Alimentary Tract

Adverse events of computed tomography colonography: An Italian National Survey

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ABSTRACT

Aim: To retrospectively study the frequency and magnitude of complications associated with computed tomography (CT) colonography in clinical practice.

Methods: A questionnaire on complications of CT colonography was sent to Italian public radiology departments identified as practicing CT colonography with a reasonable level of training. The frequency of complications and possible risk factors were retrospectively determined. Responses were collated and row frequencies determined. A multivariate analysis of the factors causing adverse events was also performed.

Results: 40,121 examinations were performed in 13 centers during the study period. No deaths were reported. Bowel perforations occurred in 0.02% (7 exams). All perforations were asymptomatic and occurred in patients undergoing manual insufflation. Five perforations (71%) occurred in procedures performed following a recent colonoscopy. There was no significant difference between perforations associated with rectal balloon (0.017%) and those that were not (0.02%). Complications related to vasovagal reaction (either with or without spasmolytic) occurred in 0.16% (63 exams). All vasovagal reactions resolved in less than 3 h, without any sequelae.

Conclusions: Perforation rate at CT colonography in Italy is comparable with elsewhere in the world, occurring regardless of the experience of radiology centers. Although the risk is very small, it may not be negligible when compared with the risk of diagnostic colonoscopy.

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1. Introduction

Computed tomographic colonography (CTC) is increasingly used as a relatively non-invasive method of colonic investigation both for colorectal cancer (CRC) screening [1–3] and for patients with symptoms suggestive of CRC [4–7]. Data from large studies on screening cohorts have suggested that CTC and conventional colonoscopy have similar sensitivity for polyps ≥6-mm in diameter [8,9]. Moreover, patients generally prefer CTC instead of barium enema examination or colonoscopy [10–13]. However, concerns were raised about recommending CTC as routine screening tool because of potential harm [14,15]. While CTC is widely considered to be much safer than colonoscopy [16–18], it is not exempt from potential serious complications, mainly represented by large bowel perforations [18–22]. The National Survey of United Kingdom [18] has suggested a perforation rate, for diagnostic studies, of 1 in every 1889 examinations. Similarly, in a large population-based cohort, the incidence of perforations was 0.058%, or one in 1969 studies, with one in 2967 patients requiring surgical intervention [19]. These rates are higher than those reported by the International Working Group on Virtual Colonoscopy [20,21]. In this survey the total perforation rate for all patients was 0.009% (2 in 21,923 studies) and symptomatic perforation rate (requiring further treatment) was 0.0054% (1 in 21,923). Higher rates of adverse events (AEs) may be a sign of poor quality hospital care and many complications can be prevented if hospitals follow procedures based on the best practice and scientific evidence [20,21]. Ideally, for the standard best practice, continuing training should be required to
radiologists or technologists performing CTC examinations at their institutions [19,23,24].

Thus, the purpose of this nationwide survey is to assess the frequency and the magnitude of complications associated with CTC in daily clinical practice at well-trained centers. This setting is of interest since previous studies have provided data from specialized centers [19,20] and it remains unknown whether results from these studies can be generalized.

2. Methods

A questionnaire about complications of CT colonography was sent to Italian public radiology departments identified as practicing CT colonography with a reasonable level of training. The frequency of complications of CT colonography and possible risk factors were retrospectively determined. Ethical approval and informed consent were waived, since this study was deemed a clinical audit and patients would not be approached. At the time of this survey, in Italy, there were 40 public Departments offering CTC in their everyday clinical practice with different levels of standard care and another unknown number of private centers, whose expertise is unknown [25]. A preliminary letter was mailed to the clinical directors of all public departments. The letter included a brief description of the study and the permission to collect anonymous data from the Institution. The respondent centers were re-contacted to establish eligibility. To be eligible, departments had to attend or organize at least 2 CTC courses recognized by the Italian Society of Radiology (SIRM). This criterion was applied to select centers attaining the goal of providing best practice. Although there were no rules to define principles of best practice, it was assumed that radiologists and technicians at qualified centers had to undergo training including continuing medical education accredited courses [23,25]. Thus, two approved training programs was the minimum requirement. Of the 24 (60%) respondents, 8 centers were excluded because they did not meet our inclusion criterion; three additional centers were also excluded because eligibility was never established despite multiple attempts. Between December 2010 and December 2012, an email was sent to the Lead Gastrointestinal Radiologist of each participant center asking to complete a detailed questionnaire (supplementary Table S1). The questionnaire included when the CTC service was started (year) and the total number of examinations performed at the time of the present survey. The radiologists were asked how many complications (e.g., colonic perforations and vasovagal effects) they had experienced in their institution. Additional questions were asked including the type of gas inflated (air or carbon dioxide – CO₂), the type of catheter used for inflation (rigid or flexible, with or without balloon), the use of spasmyloytics (i.e. Hyoscine N-butylbromide 20 mg/ml, 1 ml injectable vials), the bowel preparation given to the patient (including diet, the use of laxatives and fecal tagging agents); complications were registered along with possible deaths. If a complication was recorded, additional details related to that event were asked. If a perforation occurred, the staff member performing the inflation (radiologist, resident, nurse or technician), the severity of the event, the perforation site (intra or retroperitoneal, determined on CT images by the distribution of gas in the abdomen) and the type of treatment (conservative or surgical) were recorded. Additional information on patient demographics including sex, age, comorbidities, previous surgical intervention and previous recently performed CC was also reported.

