Diabetes mellitus and colorectal cancer screening in the population of the Italian region Friuli Venezia Giulia

Francesca Valent [1], Michele Gobbato [1], Antonella Franzo [1], Francesco Gongolo [1]

(1) Direzione centrale salute, integrazione sociosanitaria, politiche sociali e famiglia – Regione autonoma Friuli Venezia Giulia – Via Pozzuolo 330, 33100 Udine, Italy

CORRESPONDING AUTHOR: *Francesca Valent, Direzione centrale salute, integrazione sociosanitaria, politiche sociali e famiglia – Regione autonoma Friuli Venezia Giulia – Via Pozzuolo 330, 33100 Udine, Italy - Telephone: +39 0432 805616 – Email: francesca.valent@asuiud.sanita.fvg.it*

DOI: ***10.2427/11958***
Accepted on September 27, 2016

ABSTRACT

Background: Colorectal cancer is the most common cancer in Italy, where screening programs are now in place all over the country. We conducted a research to assess whether the use and outcomes of colorectal cancer screening are different between diabetics, who are at increased risk of developing colorectal cancer, and non-diabetics in the Italian Northeastern region Friuli Venezia Giulia.
Methods: This was a retrospective population-based study which used the administrative databases of the regional health information system of Friuli Venezia Giulia as sources of information. We compared screening adherence and results among diabetic and non-diabetic residents in the period 2010-2013 (2 screening rounds).
Results: Overall, more than 300,000 persons were invited for the colorectal cancer screening in each round. Of them, approximately 8.8% had diabetes.Adherence to the screening program was significantly lower among diabetics than among non-diabetics: in women, adherence was respectively 43.8 and 47.3 % in the first round and 56.2 and 58.8 % in the second; in men, adherence was respectively 40.1 and 42.1% in the first round and 53.0 and 53.8% in the second. The proportion of positive fecal occult blood tests and the detection rate for initial and advanced adenomas among diabetics were higher than among non-diabetics, whereas no clear pattern was observed for the detection of cancers.
Conclusion: In Friuli Venezia Giulia, efforts should be directed at improving the management of diabetic patients and at reducing the inequalities in access to care due to this comorbidity.

Key words: colorectal cancer screening; diabetes mellitus; Italy; screening participation

INTRODUCTION

In Italy, colorectal cancer is the most common malignancy, with annual incident cases representing approximately 13% of all new cancers in both sexes [1,2] in the areas covered by the cancer registry [3]. Both standardized incidence and mortality have started to decrease since 2007 [1]. One of the reasons may be the increasing implementation of colorectal cancer screening programs, which started in Italy in a few areas in 2000 [4] and are now in place in all the Italian administrative regions with a theoretical coverage of more than 70%

of the eligible population [5]. In fact, the detection and removal of precancerous polyps prevents the development of cancers and consequent deaths.

In Italy, the likelihood of developing colon and rectum cancer has been shown to be significantly higher among diabetics than in the non-diabetic population (HR=1.48 and 1.26, respectively) [6]. The association between diabetes mellitus and colorectal cancer incidence has been known for a long time [7], and recently diabetes and colorectal cancer have been shown to share common features, including inflammation, imbalanced intestinal microbiota, and a molecular cross talk between several signaling pathways [8]. In addition, diabetes has been shown to be a negative prognostic factor for colorectal cancer, increasing the likelihood of cause-specific death by 36% [9]. Therefore, diabetic populations might have a great benefit from adhering to screening, despite cost-effectiveness of colorectal screening may be affected by a person's comorbidities, such as diabetes [10].

The international literature is not unanimous about the use of colorectal screening among diabetic patients: a US survey found that colorectal cancer screening did not differ between diabetic and non-diabetic men and women <65 years of age, whereas older men with diabetes had higher prevalence of guideline-concordant screening [11]. Another study showed that women with diabetes were more likely to be screened than non-diabetics [12], whereas in another there was no significant difference between diabetics and non-diabetics [13].

