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Professional paper

Cervical Cancer in Croatia: State of the Art and Possibilities for Prevention

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A B S T R A C T

In Croatia, there are about 355 incident cases and about 100 deaths from cervical cancer every year. The aim of this study is to present the trends of cervical cancer incidence and mortality and to propose preventive strategies for cervical cancer in Croatia. Age-standardised and age-specific cervical cancer incidence rates were calculated for the period 1985–2004. For cervical cancer mortality data, the WHO Mortality Database was used. After an early decrease of cervical cancer incidence and mortality following the introduction of opportunistic screening in Croatia, no further decrease has been observed since the 1990s. An increase in incidence over the last 20 years was observed in the age-groups 40–44 and 45–49 years. To reduce cervical cancer rates, an organised cervical cancer screening programme is essential. In addition, HPV vaccination should be introduced in the school vaccination programme to achieve further reductions in cervical cancer incidence in the future.

Key words: *cervical cancer, prevention, Croatia*

Introduction

Cervical cancer is the second most common female cancer worldwide with about 493,000 incident cases per year, and it is the most common female cancer in Africa, South America and Asia[1]. There are about 273,000 cervical cancer deaths in the world yearly, 85% of which take place in developing countries[1]. In Europe, there are about 50,000 new cases, and about 25,000 deaths yearly[2]. The majority of incident cases occur between ages 30 and 50. The highest incidence of cervical cancer in Europe is observed in Eastern European countries. As a consequence of cervical cancer screening by Papanicolaou (Pap) smear, cervical cancer incidence and mortality rates have been decreasing over the last three decades in most of the European countries. In countries with organised cervical cancer screening programmes, cervical cancer is usually the 10th most common female cancer[1–3].

The Croatian population as assessed by the 2001 census was 4.4 million[4]. The annual cancer incidence is about 20,000 cases and cervical cancer is the 8th most common female cancer in this country. There are on average 355 new cases, and about 100 deaths each year[5,6]. Croatia has a lower cervical cancer incidence than most Central and Eastern European countries, but it is still much higher than in countries with organised cervical cancer screening programmes[1]. Relative 5-year survival of cervical cancer patients in Croatia diagnosed in the period 1994–1998 was 74%[7].

A possibility for primary prevention of cervical cancer is vaccination against the Human papillomavirus (HPV) that has been identified as a necessary cause of cervical cancer[8]. About 60% of cervical cancer cases are attributed to HPV type 16, and additional 10–20% to HPV type 18 infection[9–12]. The currently available HPV vaccines that have recently been approved in the US and Europe, protect against the oncogenic HPV 16 and HPV 18 (quadrivalent HPV [types 6, 11, 16, 18] recombinant vaccine GARDASIL®, Merck and Co.). Because the genital types of HPV are primarily transmitted by sexual contact, the optimal age for vaccination of girls is before the onset of sexual activity. Vaccination of males has not been considered cost-effective[13–15]. The report on GARDASIL® efficiency provided to the US Food and Drug Administration and the European Medicines Agency, states that the vaccine can reduce HPV 16 or 18 related cervical intraepithelial neoplasia grade 2 and 3 (CIN 2/3) or adenocarsinoma *in situ* (AIS) by 39.0% (95% CI: 23.3–51.7), while reducing treatment rates for any CIN by 16.5% (95% CI 2.9–28.2)[13,14].

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The current HPV vaccines will not prevent all oncogenic HPV infections and therefore cannot replace the traditional cervical cancer screening. However, screening methods and intervals may be modified to account for changes in population risk for the development of this disease[15–18].

Historically, cervical cancer screening by Pap smear, when followed by adequate therapy, has been proven to substantially reduce cervical cancer incidence and mortality. Following the introduction of such effective programmes, cervical cancer incidence and mortality has been reduced by more than 80% particularly in British Columbia and the Nordic countries[19]. The Pap smear was introduced in the mid 1940s, and entered wider use in the late 1950s. Organised national cancer screening programmes are currently available only in 8 EU countries (Finland, Denmark, Iceland, Italy, Norway, Sweden, Slovenia and UK). The European guidelines specify that cervical cancer screening programmes should target the age-group 25–64 years[20–22]. The International Agency for Research on Cancer (IARC) also recommends the introduction of HPV-DNA screening within organised programmes in such a way that the efficacy and effectiveness can be evaluated[9].

