Oncology

Rural–urban differences in the long-term risk of colorectal cancer after adenoma removal: A population-based study

Isabelle Fournel [a,b,c], Vanessa Cottet [c], Christine Binquet [a,b,c], Valérie Jooste [c], Jean Faivre [c], Anne-Marie Bouvier [a,b,c], Claire Bonithon-Kopp [a,b,c,*]

[a] CHRU Dijon, Centre d'investigation clinique, Dijon F-21000, France
[b] INSERM CIC 1432, Dijon F-21000, France
[c] INSERM U866 (Registre Bourguignon des Cancers Digestifs), Université de Bourgogne, Dijon, France

ARTICLE INFO

ABSTRACT

Background: We investigated the impact of municipality of residence on colonoscopic surveillance and colorectal cancer risk after adenoma resection in a French well-defined administrative area.
Methods: This registry-based study included all patients residing in Côte d'Or ($n = 5769$) first diagnosed with colorectal adenomas between January 1, 1990, and December 31, 1999. Information about colonoscopic surveillance and colorectal cancer incidence was collected until December 31, 2003.
Results: A rural place of residence reduced the probability of colonoscopic surveillance in men [HR = 0.89 (95%CI: 0.79–0.99), $p = 0.041$] and in patients without family history of colorectal cancer [HR = 0.91 (0.82–0.99), $p = 0.044$]. After a median follow-up of 7.7 years, 87 patients developed invasive colorectal cancer. After advanced adenoma removal, the standardized incidence ratio for colorectal cancer was 3.03 (95%CI: 1.92–4.54) for rural patients and 1.87 (95%CI: 1.26–2.66) for urban patients compared with the general population. The risk of colorectal cancer was higher in rural patients than in urban ones only after removal of the initial advanced adenoma [HR = 1.73 (95%CI: 1.01–3.00, $p = 0.048$)]. Further adjustment for surveillance colonoscopy, physician location, and other confounders had little impact on these results.
Conclusion: The increased risk of subsequent colorectal cancer after advanced adenoma removal in French rural patients was not explained by a lower rate of colonoscopic surveillance. The role of socio-economic and environmental factors requires further exploration.

© 2014 Editrice Gastroenterologica Italiana S.r.l. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Colorectal cancer (CRC) is one of the most common types of tumours and one of the leading causes of cancer-related death [1,2]. Most CRCs arise from adenomas, a very common lesion in the general population [3,4]. Advanced adenomas have been shown to have a high potential for malignant transformation [5], and their detection and removal during complete colonoscopy is advocated. Post-polypectomy surveillance is recommended [6,7] and in France relies on scheduled complete colonoscopy 3 years after removal of advanced adenomas and 5 years after removal of non-advanced adenomas [6].

Adenoma removal has been shown to reduce the risk of CRC and CRC-related death [8–12]. However, the long-term risk of CRC after adenoma removal was shown to remain higher than in the general population under routine clinical practice [13,14]. This suggests that the individual benefit associated with adenoma removal may not be directly applicable to the general population.

For a long time, research on health inequalities was neglected in France. In particular, very few studies dealt with inequalities in diagnosis and surveillance of colorectal tumours. The detection rate of first colorectal adenomas was previously shown to be lower in rural areas than in urban areas in a French well-defined general population [15]. This finding contrasted with the lack of rural/urban differences in CRC incidence rates whatever the stage of cancer [15], and suggested the existence of geographical inequalities in accessing initial colonoscopy only for asymptomatic subjects or patients presenting non-specific symptoms.

Whether the rural/urban disparities also affect access to surveillance colonoscopy after first adenoma removal and, thereby, affect the risk of CRC, is still open to debate. Similarly to patients diagnosed with CRC, patients diagnosed with adenomas are presumably well informed about the risk of CRC and of the need for regular colonoscopic surveillance. Thus, we hypothesized

* Corresponding author at: Claire Bonithon-Kopp – INSERM CIC 1432, Faculté de Médecine, 7 boulevard Jeanne d'Arc, BP 87900, 21079 Dijon Cedex, France.
Tel.: +33 380393337.
E-mail address: bonithon@u-bourgogne.fr (C. Bonithon Kopp).

that colonoscopic surveillance and the risk of subsequent CRC should not vary according to the place of residence. The present study, based on data collected before the implementation of the faecal occult blood test (FOBT) mass screening in France, aimed at assessing the impact of rural/urban municipality of residence on colonoscopic surveillance and CRC risk after adenoma resection in a French well-defined administrative area.

2. Methods

2.1. Population

This cohort study included all patients residing in Côte d'Or (Burgundy, France), identified from a population-based registry of colorectal polyps covering this area since 1976.

All patients with at least one colorectal adenoma diagnosed between January 1, 1990, and December 31, 1999, and followed up for at least one year after adenoma removal were included [13]. Patients with documented or suspected history of adenoma removal, known familial polyposis, hereditary non-polyposis colorectal cancer syndrome, personal history of CRC, or inflammatory bowel disease were excluded. As colonoscopies performed within the year following the initial examination may have been due to incomplete initial colonoscopy examination, findings from these repeated colonoscopies were included in the baseline data. Accordingly, patients who were diagnosed with CRC within 1 year of the initial colonoscopy were excluded because the cancer was probably missed at initial endoscopy.

