Clinical and Experimental HEPATOLOGY

Clin Exp HEPATOL 2018; 4, 1: 13–27
DOI: https://doi.org/10.5114/ceh.2018.73669
Received: 30.07.2017, **Accepted:** 21.09.2017, **Published:** 09.02.2018

Original paper

The epidemiology of hepatocellular cancer in Poland

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Abstract

Introduction: This article summarize the available data on hepatocellular carcinoma (HCC) epidemiology in Poland. Data regarding the HCC incidence rate are divergent. Statistical data presented by NFZ appear more credible in that matter than data published by the Polish Oncology Center (POC).

Material and methods: The analysis included data from the Polish Bibliography Database (GBL), the Polish National Health Fund Institution (NFZ), the scientific paper "Malignant neoplasms in Poland" issued by POC and the central liver transplant registry maintained by the Polish transplant coordinating center "Poltransplant" (2010-2015).

Results: Data regarding the HCC incidence rate are divergent. Statistical data presented by NFZ appear more credible in that matter than data published by POC.

Conclusions: The occurrence of HCC in Poland is at the average European level and is similarly rising. The incidence rate is underestimated. It is due to faulty epidemiology data collection techniques. The highest risk group comprises men over the age of 50 with concomitant liver cirrhosis. The most common HCC etiology is HCV infection.

Key words: liver transplantation, hepatocellular carcinoma, chronic liver disease.

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Introduction

Hepatocellular carcinoma (HCC) is prevalent globally, currently ranking 5th amongst malignant tumors and 3rd as their cause of death. It is prominently increased in the sub-Saharan region and in Asiatic countries, but some Western countries (e.g. USA, Europe, Australia) and Mediterranean regions are of no rare exception. Global HCC morbidity is constantly rising. Its main etiology is attributed to liver cirrhosis. Post-inflammatory HBV cirrhosis historically concerned Asiatic countries, while Western countries were dominated by post-alcoholic and HCV-related liver cirrhosis. It is presumed that over 50% of all HCC cases are diagnosed in China [1, 2]. Nowadays, wealthy countries such as Japan, South Korea and Taiwan represent a newer trend. Owing to the widely introduced hepatitis-B vaccination program, but leaning towards hepatitis-C morbidity increase (according to global tendencies), increase of alcohol intake and having a vast population with metabolic syndrome and diabetes, the proportions between etiological factors are shifting and resemble those of the Western countries [1-8].

According to the seemingly more reliable data from the USA, throughout the past 30 years HCC morbidity has significantly increased, doubling in the last 20 years [1]. The annual incidence rate increased and exceeded 18 000 cases at the end of the century [7]. Between 1999 and 2010 in the USA alone, the incidence rate increased by 3.7%.

According to WHO data, Poland, Western Europe, USA and Australia belong to a group with a low HCC

incidence rate, ranging from 2.5 to 4.9 per 100 000 [4, 5]. Those data are approximated and based on reporting of primary liver cancer classified as C22 (ICD 10), consisting of hepatocellular carcinoma and cholangiocellular carcinoma. In the majority of countries cholangiocellular carcinoma is responsible for 10% of primary liver cancer or less. Thailand is an exception to that rule, having higher rates of cholangiocarcinoma due to frequent schistosomiasis in that region [1, 2]. Mortality increases alongside HCC morbidity.

Different geographic regions present with a diverse HCC mortality. In Cameroon HCC mortality constitutes 1/3rd of all oncology-related deaths, seemingly not exceeding 5% [1, 2] in Western Europe and USA. Mean survival time is expected to be one year [9]. Without effective treatment it decreases to 5 months; 1 and 3-year survival rates are 20.9% and 5.7% [1, 2]. In Poland, between 2000 and 2002, 1, 3 and 5-year survival rates were 23%, 10.9%, 7.9%, respectively, and were three times higher than in the general population with other malignant neoplasms [10]. Disheartening data from official registries do not always correspond with clinical sample data, hence new better therapies result in improved, over previously cited, outcomes [1, 4]. On the other hand, only a small fraction with diagnosed HCC is committed to potentially therapeutic treatment [1, 7, 8, 11]. Such low survivability is related to insignificant clinical symptoms in early phases, the aggressive nature of the disease and coexisting liver failure. Onset of clinical symptoms heralds deep clinical progression at the point when therapeutic options are already severely narrowed down [1, 11]. Moreover, in western countries peak morbidity falls at 75 years old and after. In Asia, a much younger population is involved due to high incidence of hepatitis B virus (HBV) infection in childhood [1, 2, 7, 8].

