

Persistent Carcinoma in Cervical Cancer Screening: Non-Participation Is the Most Significant Cause

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Key Words

Cervical cancer screening · Carcinoma of the cervix · Screening history · Screening failures · Microinvasive carcinoma

Abstract

Objective: It was the aim of this study to determine the screening history of all invasive cervical carcinomas between 2004 and 2009 in one of the Federal States of Germany. **Study Design:** The pooled data sets of all in-state laboratories, corrected and supplemented by data of the State Cancer Registry, were used. The screening histories of all patients, their age and tumor types were collated and analyzed. **Results:** Of 617 patients with invasive carcinoma of the cervix, 373 (60%) had not had a cervical smear within the past 5 years. In 188 patients (31%), an incomplete screening history was found, whereas only 9% of women had participated regularly. In non-participants, late tumor stages (stage T1B and higher) were predominant and found in 86%. In contrast, in the group with regular screening histories more than half of all cases (54%) were microinvasive carcinomas (stage T1A) with excellent prognosis. Lack of follow-up or refusal of treatment by patients played a minor yet significant role. **Conclusions:** Non-participation is still by far the most common reason for persistent cases of cervical carcinoma in the German screening program.

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In the current discussion of future screening strategies for cervical carcinoma, much emphasis has been put on new technologies and its potential impact on the sensitivity and specificity of current screening programs [1–4]. However, only careful analysis of screening failures will give clues as to meaningful adjustments in existing programs. Yet, recent and reliable data on screening failures are limited. Furthermore, national screening programs are highly variable and require current and specific data for each individual country [5, 6]. Therefore, we analyzed the screening history of 617 patients with invasive carcinomas of the uterine cervix occurring between 2004 and 2009 in one of the Federal States of Germany.

Materials and Methods

The Federal State of Mecklenburg-Vorpommern is one of the 16 states of Germany, located on the Baltic Sea in the northeastern part of the country (fig. 1). With 1.6 million inhabitants, it is one of the lesser populated regions of the country. Currently, there are nine laboratories practicing in the state, processing approximately 350,000 smears per year. Since the year 2000, all invasive carcinomas of the cervix are to be reported to the State Quality Control Commission. In these cases, laboratories are required to provide all cytology reports for a period of 5 years preceding the diagnosis. For the current study, these data were collated and analyzed for the years 2004–2009. Subsequently, data were compared with figures of the State Cancer Registry. Thus, patients with cervical car-

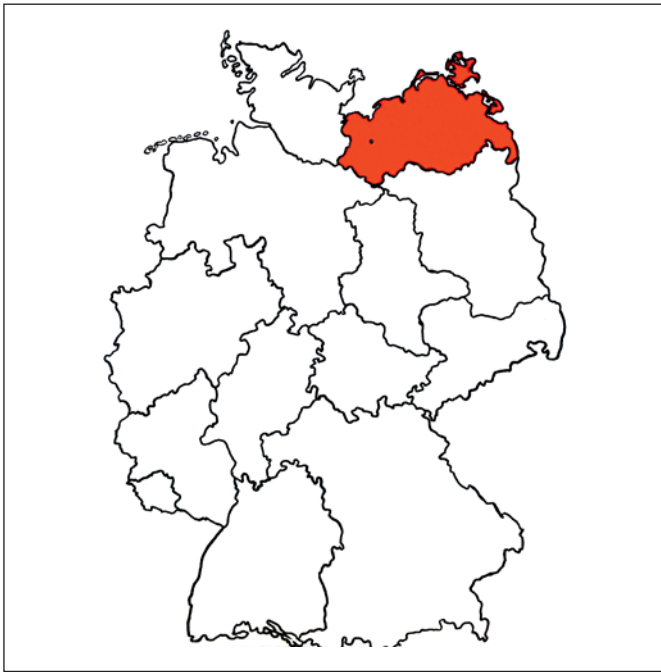


Fig. 1. Location of the Federal State Mecklenburg-Vorpommern within Germany.

cinoma were detected and included, whose smears were examined by out-of-state laboratories or who had not participated in cervical cancer screening at all. These patients were added to the data pool and their screening histories were determined by contacting their treating physicians. The data were analyzed with support of the staff of the State Medical Association. Screening participation was categorized according to one of the following three patterns: (1) regular screening history (yearly smears within the last 5 years); (2) irregular screening history (at least 1 smear within the last 5 years); (3) negative screening history (no smear within the last 5 years).