In the Italian region Friuli Venezia Giulia, approximately 1,200,000 inhabitants, a colorectal screening has been offered with a letter to all the resident population 50-69 years of age since 2009 through biannual fecal occult blood tests (FOBT) [14]. The colorectal cancer screening program is offered free of charge: FOBT is gratuitous and likewise are all the correlated medical interventions in case of positivity [15]. Subjects 70-74 are invited for the screening only if they had previously adhered to the program [15]. We conducted this research to assess whether the use and outcomes of colorectal screening in Friuli Venezia Giulia is different between diabetics and non-diabetics.

METHODS

This was a retrospective population-based study which used the administrative databases of the health information system of the Friuli Venezia Giulia region as the sources of information.

The regional health information system includes a number of health-related administrative databases which cover the entire regional population and can be linked at an individual level through an encrypted unique identifier which is periodically modified. Through this system, a regional registry of patients with diabetes mellitus has been created linking, at individual level, the following datasets: a) the regional hospital discharge database, which includes records from all the regional hospitals (either public or private accredited to the public health system) since 1986 and those regarding admissions of regional residents to extra-regional hospitals; b) the pharmaceutical prescription database, containing information on all the prescriptions made by physicians working in the public health system, whereas prescriptions paid out-of-pocket, which should be negligible in case of antidiabetic medications, are not included; c) the database of medical exemption certificates, issued to all the potential health care beneficiaries who are entitled, because of low income, age, or chronic diseases, to receive free prescriptions and outpatient specialist care. A person is defined as diabetic if he or she a) had a hospital admission with a principal or secondary discharge diagnosis of diabetes mellitus (ICD-9-CM 250 and/or subclasses), or b) a medical exemption certificate for diabetes, or c) the prescription of at least 3 packages of antidiabetic medications (ATC codes A10Axxx or A10Bxxx) in a 365-day period.

The colorectal cancer screening database is also part of regional health information system. It includes information on all the residents invited for the screening, the date when the test is processed (if the person adhered to the program), the result of the FOBT (positive/negative), and of the colonoscopy for patients with a positive FOBT.

Data from the screening database were individually linked to the diabetes registry through the anonymous unique identifier. Residents invited for the colorectal screening program in each of the two rounds 2010-2011 and 2012-2013, were considered diabetic if they were in the diabetes registry with an incidence date prior to the date of invitation for the screening.

For each round, we compared adherence to the program and the results of the FOBT and of the colonoscopy among diabetic and non-diabetic residents. Adherence was considered as the proportion of persons who actually received a FOBT among those invited to undergo the test. Detection rate was defined as the proportion of patients with the detection of cancers, advanced or initial adenomas, as the result of the colonoscopy following a FOBT test. We also calculated the proportion of cancers and adenomas detected through the colonoscopy among subjects with a positive FOBT result. The statistical significance of the differences between diabetic and non-diabetic residents was assessed through the chi-squared test. P-values <0.05 were considered significant.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Since the study was based only on administrative data without any personal identifier, no informed consent from patients was required.

TABLE 1. Adherence to the invitation for colorectal cancer screening in Friuli Venezia Giulia, Italy, 2010-2013, by screening round, sex, age class, diabetes status.