In an overwhelming majority of countries the primary liver cancer incidence rate is higher in men. The ratio between men and women ranges from 2 : 1 to 4 : 1 [1, 2, 7, 8, 12]. Likewise, male mortality attributed to HCC is higher. Major differences are seen in countries with highest HCC incidence rates [1]. It is believed to be due to a higher overall HCC cancer rate in men and higher exposure to risk factors in men. Men more often have B/C viral hepatitis, they consume alcohol, smoke and are in danger of metabolic syndrome [1, 13]. The HCC incidence rate varies not only among geographical locations but also among different populations inhabiting the same area. For example, in the USA, the incidence rate in Caucasian White is two times lower than in Latino and Afro-Americans. That seems to be related to altering viral hepatitis susceptibility in different ethnic groups [1, 14].

The aim of the study was to present Polish epidemiologic data regarding HCC and its dynamics based on the recent scientific literature.

Material and methods

The annual HCC incidence rate and rate of liver transplant secondary to HCC in the total transplant group were assessed.

Analysis included data from the Polish Bibliography Database (GBL), the Polish National Health Fund Institution (NFZ), the scientific paper "Malignant neoplasms in Poland" issued by the Polish Oncology Center (POC) and the central liver transplant registry maintained by Polish transplant coordinating center "Poltransplant" (2010-2015).

References regarding HCC in Polish language are sparse. The results of the search "hepatocellular carcinoma" in the GBL database showed 237 titles published in 1991-2014 [15], mostly in English. In comparison, the same search run on PubMed showed over 75 thousand published papers. Publications in Polish were outweighed by book chapters, case reports and overview papers. Only a small minority were original publications reviewing the diagnosis and treatment of HCC, but not epidemiology. According to that, only the latter 3 sources of listed data were used. Although the process of publishing the above-mentioned data was slightly delayed, the information contained was found to be useful to illustrate the epidemiology and determine HCC etiology in Poland.

Epidemiology data acquired from NFZ pertain to 2008-2013 and consider new cases and their onset according to geographical region. The general crude incidence rate and rate for each county were calculated using Polish demographic data [16], regarding the years 2008, 2010, 2011, 2013 (Fig. 1).

Available epidemiologic data from POC were based on reports from 2006, 2008, 2009, 2013, 2015 and statistical data from 2002 to 2013 [10, 17-20]. It consisted of data concerning the incidence rate and mortality (including division according to geographic location, age, gender, crude and standardized incidence rates) (Figs. 2-4).

Corresponding to NFZ statistical data, the crude incidence rate and mortality in geographic regions other the years 2006, 2010, 2011 and 2013, were assessed (Figs. 5, 6).

Based on the mortality and new cases onset in years 2006, 2010, 2011 and 2013 and according to geographic region, mortality rate was calculated as a result of a quotient of the above. Furthermore, based on data from POC, incidence and mortality rate were calculated for age groups encompassing a 5 years each