Results

In the 6-year period between 2004 and 2009, a total of 642 cases of invasive carcinoma of the uterine cervix had occurred in patients residing within the state. Of those, 366 cases were reported by in-state cytology laboratories. An additional 276 patients were identified by researching the data of the State Tumor Registry. For 11 patients, no information on tumor stage was available; 10 of those had not participated in screening at all, and 1 patient had been examined once in the last 5 years. Therefore, these 11 patients were excluded from further analysis. In another 14 patients, exact information on the screening history

Table 1. Screening history of patients with invasive cervical carcinoma

Year	Screening participation			Total
	regular	irregular	none	
2004	13	31	59	103
2005	10	30	71	111
2006	7	37	62	106
2007	7	30	41	78
2008	11	30	71	112
2009	8	30	69	107
Total	56	188	373	617
Percentage	9.1%	30.5%	60.4%	100%

could not be obtained. Feedback provided from treating physicians indicated that in all probability these women had not participated at all or only irregularly. These 14 patients were also excluded. Thus, for a total of 617 patients, complete data sets were available. They represent the study population.

The majority of patients with invasive cervical carcinoma had not been screened in the last 5 years (373 patients, 60%). In 188 patients (31%), an irregular screening history was found. Only 56 women (9%) had regularly participated in cervical screening in the last 5 years (table 1).

Among the entire study group of 617 patients, 141 patients (23%) presented with the early stage T1A1 and 12 patients with stage T1A2 (2%). In the group with regular screening, more than half of the patients (54%) were diagnosed with microcarcinoma (stage T1A). Stage T1B and higher was seen in 464 of 617 cases (75%), mostly in non-participants. In 21 cases, an 'advanced' carcinoma of the cervix was diagnosed without any further specification (table 2). The distribution according to histologic types is presented in table 3. As expected, squamous cell carcinoma dominates with 80%. In 15%, pure adenocarcinoma was diagnosed; mixed forms or other types were exceedingly rare. The age distribution shows the well-known 2-peak pattern with a first peak in the age group of 40–50 years and a second peak in old age (fig. 2).

Analysis of preceding cytologic diagnoses in the group of patients with regular or irregular screening histories reveals that close to 40% of patients did have significant findings, either smears with limited material or previ-

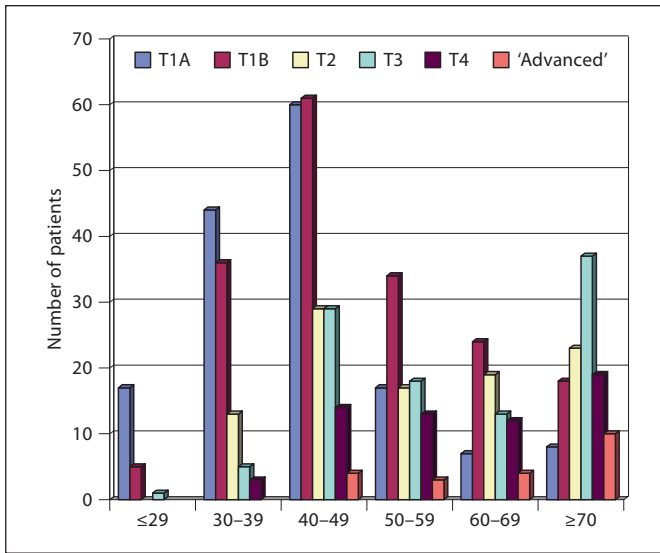


Fig. 2. Age (years) and stage distribution of all patients (n = 617).

ously abnormal smears (table 4). These findings point towards insufficient follow-up as another significant cause for screening failure.