CLASSES OF AGE	NON-DIABETICS			DIABETICS			P-VALUE TEST X^2
	INVITATION N	ADHERENCE N	ADHERENCE %	INVITATION N	ADHERENCE N	ADHERENCE %	
	ROUND II (2010-2011)						
	Females						
50-54	43.263	18.425	42,6	1.303	484	37,1	<0,001
55-59	36.675	16.920	46,1	1.849	762	41,2	<0,001
60-64	35.702	17.607	49,3	2.908	1.288	44,3	<0,001
65-69	31.823	15.353	48,2	3.747	1.598	42,6	<0,001
70-74	7.752	5.115	66,0	1.058	631	59,6	<0,001
	155.215	73.420	47,3	10.865	4.763	43,8	
	Males						
50-54	43.113	15.490	35,9	2.365	713	30,1	<0,001
55-59	33.443	13.024	38,9	3.413	1.156	33,9	<0,001
60-64	30.821	13.858	45,0	4.826	1.915	39,7	<0,001
65-69	26.406	12.409	47,0	5.844	2.489	42,6	<0,001
70-74	6.154	4.192	68,1	1.467	914	62,3	<0,001
	139.937	58.973	42,1	17.915	7.187	40,1	
	ROUND III (2012-2013)						
	Females						
50-54	47.200	24.803	52,5	1.443	633	43,9	<0,001
55-59	33.828	19.026	56,2	1.663	838	50,4	<0,001
60-64	31.112	18.777	60,4	2.520	1.361	54,0	<0,001
65-69	29.360	18.119	61,7	3.429	1.934	56,4	<0,001
70-74	11.678	9.307	79,7	1.610	1.227	76,2	0,001
	153.178	90.032	58,8	10.665	5.993	56,2	
	Males						
50-54	46.388	21.775	46,9	2.588	1.058	40,9	<0,001
55-59	30.911	15.341	49,6	2.991	1.283	42,9	<0,001
60-64	26.212	14.585	55,6	4.148	2.120	51,1	<0,001
65-69	23.691	14.255	60,2	5.230	2.886	55,2	<0,001
70-74	9.023	7.343	81,4	2.378	1.836	77,2	<0,001
	136.225	73.299	53,8	17.335	9.183	53,0	