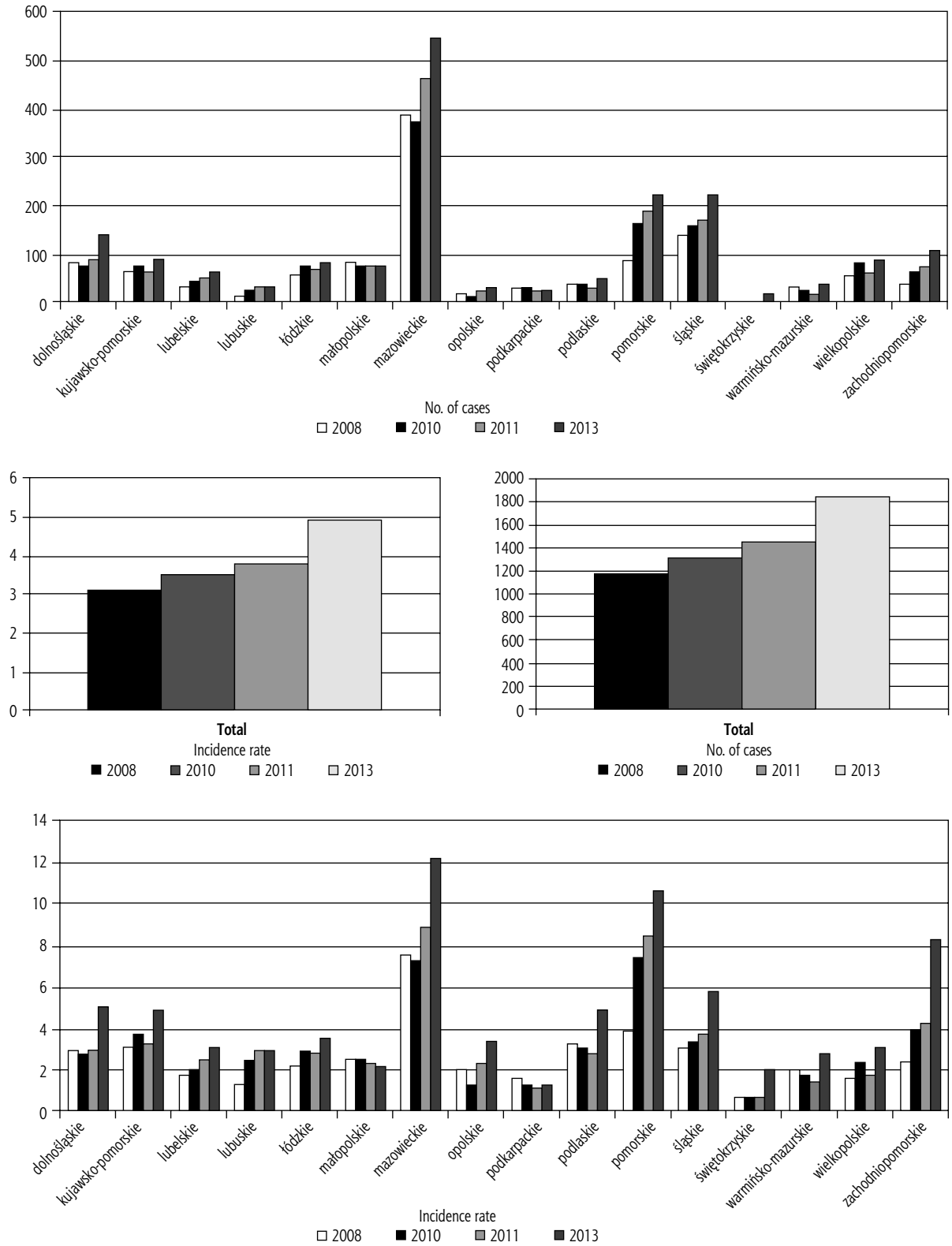


Fig. 1. Data from Polish National Health Fund Institution (NFZ) and Central Statistical Office (Polish: Główny Urząd Statystyczny – GUS) – number of hepatocellular carcinoma cases in years 2008-2013 according to geographic region; incidence rate calculated for both genders (per 100 000 of general population). The data regarding number of cases originated from NFZ and the demographic data from GUS yearly statistical reports [23, 24]

