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The fecal immunochemical test (fit): Selected aspects regarding its effectiveness for colorectal cancer screening in Quebec City

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ABSTRACT

Background and aims: FIT's value has been ascertained across Canada and worldwide, but still needs to be assessed within the province of Quebec. There also remains a gap between formal indications for FIT, and its actual use in clinical practice. This research aims to evaluate some aspects of FIT's effectiveness in our setting, and its application by prescribers.

Methods: We retrospectively identified and reviewed all the colonoscopies conducted for a positive FIT in 2014 at 2 hospitals located in Quebec City.

Results: Five hundred and fifty-nine (559) colonoscopies were reviewed. We obtained PPVs of 6.8% and 46.9% for the detection of CRC and AA, respectively. The PPV for the detection of SCL was higher in men compared to women (OR 1.56, 95%CI 1.11–2.20) and among justified FITs compared to unwarranted ones (OR 1.88, 95%CI 1.34–2.63). The PPV for CRC detection was 25.0% in the presence of unexplained iron deficiency anemia and 6.5% when anemia was absent (p = 0.0058). In 49.9% of cases, the prescription of a FIT was inappropriate.

Conclusion: The FIT holds a better PPV for detecting SCL among men and when it is indicated. Anemia is associated with a higher CRC detection rate. Half of the FITs were not initially indicated.

1. Introduction

Worldwide, colorectal cancer (CCR) is the second and third most diagnosed cancer among women and men, respectively (Torre et al., 2015). It is estimated that in 2008, it was responsible for > 2400 deaths in the province of Quebec (Institut national de santé publique du Québec (INSPQ), 2008). Given this context, several reasons justify CRC screening in an average-risk population. Firstly, survival is related to the stage of the disease (0, I to IV) at the time of diagnosis. Moreover, the natural history of the disease is well known: 80% of CRC cases result from the transformation of an adenoma, which generally grows from grade 1 to grade 5 in about ten years. Polypectomy of advanced adenomas (AA) thus reduces the incidence of CRC (Potvin and Gosselin, 2012; AJCC (American Joint Committee on Cancer), 2010). In fact, colonoscopy is the gold standard for the detection of AA and CRC. However, it is not recommended as a screening tool among the general population because of its high cost, limited accessibility, and associated risk of complications. Currently, one of the endorsed screening tools for average-risk individuals is the immunochemical fecal occult blood test (FIT), followed by a confirmation colonoscopy given a positive result. This strategy allows the selection of individuals who will potentially benefit the most from a colonoscopy, and was also shown to be cost-effective (Sobhani et al., 2011; Wilschut et al., 2011). In Quebec, the guaiac fecal occult blood test (gFOBT) was replaced with the FIT in September of 2013 as part of a newly implemented provincial screening program (PQDCCR). To date, FIT's performance has not been assessed in the province of Quebec. In addition, there seems to remain a discrepancy between the formal indications for a FIT, and its actual use in clinical practice. Thus, this research aims to evaluate some aspects related to the effectiveness of the FIT in our setting and its application by prescribers.

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2. Methods

2.1. The PQDCCR

Quebec's CRC screening program (PQDCCR) was first implemented in 2011 in 8 pilot sites across the province, which includes the Québec University Hospital Center (CHU de Québec). The program is aimed at 50 to 74 year-old, asymptomatic average-risk individuals (Suppl.). Its first phase consisted in the standardization of a colonoscopy prescription, preparation, and reporting. The second phase started in September of 2013. Its purpose was to assess the use of the FIT locally. Primary care physicians request a FIT whenever they consider it is warranted, and refer test-positive patients to either of the designated centers for a confirmation colonoscopy. The third phase, which is pending, should result in the entire target population being mailed an invitation to take part in the screening program.

The technology used for sample laboratory analysis is the OC-Sensor® Diana (Eiken Chemical Co., Ltd.). Of note, the manufacturer recommends a positivity threshold value of 100 ng/mL; however, PQDCCR authorities have set the threshold at 175 ng/mL, based on available evidence regarding the performance and cost-effectiveness of the FIT, which is discussed further in more detail (Potvin and Gosselin, 2012).

2.2. Study population

We included all FIT-positive patients who underwent a confirmation colonoscopy in 2014, at either of the 2 PQDCCR designated centers in Quebec City, i.e. Saint-François d'Assise (HSFA) and Saint-Sacrement (HSS) Hospitals.