Patients included in the survey underwent CTC for both screening and diagnostic indications. All CTC procedures were acquired by using dual positioning (prone and supine scans) and a supervising radiologist or resident, that could promptly recognize the adverse event during CTC examination with real-time evaluation of images, was on call at each center.

2.1. Statistical analysis

Descriptive analysis included the calculation of rates and proportions for count data. Univariate analysis was carried out with chi-square procedures. Multivariate analysis of the main predictors of complications was performed by using logistic regression model [26,27]. Because the unit of observation (patient) was different from the unit of analysis (center), a within-center correlation of outcomes was taken into account by means of a random-effect analysis with grouping by center [28]. Centers were also separated according to the hospital academic status (academic vs. non-academic center). The number of years of experience with performing CTC procedure was also calculated for each center. The effects of factors of interest (whether categorical or continuous) were evaluated by odds ratios (ORs), along with confidence intervals (CIs) as well as model-based Wald tests. All statistical analysis was performed by using software (R; the R Foundation, Vienna, Austria) [29,30]. P-values <0.05 were considered to indicate statistical significant.

3. Results

Thirteen centers were identified as eligible and included in the analysis. Of these, 6 (46%) were located in northern Italy, 5 (39%) in central Italy and 2 (15%) in southern Italy. Overall 6 (46%) centers were academic, 7 non-academic. During the evaluated period from 2000 to 2011, the mean number of CTC procedures performed annually by each center ranged from 83 to 847. By 2011, all centers had accumulated 4 or more years of experience with performing CTC procedure. Nine (69%) centers had 8 or more years of experience in CTC procedure, with more than 1000 CTC examinations per center performed (129–847 procedures per year). Two centers (15%) reported offering CTC service in 2005, having performed a total of 500 and 1088 examinations, respectively. The remaining 2 (15%) centers offered CTC service in 2006 and 2007 (263 and 141 mean procedures/year, respectively).

3.1. Examinations performed

In total, 40,121 CTC examinations were performed at the 13 participating centers between 2000 and 2011 (mean number of exams 3086 ± 2773; range, 500–9322). Table 1 reports the distribution of CTC exams per center. The six academic centers contributed 28,752 patients to the total 40,121 (72%).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the included centers.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center 1</td>
<td>CTC studies n (%)</td>
</tr>
<tr>
<td>Center 2</td>
<td>565 (1.5)</td>
</tr>
<tr>
<td>Center 3</td>
<td>1,190 (2.9)</td>
</tr>
<tr>
<td>Center 4</td>
<td>1,088 (2.7)</td>
</tr>
<tr>
<td>Center 5</td>
<td>1,267 (3.2)</td>
</tr>
<tr>
<td>Center 6</td>
<td>3,420 (8.5)</td>
</tr>
<tr>
<td>Center 7</td>
<td>500 (1.3)</td>
</tr>
<tr>
<td>Center 8</td>
<td>9,322 (23.2)</td>
</tr>
<tr>
<td>Center 9</td>
<td>6,029 (15.0)</td>
</tr>
<tr>
<td>Center 10</td>
<td>6,177 (15.4)</td>
</tr>
<tr>
<td>Center 11</td>
<td>5,034 (12.5)</td>
</tr>
<tr>
<td>Center 12</td>
<td>3,183 (7.9)</td>
</tr>
<tr>
<td>Center 13</td>
<td>1,316 (3.3)</td>
</tr>
<tr>
<td>Total</td>
<td>40,121 (100)</td>
</tr>
</tbody>
</table>
Table 2
Details of seven perforations. All perforations were asymptomatic and performed with manual insufflation method.