Croatia does not have an organised national cervical screening programme. Following the recommendations for cervical cancer screening in Europe, a Working Group of the Croatian Ministry of Health and Welfare has proposed a national cervical cancer screening programme, although this has not yet been introduced[23]. The proposed programme comprises screening of women aged 25–64 years every three years by Pap smear in the first phase. In the second phase of the programme, in addition to Pap smear, HPV test would be introduced for women aged 30–64, with five-year screening intervals[23].

The aim of this study was to present the trends of cervical cancer incidence and mortality between 1985 and 2004 in Croatia, and to propose preventive strategies for cervical cancer in Croatia.

Materials and Methods

The source of data on cervical cancer mortality in Croatia for the period 1985–2004 was the WHO mortality database[24]. Only the data for cervical cancer (ICD-10 code C53), without data on death associated to »Uterus not otherwise specified« (NOS) (ICD-10 code C55) are presented. However, the data on cervical cancer deaths are likely to be underestimates since there are over one hundred deaths per year from cancer of uterus NOS in Croatia and a proportion of these will be due to cervical cancer as well. For the data on cervical cancer incidence, we used the Croatian National Cancer Registry data[5]. To calculate the age-specific rates for the year 1985, we used the Croatian population census for 1981; for the period 1986–1995 we used the Croatian population census for 1991; and for the period 1996–2004, we used the Croatian population census for 2001[4,25,26]. Age-standardised rates of cancer incidence in Croatia for the period 1985–2004 were calculated by the direct standardization method, using the World standard population as a reference[27].

Results

The age-standardised cervical cancer incidence rates show a decreasing trend until the year 1991 but no further consistent decrease in cervical cancer incidence has been observed afterwards. The age-standardised rates of cervical cancer mortality remained at a low level during the entire period but no decrease was observed over the last decade (Figure 1).

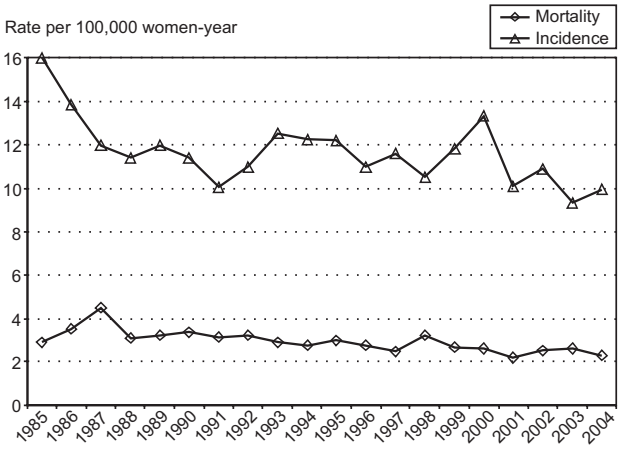

Fig. 1. World age-standardised rates (ASRW per 100,000 women-year) of cervical cancer incidence and mortality in Croatia, 1985–2004.

Table 1 shows the age-specific rates of cervical cancer in Croatia for the age-groups targeted by the proposed screening programme[23]. In the age groups between 25–39 years, a decreasing trend of cervical cancer incidence is observed. An increase of cervical cancer incidence over the last 20 years has been observed in the age-groups 40–44 and 45–49 years. In the age groups between 50 and 64 years, a decrease of cervical cancer incidence is observed, which is most prominent in the age group 60–64, being over 5-fold over the 20-year period.

Discussion

Opportunistic cervical cancer screening was introduced in Croatia in the 1960s and this was accompanied by decreasing cervical cancer incidence and mortality trends through to 1991. However, no substantial further decreases in cervical cancer incidence and mortality were observed subsequently (Figure 1). The largest decrease of cervical cancer incidence over time is observed in women between 25 and 39 years of age (Table 1). In addition to a higher awareness of the importance of preventive medical examinations in these women, this could be accounted for by opportunistic screening in scope of gynecological examinations for either pregnancy or con-