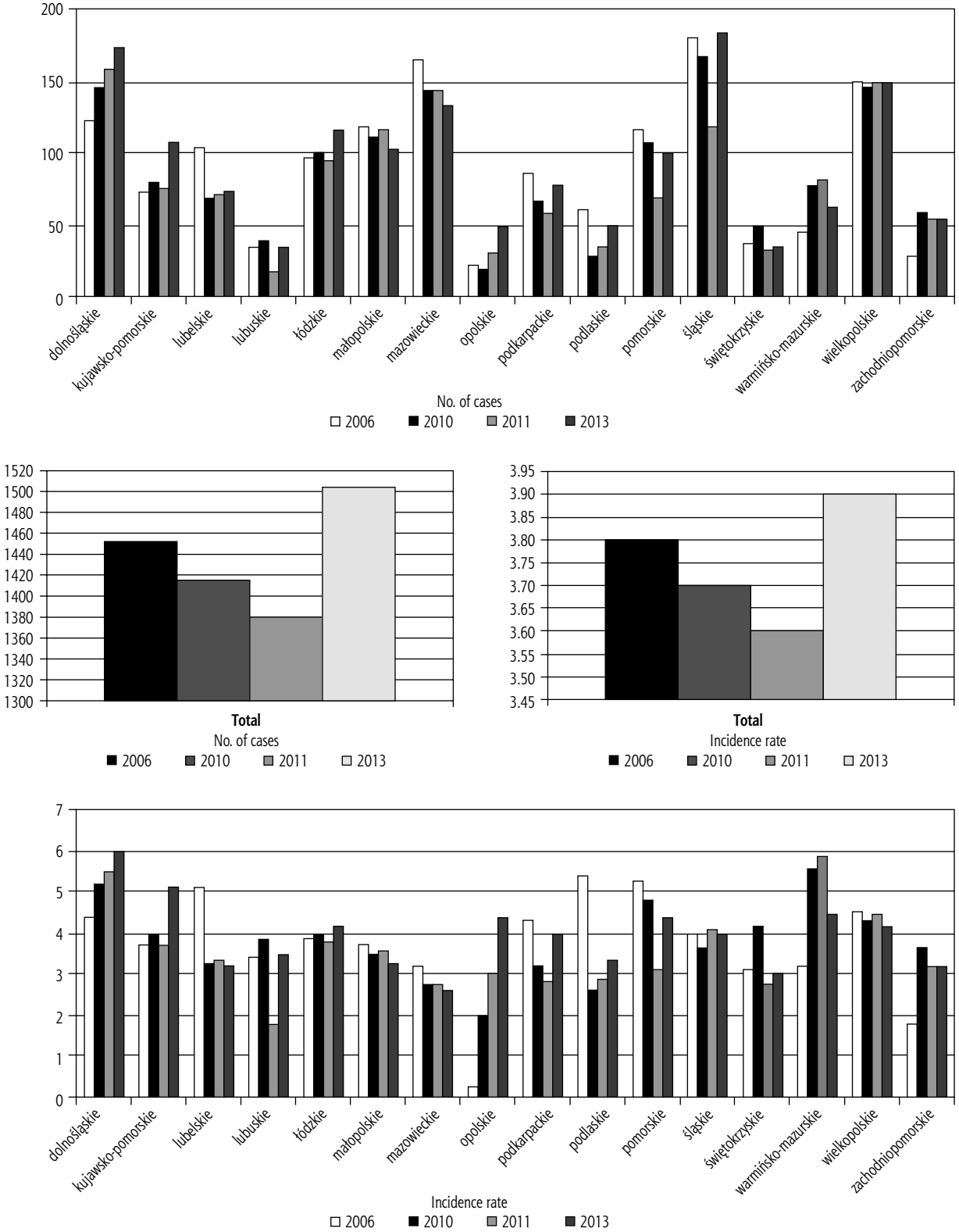
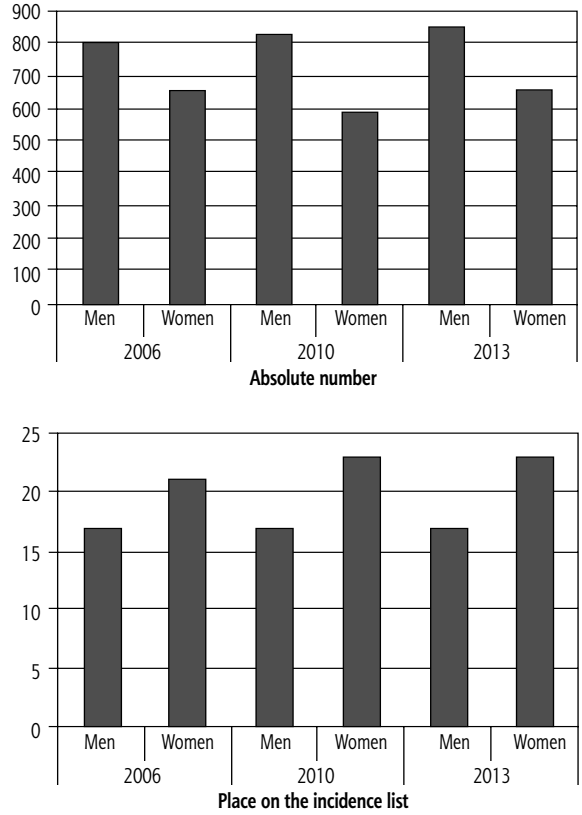