<table>
<thead>
<tr>
<th>Center no.</th>
<th>Treatment</th>
<th>Catheter</th>
<th>Operator</th>
<th>Site</th>
<th>Gas distribution</th>
<th>Prior CC</th>
<th>Prior biopsy</th>
<th>Comitant* disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Surgery</td>
<td>Foley</td>
<td>Technician</td>
<td>Rectum</td>
<td>Retroperitoneal</td>
<td>Yes 2 weeks before</td>
<td>Yes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Surgery</td>
<td>Rigid with balloon</td>
<td>Nurse</td>
<td>Sigmoid</td>
<td>Peritoneal and retroperitoneal</td>
<td>Yes same-day</td>
<td>No</td>
<td>Diverticulosis</td>
</tr>
<tr>
<td>3</td>
<td>Surgery</td>
<td>Rigid with balloon</td>
<td>Radiologist</td>
<td>Rectum</td>
<td>Retroperitoneal</td>
<td>Yes same-day</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Conservative</td>
<td>Flexible without balloon</td>
<td>Radiologist</td>
<td>Sigmoid</td>
<td>Retroperitoneal</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Conservative</td>
<td>Foley</td>
<td>Nurse</td>
<td>Sigmoid</td>
<td>Intraperitoneal</td>
<td>Yes 3 days before</td>
<td>No</td>
<td>Diverticulosis</td>
</tr>
<tr>
<td>6</td>
<td>Conservative</td>
<td>Foley</td>
<td>Resident</td>
<td>Sigmoid</td>
<td>Peritoneal and retroperitoneal</td>
<td>Yes same-day</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Conservative</td>
<td>Rigid with balloon</td>
<td>Radiologist</td>
<td>Sigmoid</td>
<td>Peritoneal and retroperitoneal</td>
<td>Yes same-day</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

\* Pre-existing medical conditions such as inguinal hernia, carcinoma, diverticulosis.

<sup>b</sup> Without electrocautery using cold biopsy forceps.

3.2. CTC technique

Colon distension was achieved via room air insufflation in 73% (29,373/40,121) of the patients; in the remaining 10,748 cases (27%) an automatic CO₂ insufflator was used. Gas was inflated through Foley catheters in 63% of the patients (25,361/40,121); ballooned-tipped flexible catheters in 14% (5513/40,121); flexible catheters without balloon in 3% (1032/40,121); ballooned-tipped plastic large-bore rigid catheters in 11% (4501/40,121) and plastic large-bore rigid catheters without balloon in 9% (3714/40,121). Spasmolytic agents were used in 25,164 patients (64%) to achieve a better colonic distension; this was not necessary in 14,957 patients (36%).

3.3. Adverse events

3.3.1. Vasovagal reactions

Sixty-three self-limiting vasovagal episodes were reported overall (0.16%; 95% CIs, 0.09–0.3%; event occurrence, one every 638 procedures).

All vasovagal reactions were managed without additional medications and resolved in less than 3 h, without any sequelae. As shown in Table 1, vasovagal reactions rates varied widely between centers from 0% to 0.86%.

Multivariate analysis showed that patients from academic centers were less likely to experience vasovagal episodes than those from non-academic centers (ORs, 0.33; 95% confidence interval, 0.12–0.89; P = 0.04).

3.3.2. Bowel perforations

There were 7 cases of bowel perforation (0.02%; 95% CIs: 0.007–0.04%, event occurrence, one every 5732 studies), which occurred at 4 (2 academic and 2 non-academic) centers. At all four centers, a total of 1000 or more exams had been performed, and, collectively these centers contributed to 11,509 (29%) examinations included in our analysis. Patients who experienced perforation were 71.4% male, mean age was 73 years (range, 64–78 years). None of the patients were symptomatic. Characteristics for the seven perforated patients are summarized in Table 2.

