Computer-Aided Detection of Colorectal Polyps at CT Colonography: Prospective Clinical Performance and Third-Party Reimbursement

OBJECTIVE. We assessed the initial clinical performance and third-party reimbursement rates of supplementary computer-aided detection (CAD) at CT colonography (CTC) for detecting colorectal polyps 6 mm or larger in routine clinical practice.

MATERIALS AND METHODS. We retrospectively assessed the prospective clinical performance of a U.S. Food and Drug Administration–approved CAD system in second-reader mode in 347 consecutive adults (mean age, 57.6 years; 205 women, 142 men) undergoing CTC evaluation over a 5-month period. The reference standard consisted of the prospective interpretation by experienced CTC radiologists combined with subsequent optical colonoscopy (OC), if performed. We also assessed third-party reimbursement for CAD for studies performed over an 18-month period.

RESULTS. In all, 69 patients (mean ± SD age, 59.0 ± 7.7 years; 32 men, 37 women) had 129 polyps ≥ 6 mm. Per-patient CAD sensitivity was 91.3% (63 of 69). Per-polyp CAD-alone sensitivity was 88.4% (114 of 129), including 88.3% (83 of 94) for 6- to 9-mm polyps and 88.6% (31 of 35) for polyps 10 mm or larger. On retrospective review, three additional polyps 6 mm or larger were seen at OC and marked by CAD but dismissed as CAD false-positives at CTC. The mean number of false-positive CAD marks was 4.4 ± 3.1 per series. Of 1225 CTC cases reviewed for reimbursement, 31.0% of the total charges for CAD interpretation had been recovered from a variety of third-party payers.

CONCLUSION. In our routine clinical practice, CAD showed good sensitivity for detecting colorectal polyps ≥ 6 mm or larger, with an acceptable number of false-positive marks. Importantly, CAD is already being reimbursed by some third-party payers in our clinical CTC practice.

Keywords: colonography, computer-aided detection, CT, polyps, screening

DOI:10.2214/AJR.16.17499

Received October 1, 2016; accepted after revision November 28, 2016.

D. H. Kim is a cofounder of VirtuoCTC and a consultant for Viaftronix and serves on the medical advisory board for Digital Artforms. M. G. Lubner receives research funding from GE Healthcare, Neuwave Medical, and Philips Healthcare. P. J. Pickhardt is a cofounder of VirtuoCTC and a shareholder in Cellectar Biosciences, Elucent, and SHINE.

Based on a presentation at the Radiological Society of North America 2016 annual meeting, Chicago, IL.

© American Roentgen Ray Society

AJR:208, June 2017

1All authors: Department of Radiology, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, MC 3252, Madison, WI 53792. Address correspondence to T. J. Ziemlewicz (tziemlewicz@uwhealth.org).
**Patient Population**

Asymptomatic adults undergoing routine screening CTC in a single health care system over a 5-month period formed the initial study population of 393 patients. CAD failed to build on at least one series in 41 patients. Patients had all marks identified by CAD recorded by the interpreting radiologist in a clinical database. Marks were not recorded for five patients for unknown reasons. A total of 347 patients were included in the final analysis (Fig. 1).

**CT Colonography Technique**

We employed a standard CTC technique described in detail elsewhere [1, 14–16]. Patients undergo a bowel preparation protocol beginning 1 day before CTC consisting of complete colonic catharsis and tagging of residual material. The cathartic cleansing agent was magnesium citrate; polyethylene glycol was substituted as needed in a small number of patients. Contrast material tagging of residual fluid and fecal material was achieved with 2.1% weight/volume barium and diatrizoate (Gastrografin, Bracco). During the CTC examination, colonic insufflation was achieved and maintained throughout image acquisition using automated continuous carbon dioxide delivered through a rectal catheter [17]. Patients were routinely scanned in both supine and prone positions with decubitus positioning as needed [18]. Images were acquired with 8- to 64-MDCT scanners using 1.25-mm collimation, a 1-mm reconstruction interval, 120 kVp, and tube current modulation (range, 30–300 mA).