Fig. 2. Data from Polish Oncology Center (POC) and Central Statistical Office (Polish: Główny Urząd Statystyczny – GUS) – hepatocellular carcinoma total number of cases and incidence rate according to geographic region in years 2006, 2010, 2011 and 2013. Data concerning number of cases derived from POC, demographic data from GUS yearly statistical reports [16, 17, 19, 20]



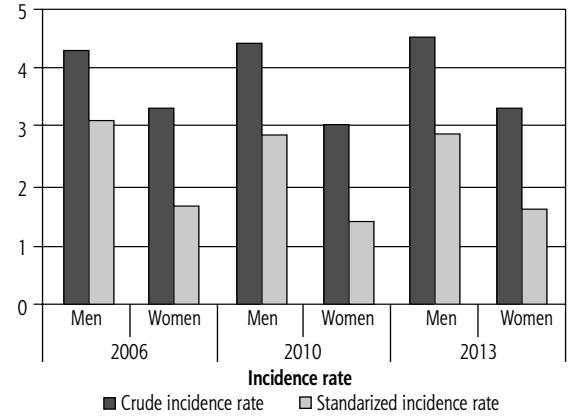
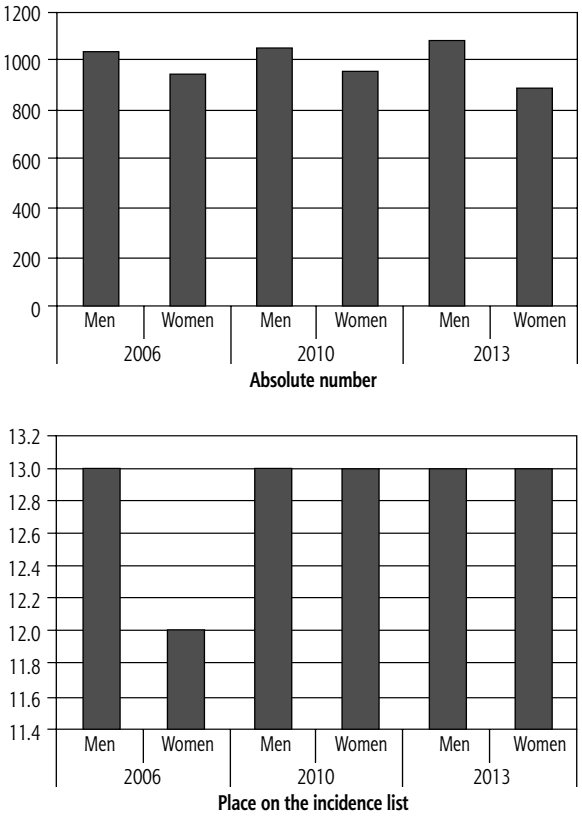


Fig. 3. Data from Polish Oncology Center (POC) – hepatocellular carcinoma incidence among men and women; absolute case numbers, incidence rate cruel and standardized, position on the neoplasm incidence list [17]



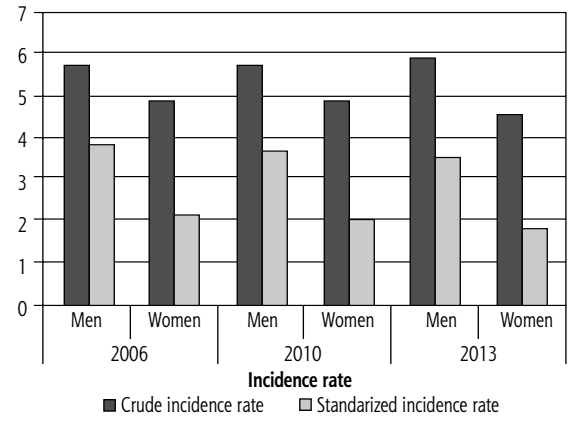


Fig. 4. Data from Polish Oncology Center (POC) – hepatocellular carcinoma mortality among men and women in 2006, 2010, 2013; absolute case numbers, incidence rate cruel and standardized, position on the neoplasm incidence list [17]