2.2. Data collection and definitions

Information on cases of adenoma is routinely obtained from public and private pathology laboratories in the area. Endoscopic data were retrospectively collected from Gastroenterologists' reports (14 private practices in urban areas and 2 in rural areas, 1 university hospital and 1 general hospital in urban areas, and 2 general hospitals in rural areas). The index colonoscopy was considered complete if the intubation reached the caecum. Advanced adenomas were defined as: adenomas ≥10 mm, and/or with villous component, and/or non-invasive high-grade dysplasia (severe dysplasia), or in situ carcinoma limited to the muscularis mucosae. The municipality of residence was categorized into predominantly urban and predominantly rural areas according to the official classification established by the French National Statistics and Economic Studies Institute (INSEE) (Appendix A).

2.3. Follow-up

For the present study, data collection started in 2004. All surveillance colonoscopies performed between 1990 and 2003 were collected reviewing Gastroenterologists' medical records and their recorded findings until the end-point date (December 31, 2003). A surveillance colonoscopy was defined as an examination performed between 1 year after first adenoma removal and the end-point date, or the date of cancer diagnosis or death, whichever came first. The colonoscopy that detected CRC was considered as a surveillance colonoscopy only if the reason for colonoscopy was clearly stated as surveillance of previous colorectal lesions or if the patient was asymptomatic. The vital status of adenoma patients was obtained from the national mortality files, Gastroenterologists' and primary care physicians' (PCPs) medical records, and hospital discharge files. Follow-up information was obtained for 96% of the patients.

Data from the Burgundy Digestive Cancer Registry were used to identify adenoma patients with a history of CRC or synchronous CRC and patients who developed CRC after adenoma removal, as well as to provide reference incidence data for the Côte d'Or population. Cancer stage at the time of diagnosis was classified according to the TNM classification and categorized as 'early stage', including stages I/II (T1-4 N0M0), or 'late stage', including stage III (N1)/IV (M1)/unstaged cancers (non-resected cancers with no evidence of visceral metastasis).

2.4. Statistical analysis

Statistical analyses were systematically performed including all adenoma patients as well as in the sole patients with advanced adenomas. Standardized incidence ratio (SIR) and cumulative CRC probabilities were calculated. Cox regression models were used to assess the independent impact of municipality of residence on the probability of colonoscopic surveillance and the risk of subsequent CRC (see Appendix A).

Statistical analyses were performed using SAS software version 9.1 (SAS Institute, Inc, Cary, NC), STATA software version 10.0 (Stata corporation. College Station, TX, USA), and PAMCOMP software version 1.41 (Institute of Epidemiology and Social Medicine, University of Muenster, Muenster, Germany). A p-value <0.05 was considered significant.

3. Results

3.1. Baseline characteristics of the cohort

After exclusion of 10 patients with unknown municipality of residence, 5769 patients were retained in the analysis (Fig. 1).

On the whole, 28% of the patients lived in rural areas. The proportion of patients living in a municipality with a practicing physician was smaller for rural patients than for urban patients (presence of a local PCP: 55% vs 84%, $p < 0.001$; presence of a local Gastroenterologist: 16% vs 51%, $p < 0.001$). The proportion of men (58%) did not differ according to the municipality of residence ($p = 0.422$). Compared to rural patients, the urban ones had more often a family history of CRC (8% vs 11%, $p = 0.001$) and were slightly younger (63.9 ± 12.6 vs 61.3 ± 13.3, $p < 0.001$). Additionally, rural patients had advanced adenomas more often than urban patients (35% vs 32%, $p = 0.028$).

Among the 3831 patients with available information on caecal intubation, 3322 had initial complete colonoscopy. Initial incomplete colonoscopy was more frequent in rural than in urban patients (17.8% vs 11.5% respectively, $p < 0.001$).

3.2. Factors associated with colonoscopic surveillance

The median follow-up was 7.7 years (interquartile range, IQR: 5.2–10.5) for the whole cohort, and 7.2 years (IQR: 4.9–9.9) for patients with advanced adenoma, without significant differences according to municipality of residence. Information about surveillance colonoscopies was available for 4877 patients (Fig. 1), and more often was available after 1994, and in cases of family history of CRC or initial advanced adenoma (Table 1). Patients without information about colonoscopic surveillance were slightly older (63.4 years old vs 61.8, $p < 0.001$).

Factors associated with colonoscopic surveillance were examined among the 4877 patients with available information. Compared to urban patients, the rural ones had less often at least one surveillance colonoscopy (59% vs 56%, $p = 0.038$). The same trend was observed when the analysis was limited to patients with advanced adenomas (64% vs 59%, $p = 0.085$). The median time to the first surveillance colonoscopy (excluding the first year after adenoma removal) was 4.1 years (95% CI: 3.9–4.4) for urban patients and 4.7 years (95% CI: 4.1–5.2) for rural patients ($p = 0.096$). The corresponding figures in case of initial advanced adenoma were 2.8