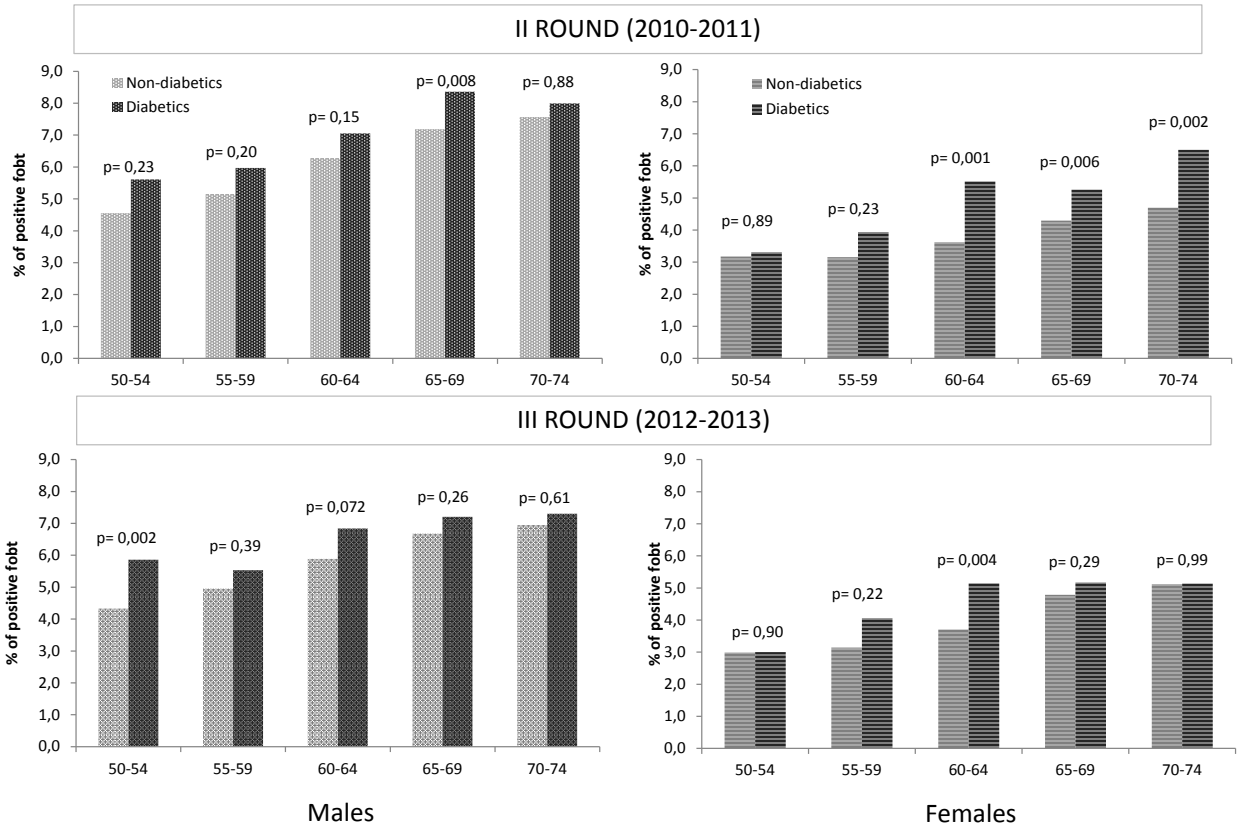
RESULTS

Overall, in the Italian region Friuli Venezia Giulia, 323,932 persons were invited for the colorectal cancer screening in round 2010-2011 and 317,403 in round 2012-2013. Of them, approximately 8.8% were diabetic. The proportions of persons who adhered to the invitation, stratified by age, sex, and diabetic status at the time of invitation are reported in Table 1. Overall, adherence was higher among females than among males and it increased from round 2010-2011 to round 2012-2013. Adherence also increased with age, but, within each age group, it was significantly lower among diabetics than among non-diabetics.

Figure 1 depicts the results of the FOBT among adherent persons. The proportion of positive FOBTs increased with age, was higher in men than in women and was slightly lower in round 2012-2013 than in round 2010-2011, and was higher among diabetics than among non-diabetics, in all age groups, although the difference was statistically significant only in some subgroups.

The results of colonoscopy in persons with positive

FIGURE 1. Positive FOBT among residents adherent to the invitation for the colorectal cancer screening in Friuli Venezia Giulia, Italy, 2010-2013, by screening round, sex, age class, diabetes status.



FOBT=fecal occult blood test

FOBT are shown in Table 2. Among diabetics, the detection rate for initial and advanced adenomas was higher than among non-diabetics, particularly in round 2010-2011. No clear pattern was observed for the detection of cancers.

Figure 2 summarizes findings from this study collapsing figures from the two rounds. Among residents with a positive FOBT, the frequency of detection of cancers and adenomas was similar between diabetics and non-diabetics.

DISCUSSION

This study showed that adherence to the colorectal cancer screening in the Italian region Friuli Venezia Giulia was lower in the diabetic population than among non-diabetics. On the other hand, the proportion of positive FOBT among subjects adhering to FOBT was higher among diabetics, especially in the former of the two rounds we analyzed. Among all the persons who adhered to the FOBT, the detection rate of adenomas was higher in the diabetic group. However, when considering only subjects with a positive FOBT, the proportion of those with detected adenoma was similar between diabetics and non-diabetics.

Two findings deserve particular attention. First, in this Italian region adherence to colorectal cancers screening in the diabetic population is lower than in non-diabetics. This is inconsistent with North American findings [11-13].

Differences in health system reimbursement policies, in cancer screening organization, in the use of screening by the population, and in the management of diabetic patients may explain the different findings in the US and in Italy. The reasons for the less-than-optimal management of diabetic patients needs to be investigated in our region. Public health professionals, general practitioners, and diabetologists should reconsider the diagnostic and therapeutic care pathway of diabetic patients and identify strategies (e.g., reminder systems, effective information and communication strategies [16]) that could be effective in this context in promoting screening adherence in this increased-risk population. Surveying both the diabetic population in the age group 50-74 and the physicians who provide care to diabetic patients may be a first step in this process.

The second important finding of this study is that the proportion of positive FOBTs and the adenomas detection rate were higher among diabetics than among non-diabetics. This suggests that pre-cancerous lesions are more common among diabetics and supports the idea that colorectal screening can be particularly effective in this group of patients. Dinh et al. reported that colorectal cancer screening is not cost-effective after age 70 in diabetics,

TABLE 2. Results of colonoscopy among residents with positive FOBT and adhering to the second-level examination in Friuli Venezia Giulia, Italy, 2010-2013, by screening round, age class, and diabetes status.