Analysis of Screening Failure

In order to analyze the reasons for screening failure more closely, we examined the data sets of the 56 patients with regular participation in detail. There was a slight yet non-significant preponderance of adenocarcinoma (23 vs. 15%; table 3). Eleven of the 56 patients (20%) had their smears examined in out-of-state laboratories; among them, 5 patients with stages T3 and T4.

To narrow down the cases to true screening failures, we excluded the 30 patients with stage T1A, because the detection of microcarcinomas is still considered meeting the screening target because of its excellent prognosis [7]. In addition, we excluded 3 patients who did have positive smear diagnoses of high-grade disease, but were not followed and treated. Of the remaining 23 patients, 4 did have a cytologic diagnosis of low-grade disease, with 2 patients having biopsies. In a further 7 patients, there were suspicious or non-representative smears but follow-up was either negative or refused.

This leaves 12 patients (2%) who in our opinion represent true screening failures, i.e. regular participation with negative smears and development of an invasive cervical carcinoma of stage T1B or higher. The smears of these 12 patients were not rescreened, they were considered false negative.

Table 2. Tumor stage and screening history

Tumor stage	Screening participation			Total
	regular	irregular	none	
T1A1	26	67	48	141 (23)
T1A2	4	3	5	12 (2)
T1B	17	77	84	178 (29)
T2	4	25	72	101 (16)
T3	3	10	90	103 (17)
T4	2	3	56	61 (10)
'Advanced'	0	3	18	21 (3)
Total	56	188	373	617 (100)

Figures in parentheses are percentages.

Table 3. Histologic tumor type and screening history

Histologic tumor type	Screening participation			Total
	regular	irregular	none	
Squamous cell carcinoma	42	139	315	496 (80)
Adenocarcinoma	13	40	41	94 (15)
Mixed	0	5	7	12 (2)
Other	1	4	5	10 (2)
Unknown	0	0	5	5 (1)
Total	56	188	373	617 (100)

Figures in parentheses are percentages.

Table 4. Preceding cytologic diagnoses in patients with invasive carcinoma and regular or irregular participation

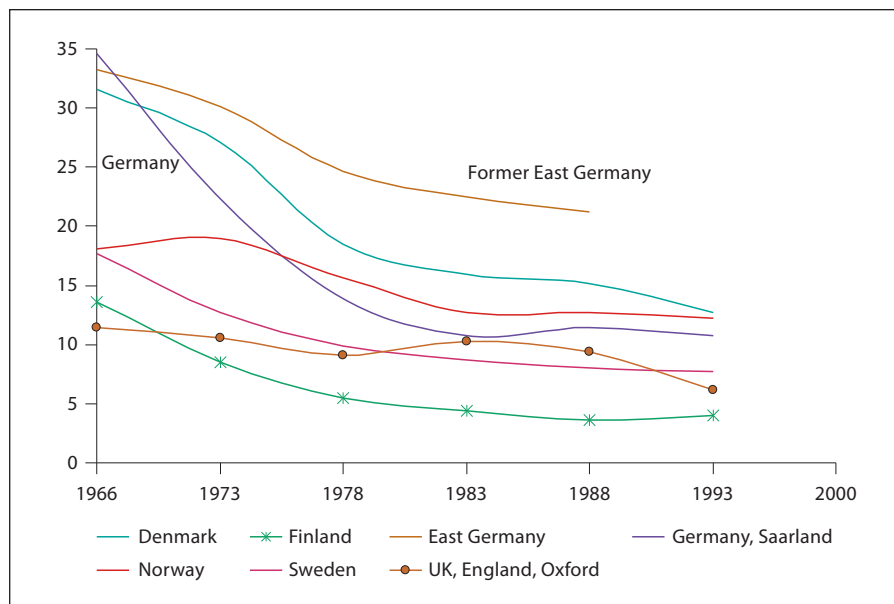
Screening participation	Previous abnormal smear	Limited material	Total
Regular (n = 56)	20	6	26 (46)
Irregular (n = 188)	48	22	70 (37)
Total (n = 244)	68	28	96 (39)

Figures in parentheses are percentages.