CT interpretation was performed for both the supine and prone (as well as decubitus in 45 patients) positions on a V3D workstation (Viatronix) with a combined 2D read for evaluation of the pooled fluid and 3D read as the means of primary polyp detection. For cases in which more than two series were created, the two with greatest luminal distention were used for luminal, and therefore CAD, evaluation. Initially, a primary read was performed by one of six abdominal radiologists (2–10 years’ experience with CTC). At the completion of the primary read, CAD (Veralook version 1.0, iCAD) was applied in the second-reader mode. The CAD-identified marks (i.e., potential lesions) were carefully reviewed by the interpreting radiologist using 2D or 3D images (both). At the time of image analysis, the interpreting radiologist recorded the number of CAD marks in each position and whether they were thought to be true-positives or false-positives. To be considered a true-positive CAD result, at least a portion of the lesion had to be seen within the ROI of the 2D mark (Fig. 2). Findings from optical colonoscopy (OC), pathologic evaluation, or both, if done, were also incorporated into all applicable cases. A subset of the CAD recordings included a determination of a cause for each false-positive CAD recording.

**CAD of Colorectal Polyps at CTC**

**Reference Standard and the Computer-Aided Detection System**

In all cases, initial interpretation by the radiologist served as the reference standard. Of the 69 patients with positive CTC findings, 45 were also evaluated with subsequent OC and one underwent surgery after discovery of a colonic mass. All of the polyps measuring 6 mm or larger found at OC, regardless of CTC detection, were recorded; the corresponding CTC was reviewed for re-

---

**Fig. 2—**65-year-old man with 7-mm sessile polyp identified at screening CT colonography (CTC).
A, Three-dimensional colon map shows location of polyp in descending colon (red dot adjacent to blue arrow).
B, Three-dimensional endoluminal rendering showing computer-assisted detection (CAD) mark (blue) of polyp.
Yellow arrow and green line are function of software.
C, Prone transverse CTC image with yellow ROI around blue marked polyp (arrow); both markings are from CAD program.
D, Optical colonoscopy image of polyp before retrieval. Polyp was tubular adenoma at histopathology.
confirmation. The remaining 23 patients did not undergo optical colonoscopy either because their polyps were classified as CT Colonography Reporting and Data System category C2 and the patients elected 3-year CTC follow-up or because the patient had not yet undergone optical colonoscopy (two patients) [19, 20]. OC was attempted with no polyp identified in one patient with positive CTC findings. This case was reviewed in consensus by two additional radiologists who confirmed the presence of a polyp. This patient was scheduled to undergo a repeat OC [21].

With respect to the reference standard, CTC cases with at least one true-positive, one false-negative, or both types of CAD hits were regarded as positive for true polyps. The per-polyp and per-patient sensitivities of CAD polyp detection were calculated according to these stratifications.

Reimbursement Evaluation

In an expanded population of 1225 patients consecutively enrolled over an 18-month period, billing data were searched for Current Procedural Terminology code 76497 to identify cases in which CAD was used and a $30 charge applied. The volume, total charges, and balance of reimbursement from all private and public payers were recorded for this cohort.

Data and Statistical Analysis

Means, SDs, and sensitivities were calculated using Excel (version 2010, Microsoft).

Results

Computer-Aided Detection Evaluation

The study population consisted of 347 patients (205 women, 142 men) with a mean age of 57.6 years (range, 34–88 years). Of this population, 69 patients (19.9%) had 129 polyps 6 mm or larger identified (Table 1). The mean age of the 37 women and 32 men with positive CTC findings was 59.0 years (range, 39–83 years). Of the 129 colorectal polyps measuring at least 6 mm, 72.9% (94/129) were 6–9 mm, 11.6% (15/129) were ≥10 mm in diameter.