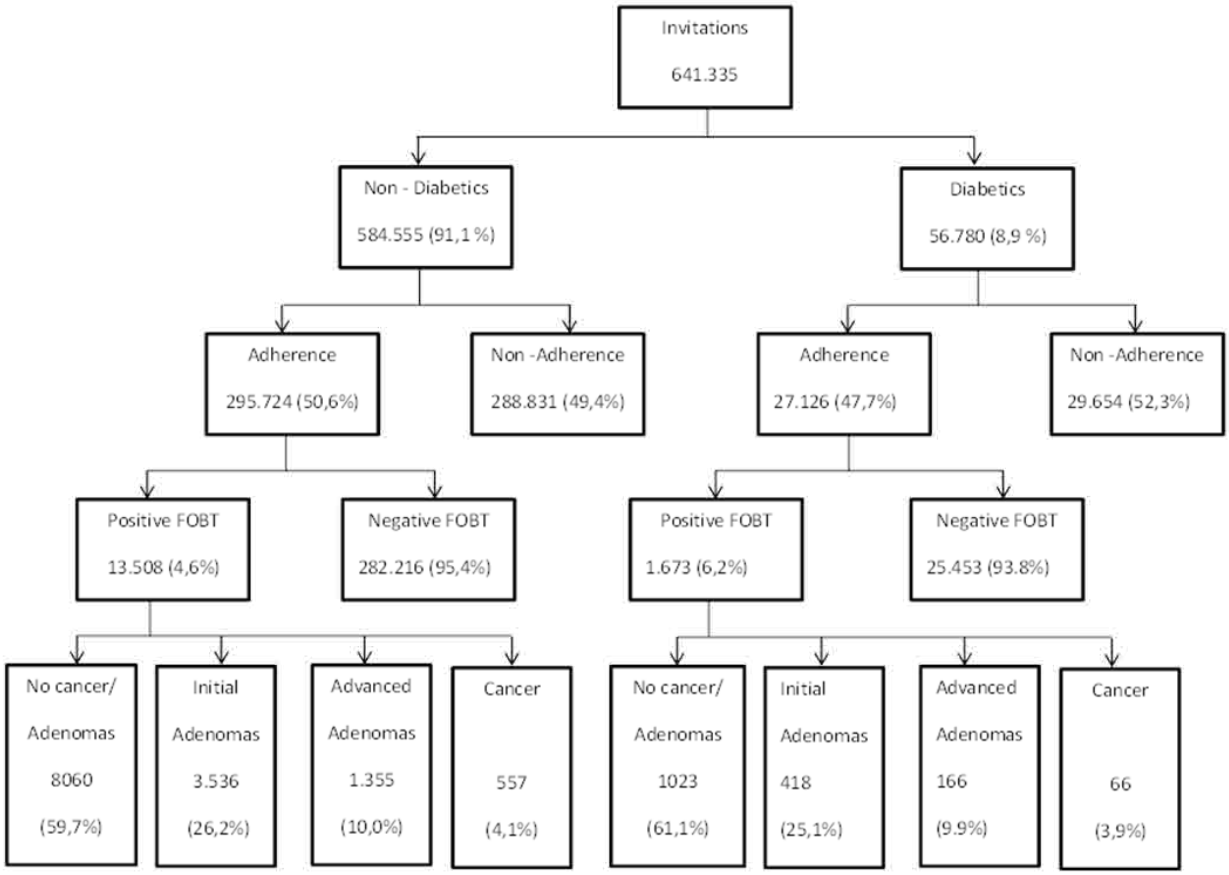
CLASSES OF AGE	NON-DIABETICS						
	PERSONS WITH A SCREENING EXAM	CANCER DIAGNOSIS N	ADVANCED ADENOMA DIAGNOSIS N	INITIAL ADENOMA N	DR FOR CANCER ‰	DR FOR ADVANCED ADENOMA ‰	DR FOR INITIAL ADENOMA ‰
	ROUND II (YEARS2010-2011)						
50-54	33.915	43	133	294	1,27	3,92	8,67
55-59	29.944	48	164	312	1,60	5,48	10,42
60-64	31.465	80	169	423	2,54	5,37	13,44
65-69	27.762	94	173	474	3,39	6,23	17,07
70-74	9.307	30	58	163	3,22	6,23	17,51
Total	132.393	295	697	1.666	2,23	5,26	12,58
	ROUND III (YEARS 2012-2013)						
50-54	46.578	41	138	368	0,88	2,96	7,90
55-59	34.367	49	130	346	1,43	3,78	10,07
60-64	33.362	54	141	419	1,62	4,23	12,56
65-69	32.374	83	147	478	2,56	4,54	14,76
70-74	16.650	35	102	259	2,10	6,13	15,56
Total	163.331	262	658	1.870	1,60	4,03	11,45
CLASSES OF AGE	DIABETICS						
	PERSONS WITH A SCREENING EXAM	CANCER DIAGNOSIS N	ADVANCED ADENOMA DIAGNOSIS N	INITIAL ADENOMA N	DR FOR CANCER ‰	DR FOR ADVANCED ADENOMA ‰	DR FOR INITIAL ADENOMA ‰
	ROUND II (YEARS2010-2011)						
50-54	1.197	2	5	12	1,67	4,18	10,03
55-59	1.918	3	13	32	1,56	6,78	16,68
60-64	3.203	11	20	62	3,43	6,24	19,36
65-69	4.087	15	29	75	3,67	7,10	18,35
70-74	1.545	3	13	27	1,94	8,41	17,48
Total	11.950	34	80	208	2,85	6,69	17,41
	ROUND III (YEARS 2012-2013)						
50-54	1.691	1	9	13	0,59	5,32	7,69
55-59	2.121	2	10	18	0,94	4,71	8,49
60-64	3.481	7	24	51	2,01	6,89	14,65
65-69	4.820	11	27	82	2,28	5,60	17,01
70-74	3.063	11	16	46	3,59	5,22	15,02
Total	15.176	32	86	210	2,11	5,67	13,84