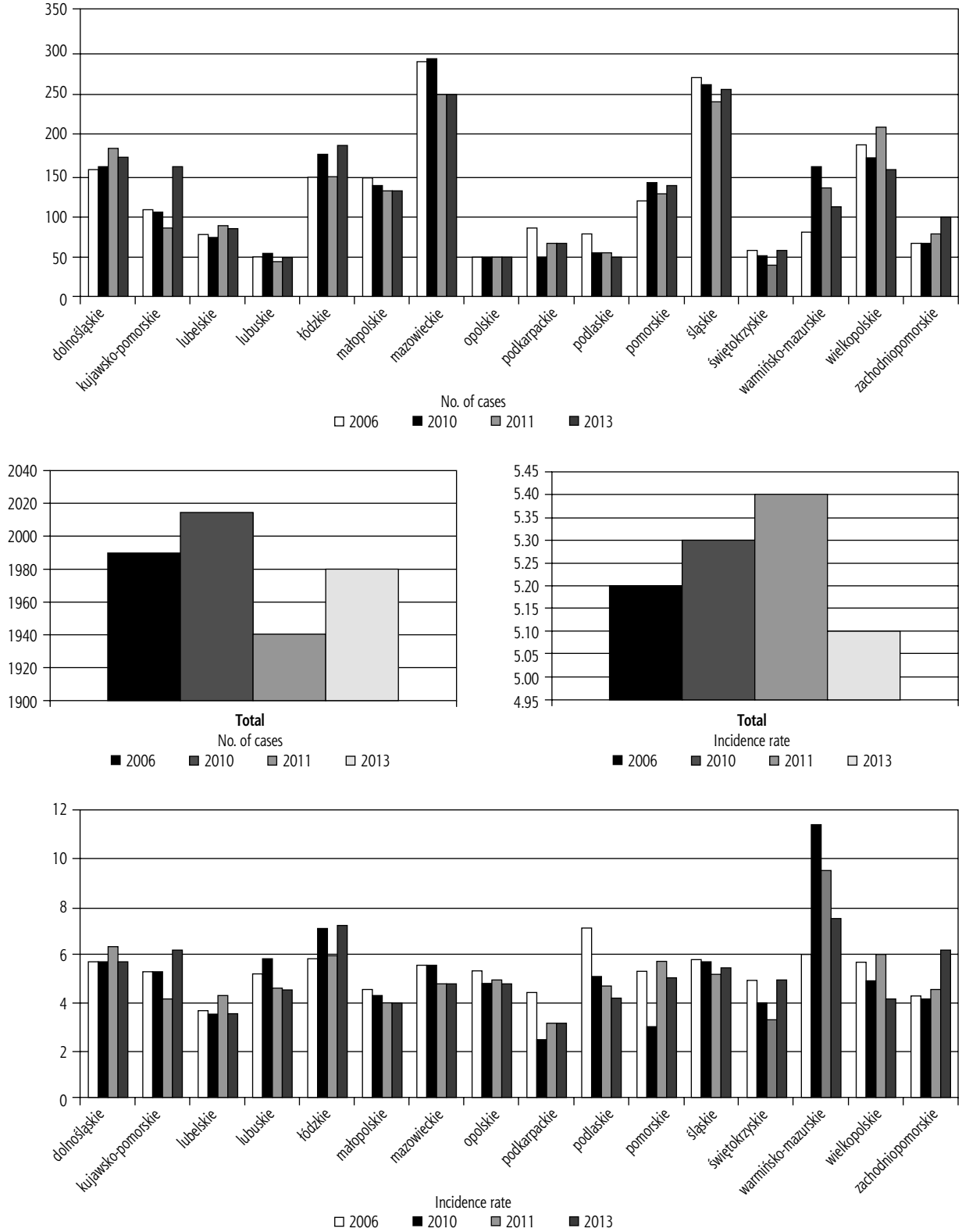


Fig. 5. Data from Polish Oncology Center (POC) and Central Statistical Office (Polish: Główny Urząd Statystyczny – GUS) – hepatocellular carcinoma mortality, mortality rate according to geographic region, years 2006, 2010, 2011 and 2013. Data concerning number of cases derived from POC, demographic data from GUS [16, 17, 19, 20]