No perforations occurred in patients who underwent mechanical CO₂ insufflation. Five cases of perforations (71%) occurred in CTC examinations performed as studies following CC: three occurred after same-day CC (Fig. 1) and two others occurred within 1–2 weeks after CC. Four (57%) cases of perforations occurred in the rectum (Fig. 2); and three in the sigmoid colon. Overall, 35,375 CTC examinations were performed by using an inflated balloon in the rectum, and among these, there were six perforations. Further, 4746 examinations were performed without an inflated balloon, and among these, there was one perforation. The proportion of perforations associated with rectal balloon was similar to the proportion of those that were not (0.017% vs. 0.02%; P = 0.5). Three perforations occurred among 8215 patients previously distended by using a rigid catheter (0.036%; one every 2738 exams); the perforation rate from studies performed with a flexible catheter was 0.012% (4/31,906; one every 7978 exams; P = 0.3). Three perforations occurred at two academic centers, the remaining four perforations at two non-academic centers. Multivariate analysis showed that there were no significant differences in perforation occurrence between academic and nonacademic centers (ORs, 0.37; 95% CIs, 0.05–2.6; P = 0.4). Bowel distension was performed in three cases (43%) by an attending physician, in two cases (29%) by a nurse.

Fig. 1. 71-Year-old male undergoing CT colonography on the same day of conventional colonoscopy. The images show a large amount of free air in the peritoneal cavity due to sigmoid perforation.

Fig. 2. 68-Year-old male undergoing CT colonography for screening. The images show free retroperitoneal air due to perforation of the rectum. A few air bubbles are also seen in the peritoneal cavity. The patient underwent conservative treatment.
in one case (14%) by a resident in Radiology and in the last one (14%) by a technician. Distribution of air was retroperitoneal in 4 patients (57%) and in the three remaining cases (43%) gas distribution involved both retroperitoneum and peritoneal space. Three patients underwent surgery (0.0075% surgery rate for CTC-related perforation, one event in 13,374 procedures); the remaining four patients received successful conservative treatment.

No deaths were reported.

4. Discussion

In our national survey, the majority (90%) of all complications of CTC were vasovagal reactions of mild severity. There was no need for medical treatment during vasovagal episodes and no post-procedural sequelae occurred. Vasovagal reactions, which can result from overstimulation of the nerve, may be easily avoided [31,32]. According to our data, vasovagal reactions can be expected in approximately 0.16% of patients, one in 638 examinations. These figures compare favorably with results of routine colonoscopy practice, where vasovagal reactions have been reported in 16% of cases [33–37]. On the other hand, our estimate is considerably higher than those reported in prior studies on CTC complications. [18,37]. Colonic perforation is the most dreadful complication of a colorectal diagnostic examination. In our survey cohort, the incidence of colonic perforation was 0.02%, one in 5731 CTC examinations, though. Only 3 of the 7 perforated patients eventually needed post-CTC surgery. When comparing our data with the endoscopic series, the perforation rate at colonoscopy, whether diagnostic or therapeutic, would appear to be higher than that of CTC. The reported perforation rates for colonoscopy range from one case in 3115 procedures (0.032%) to one case in 510 procedures (0.196%) [17,39–44]. Thus, our 0.02% estimate of post-CT colonography perforations imparts a significantly more favorable profile for CTC compared to colonoscopy. In our series, no symptomatic perforations were identified. Estimates of perforation rate following colonoscopy were based only on those patients in whom the colonoscopist was aware of the event or subsequent symptoms alerted clinicians to this complication following the procedure. So it is to be expected that asymptomatic perforations are underreported at colonoscopy. Literature reports that up to 50% of the colonoscopy-related perforations are not recognized at time of colonoscopy [18]. Therefore, our study supports previous evidence that the risk of symptomatic perforations is lower for CTC than colonoscopy [20,22]. No deaths were recorded in our series. Mortality from colonoscopy has been reported to be as high as 0.07% (1 death every 1500 colonoscopies) [41] though the rate is much lower when colonoscopy is used for screening purposes [42]. Our data on perforations is similar to that reported by the American survey [20,21] and favorably compares with the data from the survey performed in UK and Israel [18,19].

All seven perforations in our survey occurred in CTC examinations performed using air as gaseous medium in manually controlled insufflations. According to the literature, the use of an automated low-pressure CO₂ delivery reduces perforation rate, having the possibility to control gas pressure and volume during the inflation, and to maintain both of them constant during the procedure. Inflating the colon manually with air does not give this opportunity and could generate unknown (possibly high) pressure and volume values that can only be estimated and potentially harmful [22]. However, given that the occurrence of perforation at CTC is a rare event, we were unable to demonstrate a causal relationship between manual insufflation, as opposed to automatic insufflation, and perforation. Rectal tubes are rigid catheters with large caliber are associated to a major risk of complications due to the fact that its rigidity has the potential to breach a normal rectal wall if forcefully inserted. In our survey the use of rigid catheters was limited to 21% exams and, notably, they have been used much more frequently until 2004. In our population 3 perforations occurred in patients previously distended with the use of a rigid catheter, but, as previously stated, these events occurred in the period ranging from 2000 and 2003. To our knowledge, since 2005 no CTC examinations have been performed by using that type of catheter, thus decreasing dramatically the number of perforations occurred. Hence, our estimate of perforation rate among patients distended with a flexible catheter (0.012%; 1 every 7980 examinations) may be a more relevant metric reflecting what could be expected in the future.