FOBT=fecal occult blood test
DR=detection rate

based on US data [10]. Cost-effectiveness analyses with Italian data could be useful to guide screening decisions and to develop individualized screening recommendations in our context.

Our results imply that, in this region, there is room for improvement in diabetes care. Public health professionals, general practitioners, and diabetologists should not simply aim to manage glucose levels in persons with diabetes: they should

FIGURE 2. Summary of study design and findings of colorectal cancer screening in Friuli Venezia Giulia, Italy, 2010-2013.



FOBT=fecal occult blood test

instead look at these patients with a broader perspective.

This study has the advantage of using administrative health databases with complete coverage of the regional population, linkable with one another at the individual level respecting a patient's privacy. The use of administrative data also avoided recall bias that may be an issue in studies based on self-reports. The disadvantage of using administrative data is that information on a number of clinical, lifestyle, socioeconomic, cultural variables is not available, because those data are not routinely collected for administrative purposes. Thus, we could not adjust for the potential confounding effect that some of those variables might have on the association between screening participation and cancer incidence. For example, unhealthy diet, overweight, physical inactivity, ethnicity, which are all associated with diabetes incidence [17], might also affect screening participation, but we could not assess the influence of those factors on our results.

CONCLUSION

In conclusion, we observed that diabetic patients in Friuli Venezia Giulia undergo colorectal cancers screening less than non-diabetics, although they have a higher detection rate for adenomas. Efforts should be directed at improving the management of diabetic patients and at reducing the inequalities in access to care due to comorbidities.

Conflict of Interest

The authors declare that they have no conflict of interest.

This article does not contain any studies with human or animal subjects performed by any of the authors.

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