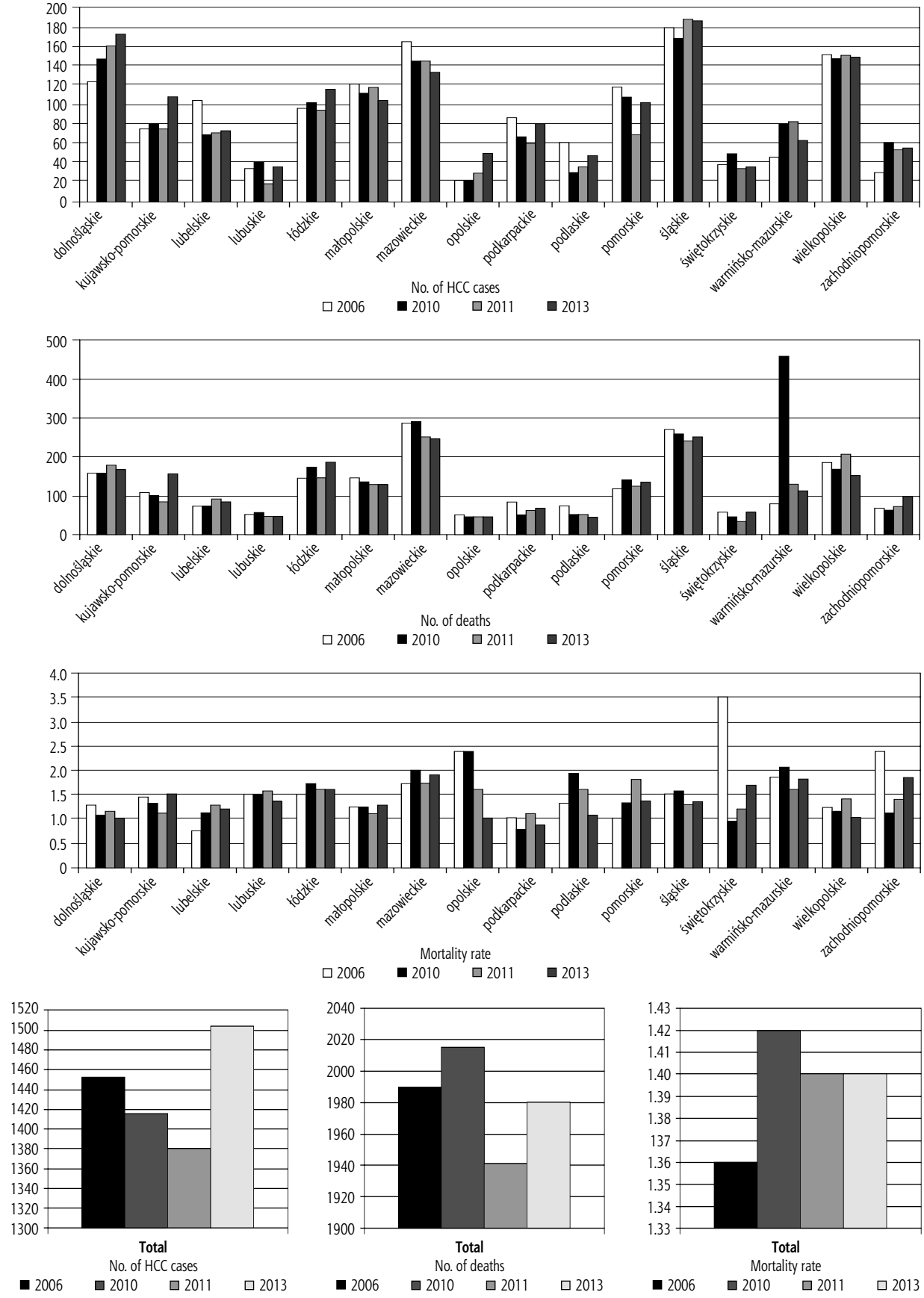


Fig. 6. Data from Polish Oncology Center (POC) – hepatocellular carcinoma incidence rate and mortality according to geographic region, years 2006, 2010, 2011 and 2013 [17, 19, 20]