TABLE 1: Polyp Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total No.</th>
<th>Largest Polyp Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with a polyp</td>
<td>69</td>
<td>30</td>
</tr>
<tr>
<td>CTC-identified polyps</td>
<td>129</td>
<td>35</td>
</tr>
<tr>
<td>CTC-identified polyps detected by CAD</td>
<td>114</td>
<td>83</td>
</tr>
<tr>
<td>No. of patients undergoing OC</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td>CTC-identified polyps examined with OC</td>
<td>100</td>
<td>66</td>
</tr>
<tr>
<td>CTC-identified polyps confirmed at OC</td>
<td>89</td>
<td>60</td>
</tr>
<tr>
<td>Polyps found at OC that were not identified at CTC</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>CAD-identified polyps found at OC that were dismissed at CTC</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

Note—CTC = CT colonography, CAD = computer-assisted detection, OC = optical colonoscopy.

Overall per-polyp CAD sensitivity was 91.3% (63/69) and per-polyp CAD sensitivity was 88.4% (114 of 129), including 88.6% (83 of 94) for 6–9-mm polyps and 88.6% (31 of 35) for polyps 10 mm or larger. Of the 129 detected polyps, 45.0% (58/129) were detected by CAD on two views, and 55% (71/129) on a single view. Of the six additional polyps larger than 6 mm seen at OC but not prospectively identified at CTC, three had been detected by CAD in retrospect but were dismissed as false-positives by the reader (Fig. 3). The mean number of CAD marks was 8.3 ± 4.9 per study and 4.4 ± 3.1 per series (Table 2). There were 2911 false-positive CAD marks, 1026 of which had a cause recorded. Of these 1026 in 167 patients, stool (28.6%), folds (26.0%), and the ileocecal valve (17.3%) were the most frequent causes of a false-positive finding.

Reimbursement Evaluation

Out of the 1225 cases within an 18-month interval for reimbursement assessment, 31.0% of the total charges were recovered. Across all private payers covering CAD, charge recovery ranged from 18.0% to 72.8%.

Discussion

The role of CAD software in the daily performance of CTC is as a second-reader assistive software. Although previous studies have found CAD to be useful as a stand-alone software tool, to our knowledge this is the first report of the prospective use of the software in a clinical CTC practice. The sensitivity and false-positive rate of CAD in second-reader mode during routine CTC reading were acceptable and comparable with prior nonclinical experiences. In addition, several CAD-identified lesions were dismissed by the radiologist but subsequently identified at OC.

TABLE 2: Computer-Assisted Detection Data by Imaging Position

<table>
<thead>
<tr>
<th>Imaging Position</th>
<th>No. of Hits</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine</td>
<td>1344</td>
<td>4.0 ± 3.0</td>
</tr>
<tr>
<td>Prone</td>
<td>1536</td>
<td>4.8 ± 3.2</td>
</tr>
<tr>
<td>Decubitus</td>
<td>208</td>
<td>4.8 ± 2.8</td>
</tr>
<tr>
<td>All positions</td>
<td>3088</td>
<td>4.4 ± 3.1</td>
</tr>
</tbody>
</table>

TABLE 3: False-Negative Computer-Assisted Detection Description

<table>
<thead>
<tr>
<th>Description</th>
<th>No. of Polyps</th>
<th>Rectum</th>
<th>Sigmoid</th>
<th>Transverse</th>
<th>Ascending</th>
<th>Hyperplastic or Serrated Polyp</th>
<th>Tubular Adenoma</th>
<th>Tubulovillous Adenoma</th>
<th>Villous Adenoma</th>
<th>No OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flat polyp</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Between folds</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Adjacent larger polyp</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Unclear nature</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Note—OC = optical colonoscopy.
Beyond the clinical utility, for any software tool to undergo clinical adoption, monetary factors need to be considered. CTC and the addition of CAD to its interpretation have proven cost-effective [13, 22, 23]. However, some actual recovery from payers, even if only partial, is likely necessary for broad adoption. In the first study, to our knowledge, to evaluate this aspect of the technology, we found a reimbursement rate of 31.0% on charges from a variety of third-party payers for CAD added to routine CTC.