TABLE 1
AGE-SPECIFIC INCIDENCE RATES (PER 100,000 WOMAN-YEARS) OF CERVICAL CANCER IN CROATIA IN THE PERIOD 1985–2004

Year	Age-group							
	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64
1985	9.4	22.6	38.7	17.7	20.7	28.7	39.1	66.1
1986	10.6	14.4	17.5	22.5	36.8	31.7	36.4	40.0
1987	10.0	15.0	19.1	17.8	29.1	24.6	32.1	36.7
1988	7.1	18.8	14.2	17.8	16.9	31.7	25.9	35.4
1989	15.3	15.5	20.2	18.4	23.0	24.6	31.4	42.0
1990	10.6	13.8	24.6	26.7	16.1	16.8	25.3	26.9
1991	5.9	18.3	20.2	18.4	26.1	16.2	18.5	30.2
1992	5.3	14.4	17.5	27.2	23.8	17.5	25.3	28.2
1993	11.8	17.7	38.8	26.7	19.9	25.3	21.0	23.0
1994	9.4	17.7	27.3	26.7	29.1	22.0	20.3	31.5
1995	7.1	15.5	26.2	34.9	30.7	22.7	26.5	26.2
1996	6.2	10.9	21.4	32.4	24.2	20.5	30.6	24.8
1997	9.6	13.6	30.9	30.0	24.2	19.8	19.0	21.2
1998	6.2	11.5	20.2	28.2	25.4	19.1	25.6	25.5
1999	6.9	20.3	21.4	25.2	21.8	23.8	32.2	33.3
2000	11.0	21.7	29.0	29.4	39.9	23.8	22.3	23.3
2001	7.5	12.9	30.9	28.2	21.8	18.5	13.2	21.9
2002	4.8	16.9	25.8	26.4	23.0	29.0	16.5	24.1
2003	4.8	10.8	18.3	24.6	25.4	19.8	23.9	18.4
2004	5.5	9.5	22.7	21.6	34.5	22.4	28.1	12.0

traceptive use counselling. However, the lack of a decreasing trend in women between 40 and 49 years of age is more worrying, since this age-group comprises over a quarter of the incident cervical cancer cases in Croatia (Table 1). Meanwhile, the decrease of incidence in age-groups 50–64 probably reflects higher awareness of postmenopausal women about the importance of gynecological examinations (Table 1).

The available evidence indicates that opportunistic cervical cancer screening in Croatia has had an impact. The number of Pap smears taken yearly is still increasing and reached 433,671 in 2005. However, in the absence of an organised population-based programme it is difficult to assess the efficacy of this screening and it is clear that a large proportion of target population still remains un-screened or under-screened[23].

In spite of the decrease of cervical cancer incidence following its introduction, opportunistic screening is not an optimal method for the prevention of this disease as it tends to overscreen the wealthy and well-educated while under-screening the less affluent and minorities, thereby creating inequalities in the healthcare that is delivered to the population[20]. The only way to resolve this problem and to achieve further reductions in cervical cancer cases is through the introduction of an organised cervical cancer screening programme. Following the introduction of such programmes, cervical cancer incidence and mortality has been reduced by more than 80% particularly in British Columbia and the Nordic countries (Finland, Denmark, Iceland, Norway and Sweden)[19]. In addition, organised screening programmes are the only way that countries will be able to derive the maximum benefit from the new HPV vaccines that will soon be launched in Croatia.

Conclusion

There is now a very urgent need to move forward with the introduction of a comprehensive organised cervical cancer prevention programme in Croatia. Indeed, this is the only way that we will be able to further reduce cervical cancer rates while providing equitable, cost-effective protection to all the women of Croatia.

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RAK VRATA MATERNICE U HRVATSKOJ: POSTOJEĆE STANJE I MOGUĆNOSTI ZA PREVENCIJU

SAŽETAK

U Hrvatskoj godišnje oko 355 žena obolijeva, a oko 100 umire od raka vrata maternice. Cilj ovog rada bio je prikazati trendove incidencije i mortaliteta od raka vrata maternice u Hrvatskoj te predložiti strategije za prevenciju. Izračunate su dobno-standardizirane i dobno-specifične stope incidencije raka vrata maternice za razdoblje 1985–2004. Za podatke o mortalitetu od raka vrata maternice koristili smo bazu podataka Svjetske zdravstvene organizacije. Nakon ranog pada incidencije i mortaliteta od raka vrata maternice u Hrvatskoj koji je pratio uvođenje oportunističkog probira, daljnji pad se ne primjećuje nakon 1990-ih godina. Opažen je porast incidencije u zadnjih 20 godina u dobnim skupinama 40–44 i 45–49 godina. Da bi se smanjile stope incidencije i spriječile smrti od raka vrata maternice, potrebano je što prije uvođenje organiziranog programa probira. Da bi se postiglo daljnje smanjenje incidencije raka vrata maternice, potrebno je također uvođenje cjepiva protiv humanog papilomavirusa (HPV) u program obaveznog cijepljenja školske djece.