We excluded FIT-positive patients who were referred for a colonoscopy which was not performed, for any reason (e.g. refusal), or incomplete because of poor bowel preparation. We also excluded patients who were referred for a positive gFOBT rather than a FIT, whose medical records were unavailable, and whose colonoscopy was performed for another reason than a positive FIT result.

2.3. Data collection

At the CHU de Québec, which is comprised of the HSFA and HSS, all gastrointestinal (GI) endoscopy reports are generated in a standardized manner and electronically stored via Endoworks® (Olympus®) software. In addition, all medical records from the 5 hospitals of the CHU are digitized and merged into a single source. We launched a search in Endoworks® for all reports of colonoscopies performed at HSFA and HSS between January 1st and December 31st 2014 containing the keywords “FIT” or “RSOSi (French equivalent of FIT)”. We then consulted each corresponding medical record to complete data collection. When a record was only partially digitized, we consulted the print version at the Health Records Department.

All colonoscopy reports and medical records were reviewed manually by either one of the two first authors (MC, GL). A data collection tool was created, as well as a database to allow statistical analyses.

2.4. Objectives

The primary objective of the study was to determine the positive predictive value (PPV) of the FIT for the detection of CRC, significant colorectal lesions (SCL), and AA. The secondary objectives were to (i) describe the anatomical site and staging of detected cancers, (ii) identify the false-positive FIT results, (iii) examine the influence of specific variables on the test's PPV, such as age, sex, adequacy of the prescription of a FIT, presence of warning features, and the hospital where the colonoscopy was performed, and (iv) identify the FITs that were unjustified, i.e. that were requested for other than asymptomatic, average-CRC risk patients. Definitions for SCL, AA, and average- CRC risk patients are listed in the Supplementary Material.

2.5. Statistical analyses

Continuous data are presented as means and their corresponding 95% confidence intervals (95% CI), whereas categorical data are shown as frequencies and proportions. PPVs were estimated as the proportion of the true positive tests by the overall number of positive results and are displayed as percentages. The Wald 95% CIs for binomial proportions were estimated using the asymptotic standard error. Fisher's exact tests were used to compare true positive proportions in different subgroups of patients. Univariate and multivariate logistic regression models were arranged to estimate crude and adjusted odd ratios, and to test the association of a true positive test with different factors. Age, sex, adequacy of FIT, and warning features were used to obtain adjusted results with the multivariate analyses. The Hosmer-Lemeshow test was used to test FIT's effectiveness for the logistic regression models. All statistical tests were two-sided, and a p value of < 0.05 was considered statistically significant. The statistical analysis was carried out using SAS Statistical Software v.9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Participants

We identified 253 and 358 colonoscopies performed at HSFA and HSS, respectively, between January 1st and December 31st 2014, for a total of 611 patients. Fifty-two (52) patients were excluded for various reasons (Fig. 1). The demographic and clinical characteristics of 559 retained patients are presented in Table 1.

3.2. Global PPV

Main results are shown in Tables 2, 3A, 3B and 3C. VPPs for the detection of CRC, SCL and AA were 6.8 (CI95% 4.7–8.9), 51.7 (CI95% 47.6–55.9), and 46.9% (CI95% 42.8–51.1), respectively.

Two (2) and 3 patients were excluded from the calculation of PPVs for the detection of SCL and AA, respectively, because described polyps were not retrieved.

3.3. Anatomical site and staging of CRC

Twenty-six (26) CRC were left-sided, and 12 were right-sided. In one case, 2 synchronous cancers were detected; thus, we counted it as one single patient, but reported the characteristics for both lesions. Most cancers (60.5%) were stage I or II CRCs. In one case, the lesion detected was in fact an invasive gallbladder cancer; this was not listed as a CRC in our database.

3.4. False-positive FIT results

We considered the FIT result was falsely positive when the confirmation colonoscopy was strictly normal or when the lesions found were not known to induce occult bleeding (e.g. diverticulosis). Given this definition, 10.6% of false-positive FIT results were identified.

3.5. Influence of selected covariates

Increasing age had a significant positive influence on PPVs for detection of all types of lesions, with ORs of 1.06, 1.03 and 1.02 for CRC, SCL and AA, respectively. Thus, one year of aging resulted in a 6% increase in CRC odds. Statistical significance remained for CRC detection after adjustment for the variables stated earlier. We simultaneously conducted ad hoc subgroup analyses for patients aged < 60 years, and those aged 60 years and over. PPVs were higher in the latter group for CRC (OR 5.09, $p = 0.0077$), and SCL (OR 1.71, $p = 0.0074$). Again,