68%), respectively.

Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, PPV, NPV, and accuracy of the subgroup analysis of the predicted and actual abnormal and normal differences between combined samples M1 + M0 were 75.68% (95% CI: 58.80–88.23%), 41.18% (95% CI: 24.65–59.30%), 1.29 (95% CI: 0.92–1.80), 0.59 (95% CI: 0.29–1.18), 58.33% (95% CI: 50.03–66.19%), 60.87% (95% CI: 43.68–75.73%), and 59.15% (95% CI: 46.84–70.68%), respectively.

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Dubai Med J 2022;5:171–176
DOI: 10.1159/000525390
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were 70.83% (95% CI: 55.94–83.05%), 35.42% (95% CI: 22.16–50.54%), 1.10 (95% CI: 0.83–1.45), 0.82 (95% CI: 0.46–1.48), 52.31% (95% CI: 45.39–59.14%), 54.84% (95% CI: 40.39–68.51%), and 53.12% (95% CI: 42.66–63.39%), respectively (Table 4).

### Discussion

Our findings demonstrated the use of preoperative CT scan images to predict lymph nodes with a diagnostic accuracy of 59.38% for N-stage in patients with CRC. Despite significant research with emerging technology, the reliability of preoperative CT scan imaging for predicting the histological N- and M-stage remains elusive. Consistent with earlier studies, our findings also failed to improve the accuracy and other variables [8, 15, 23, 25].

Voluminous reports indicate that preoperative CT scan supports histopathological confirmation in making treatment decisions and modifies clinical management in patients with CRC [26–28]. Moreover, a preoperative CT scan often relates to the diagnosis of metastases of the liver. We excluded patients with rectal cancer, chemotherapy, neoadjuvant radiotherapy, and distant metastases to investigate whether, contrary to conventional, preoperative CT staging could help predict outcomes. Little to few published data are available on the preoperative CT scan for predicted tumor stage with clinical outcomes. The presence of small-study effects [8] should also not be discounted. Although our analysis was performed over a period of 10 years, variability in the accuracy of our estimates might be observed as patient size increases. CT scans are also limited in their ability to distinguish lymph nodes that contain tumors.

The pathological TNM classic system of N-stage to CT staging was examined carefully with a standard proforma [17, 18]. The accuracy of N-stage prediction was 66.67% (N1 + N0) and (29) 59.15% (N2 + N0) with sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, PPV, and NPV of 72.97% versus 75.68%, 48.78% versus 41.18%, 1.42 versus 1.29, 0.55 versus 0.59, 47.44% versus 58.33%, and 56.25% versus 60.87%, respectively (Table 4).

| Table 3. Subgroup analysis of patients N1 + N0 and N2 + N0 |
|-----------------------------------------------------------|
|               | N1 + N0 |               | N2 + N0 |               |
|                | pN+ | pN− | pN+ | pN− |
| CT scan N+     | 27  | 21  | 28  | 20  |
| CT scan N−     | 10  | 20  | 9   | 14  |
| Sensitivity, % | 72.97 | 55.88–86.21 | 75.68 | 58.80–88.23 |
| Specificity, % | 48.78 | 32.88–64.87 | 41.18 | 24.65–59.30 |
| Positive likelihood ratio | 1.42 | 1.00–2.04 | 1.29 | 0.92–1.80 |
| Negative likelihood ratio | 0.55 | 0.30–1.03 | 0.59 | 0.29–1.18 |
| Positive predictive value, % | 47.44 | 36.01–59.07 | 58.33 | 50.03–66.19 |
| Negative predictive value, % | 56.25 | 47.35–64.76 | 60.87 | 43.68–75.73 |
| Accuracy, %    | 66.67 | 51.94–78.73 | 59.15 | 46.84–70.68 |

| Table 4. Subgroup analysis of patients M1 + M0 |
|------------------------------------------------|
|               | pN+ | pN− |
| CT scan N+     | 34  | 31  |
| CT scan N−     | 14  | 17  |
| Sensitivity, % | 70.83 | 55.94–83.05 |
| Specificity, % | 35.42 | 22.16–50.54 |
| Positive likelihood ratio | 1.10 | 0.83–1.45 |
| Negative likelihood ratio | 0.82 | 0.46–1.48 |
| Positive predictive value, % | 52.31 | 45.39–59.14 |
| Negative predictive value, % | 54.84 | 40.39–68.51 |
| Accuracy, %    | 53.12 | 42.66–63.39 |
blinded analyzed, and all the preoperative CT scans were examined. In particular, the preoperative CT scanning was performed with slice thicknesses 5, 3, and 2 mm. We found that subgroup analysis of N-stage with preoperative CT scan with slice thicknesses 3 and 2 mm had significant clinical outcomes than the slice thickness 5. Our findings indicate that emerging techniques with multislice and advanced CT scan images with multidimensional reconstruction may improve resolution and image quality to predict the N-staging.

Assessment of the lymph nodes using the preoperative CT scan image has several limitations and difficulties [8, 15, 22, 29, 30]. In particular, there are more inconsistent in the benchmarks for describing lymph nodes as metastatic in the preoperative CT scan image [8, 15, 22, 23, 29, 30]. Defining the radiological positive lymph nodes varies by size, morphology, clustered form, irregular borders, and combinations. Identification of benign with enlarged lymph nodes due to inflammation is challenging. In this context, there is rare literature on the relationship between the size of the lymph node and malignancy. Our findings provide evidence that the accuracy, specificity, sensitivities, and predictive value of preoperative CT scan images are poor, which could be the reason for the size of overlapping lymph nodes between benign and malignant. These findings were consistent with similar results relating to the MRI scan [29, 30, 32].

We observed a significant number of false-positive and false-negative lymph nodes, which could concern the clusters of three or more lymph nodes and the benign and metastasis: notably, bias in the radiological identification of positive lymph nodes and bias in describing or defining the lymph nodes. For instance, if a radiologist observed one or two small lymph nodes and superintended the third one with a more diminutive size. These findings might be that a significant number of preoperative CT scan images were N+, whereas these were probably not reported initially as N+. On the other hand, the patients may have large tumors with radiological positive lymph nodes and extended liver metastasis compared to patients with a small tumor or without distant metastasis.

**Statement of Ethics**

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Scientific and Research Ethics Committee of AAU-FRSMI-0034/19 on March 1, 2019. The confidentiality of the patient data was ensured. Owing to the retrospective nature of the study, the need for written informed consent was waived according to the Scientific and Research Ethics Committee and the policy of the Tertiary Hospital, Sudan.

**Conflict of Interest Statement**

The author has no conflicts of interest to declare.

**Funding Sources**

This research received no external funding.

**Author Contributions**

The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

**Data Availability Statement**

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author A.E.
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