Other important risk factors for perforations are recent colonoscopy and presence of comorbidities. Previous recent colonoscopy, especially with polypectomy, can damage colonic wall, making perforation easier at time of insufflation. Currently, there is almost total consensus among experts that CTC should be delayed if a polypectomy and/or biopsy has recently been performed [22,45]. However, there is little evidence about a safe interval between colonoscopy and CTC [45]. Therefore, the possibility of a perforation following a recent optical colonoscopy, must be carefully investigated before CTC procedure [22,45,46]. In our study, 2 perforations occurred in patients undergoing a same-day optical colonoscopy. Of note, in these two patients the usual colonic distension was performed, a low dose scout was obtained but no CT low-dose acquisition performed, making it impossible to understand the real cause of perforation. In other three cases of perforation, patients underwent colonoscopy within 2 weeks before CTC. Hough et al. described two cases of perforation on 262 patients (0.8%) undergoing CTC after colonoscopy and then studied with a low dose CT scan before colonic inflation [47]. In our series, three (42%) perforations occurred in patients with diverticulosis; no other comorbidities such as carcinoma or left inguinal hernia containing sigmoid were noted [19,22]. Given the higher percentage of diverticulosis in the general population, it is important to proceed with caution in patients with proven or suspected diverticular disease.

As previously reported in literature by Atalla et al., even in our survey no correlation between the incidence of perforation and the institutional experience was observed [46]. This event was demonstrated by the fact that 5 out of 7 perforations occurred in two centers with a large number of monthly CTC examination performed.

Our study has some limitations. First, it must be emphasized that the data of this survey are subject to all the errors inherent in any kind of retrospective data collection. Furthermore, the surveyed centers were not a random sample of all Italian CTC centers but a representative sample of those practicing CTC after appropriate training. Our data, thus, represent the CTC practice at “well-trained” centers and this limits the generalizability to community practice. However, training is recognized as a key issue before CTC service implementation [23] and the ever-increasing experience of CTC services will probably further reduce the incidence of complications. Therefore, we believe that our results may reflect what is achievable in community care, assuming a reasonable level of basic training. Nonetheless, this survey provides information that does not exist at present in Italy. Another possible limitation was the exclusion of private hospitals. It is difficult to predict the impact of this bias. If patients with less severe illness, and low chance of complications, are more likely to be treated in private hospitals and these data were not reported, then that would likely lead to overestimation of the complications rate. If this is the case, the small percentage of perforations in our series has made even more relevant our positive findings for CTC safety. Our survey is based on self-reported practice and is, therefore, subject to recall bias. There is a natural disincentive to report complications that are managed simply and immediately [38]. Thus, many minor complications such as prolonged cramping or nausea may have not
been recorded. Furthermore, study results may have partially been affected by different criteria used by the various institutions in reporting complications. Data limitations precluded an extensive evaluation of the cause-effect relationship between factors such as the experience of the individual who performs the insufflation, comorbidities and recent colonoscopy and perforations. Specifically, we were unable to retrospectively determine the rates of these potentially risk factors in the large population in which perforations did not occur. Also a causal relationship between colon distension and spasmylytics use could not be inferred. However, the study of risk factor analysis was not the main purpose of this survey and further prospective trials will be needed to reach cause-effect conclusions. Finally, at the time of data collection, regional governments did not allow National Health Service reimbursement of CTC as a screening test. Thus, it is possible that this survey reflects symptomatic populations only.

In summary, our survey has shown that colonic perforation rate of CTC encountered in Italian hospitals is comparable with else-where in the world and events occur regardless of the experience level of the radiology centers. While severe complications are very uncommon, adverse events of mild significance, such as vasovag-al reactions, may occur more frequently. Although the perforation rate at CTC is very small, it may not be negligible when compared with the risk of diagnostic colonoscopy.

Conflict of interest statement
No conflict of interest for all the authors.

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Appendix B. Supplementary data
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References