The sensitivity of CAD per patient and per polyp in this study of 91.3% and 88.4%, respectively, is excellent when compared with prior retrospective studies. For example, a 3046-patient cohort retrospectively evaluated with the same software used in this study had per-patient and per-polyp sensitivities of 93.8% and 90.1% for polyps 6 mm or larger and 96.5% and 96.0% for polyps 10 mm or larger [3]. Another large study of 1689 patients found per-polyp and per-patient CAD sensitivities of 89.0% each for polyps 10 mm or larger [7]. However, compared with our study, the 1689-patient study had lower per-patient and per-polyp sensitivities of 61.3% and 75.8% when evaluating polyps 6 mm or larger.

Increased sensitivity in exchange for decreased specificity is acceptable and warranted when CAD is functioning as a second reader. In fact, a prior study found that use of CAD increases the area under a ROC curve [24, 25]. The average of 8.3 CAD marks per patient in this study seems to be acceptable. Positive CAD marks may also identify subtle lesions that were either not noted or discounted as unlikely to be a true-positive polyp on initial interpretation.

Three nondiminutive polyps were identified at OC that in retrospect were identified by CAD but discarded as a CAD false-positive by the radiologist. The true number of these situations may be larger than reported here, as only 65% of patients with identified polyps went on to OC. Regrettably, none of these additional lesions were recognized as true polyps by the radiologist during real-time CTC interpretation. CAD can be expected to identify more polyps missed by the primary reader when that reader is relatively inexperienced. However, lack of ultimate recognition by the radiologist will result in a missed polyp regardless of CAD detection.

The reimbursement rate in this study of 31% on a standard charge across a variety of payers shows the feasibility of adding CAD to a CTC program. Although the reimbursement on charges of one practice may be difficult to extrapolate to other practices given wide variation in charges for radiologic procedures [26], even partial reimbursement for CAD has important ramifications. Use of CAD for mammography sharply increased after coverage by Medicare and subsequently by many private insurers beginning in 2001, with the prevalence of use in screening mammograms increasing from 3.5% to 79.7% in 2009 [27]. Given the recent USPSTF decision to include CTC in screening guidelines and the evidence that reimbursement for CAD can be obtained in clinical practice, adoption is likely to increase [2].

As computer processing and deep learning improves, CAD performance will likely also improve, particularly in identification of polyps most frequently missed by human observers, such as flat polyps. In fact, three of six polyps identified by OC but not by the interpreting radiologist in this study were flat polyps. As our understanding of flat polyps grows, it is reasonable to expect that this knowledge can be incorporated into CAD algorithms to improve sensitivity [28–30].

The limitations of this study include that it was performed at a single center in a predominantly screening population, although this population is precisely the one most likely to benefit from CAD as a second reader to assist in identifying precancerous polyps. CAD systems are not in widespread use,
although their use stands to increase given the recent USPSTF guidance. Although the number of CAD marks per patient is reasonable, a true measure of time spent evaluating these marks was not performed in this study. This study also only evaluated a single CAD system when reading on a single platform and may not be generalizable.

In conclusion, CAD performance in routine clinical practice is similar to previous retrospective evaluations, with excellent sensitivity and an acceptable false-positive rate. Furthermore, we have shown that CAD is being at least partially reimbursed in our clinical practice by third-party payers. The combination of good clinical performance and third-party reimbursement would suggest that use of CAD in CTC will likely increase in the future, especially in light of the recent positive USPSTF screening recommendation for CTC.

References

30. Pickhardt PJ, Kim DH, Robbins JB. Flat (nonpolypoid) colorectal lesions identified at CT colonography in a US screening population. Acad Radiol 2010; 17:784–790