Discussion

Cervical screening by cytologic smear was introduced in Germany in 1971. The population coverage is 49% on a yearly basis, and 80% of the targeted population par-

Fig. 3. Age-adjusted incidence rate of invasive carcinoma of the cervix in Germany between 1966 and 1997, compared with other European countries. Note that only Denmark had similarly high initial incidence rates. Data sources: International Agency for Research on Cancer: Cancer Incidence in Five Continents (www.iacr.fr) and Gustafsson et al. [9].



ticipates at least once in 3 years [8]. Interestingly and significantly, the incidence of cervical carcinoma before screening was much higher in former West Germany as well as in former East Germany than in almost all other European countries [9, 10]. In the State of Mecklenburg-Vorpommern, part of former East Germany, the incidence was very high: 38.9 per 100,000 women in 1969 [11], i.e. 2–3 times higher than the figures in Finland, England or Sweden (fig. 3). The incidence has since decreased by >70% to 11.9 in 2008, testifying to a functioning screening system. In view of the current debate on alternative screening strategies [4, 12, 13], it was our goal to examine the reasons for screening failure in the state in order to provide very recent and reliable data as a basis for further discussion.

The majority (60%) of invasive cervical carcinomas occurred in non-participants. These patients did not have a single smear within the last 5 years. An additional 31% of patients were seen only irregularly. Only 9% had regularly participated according to the guidelines of the program.

These data are confirmed and remarkably similar to data in some recent studies from other countries. Among 1,230 cases of invasive cervical carcinoma in Sweden, 64% of patients had not been examined in the last 6 years [14]. In studies from California, 56% of 833 patients with cervical carcinoma had not participated in screening for at least 3 years [15, 16]. In 877 cases of cervical cancer reported from New South Wales, Australia, 67% had not

had a cervical smear within the 4 years before diagnosis [17]. In France, two thirds of 524 cervical carcinomas had not been examined cytologically for at least 3 years before diagnosis [18]. In an analysis of the Dutch national data, it was concluded that non-participation was the main reason for persistent occurrence of cervical carcinoma despite a well-organized screening program [19].

Similarly, the shift to prognostically more favorable stages in the screened population is confirmed in most studies. Cuzick [7] even suggests considering T1A carcinomas as screening successes and to exclude them from the group of failures because of their excellent prognosis. In our study, more than half of all patients (54%) of regularly screened patients were T1A cases. Yet, in the group with irregular screening histories, the proportion dropped to 37%, and in non-participants, to only 14%. In a group of French patients, the ratio of T1A tumors was 24% if a single smear was examined within the last 3 years, whereas it was only 4% in patients with complete lack of screening [18].

A second significant reason for failure was lack of follow-up or patient refusal to address suspicious or positive cytologic findings (table 4). In close to 40% of participating patients, there were either non-representative smears or outright significant positive findings. Subsequent repeat smears were either negative or patients refused further follow-up or treatment. A small group of patients strongly believe in alternative medicine and completely refuse any invasive therapies.

In summary, our data of a retrospective study of a well-defined, well-documented and very recent group of patients with invasive cervical carcinoma indicate that the majority of persistent carcinomas of the cervix occur in non-participants. Therefore, we agree with the conclusions drawn by Spayne et al. [20], based on data of the Ontario program in Canada, that the failure to detect the remaining cases of invasive cervical cancer in an established screening program can largely be attributed to a lack of participation.

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