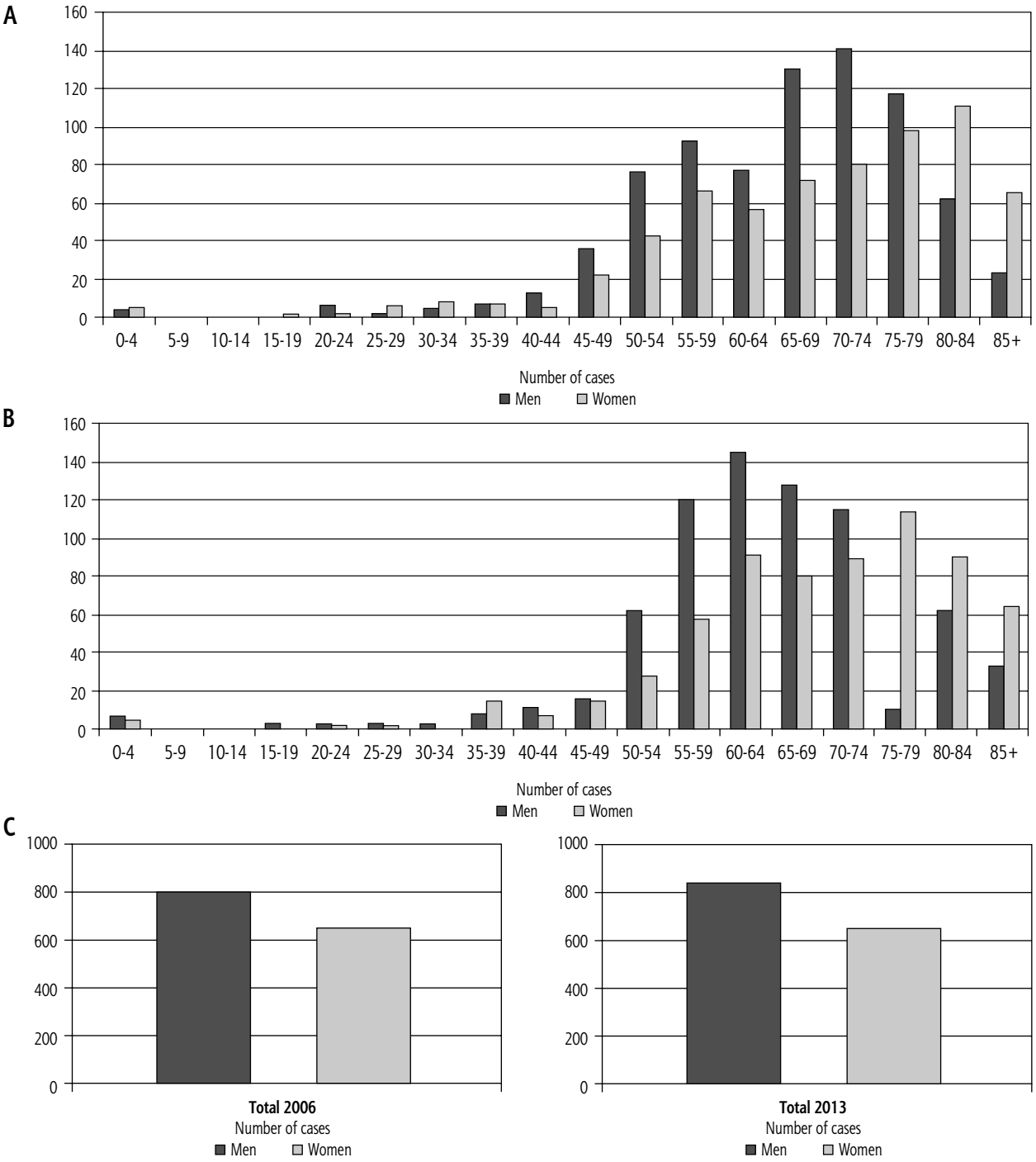


Fig. 7. Data from Polish Oncology Center (POC) – hepatocellular carcinoma incidence rate among men and women in 2006 **(A)** and 2013 **(B)** [17]; according to age. Total number of cases **(C)**

(Figs. 7, 8). Similar analysis was performed on NFZ data regarding the years 2010, 2011 and 2013.

Poltransplant data were analyzed according to the quantity of HCC-related liver transplants and etiology of liver cirrhosis leading to cancer. The analysis allowed us to establish the percentage contribution of particular etiological factors relating to HCC in Poland [21, 22] (Fig. 9).

Results

Comparison of hepatocellular carcinoma incidence rates in women, 2006 vs. 2013

There was a significant decrease in incidence rate in women aged 30-34 (Table 1). All comparisons between 2006 and 2013 groups performed using χ^2 Pearson test.

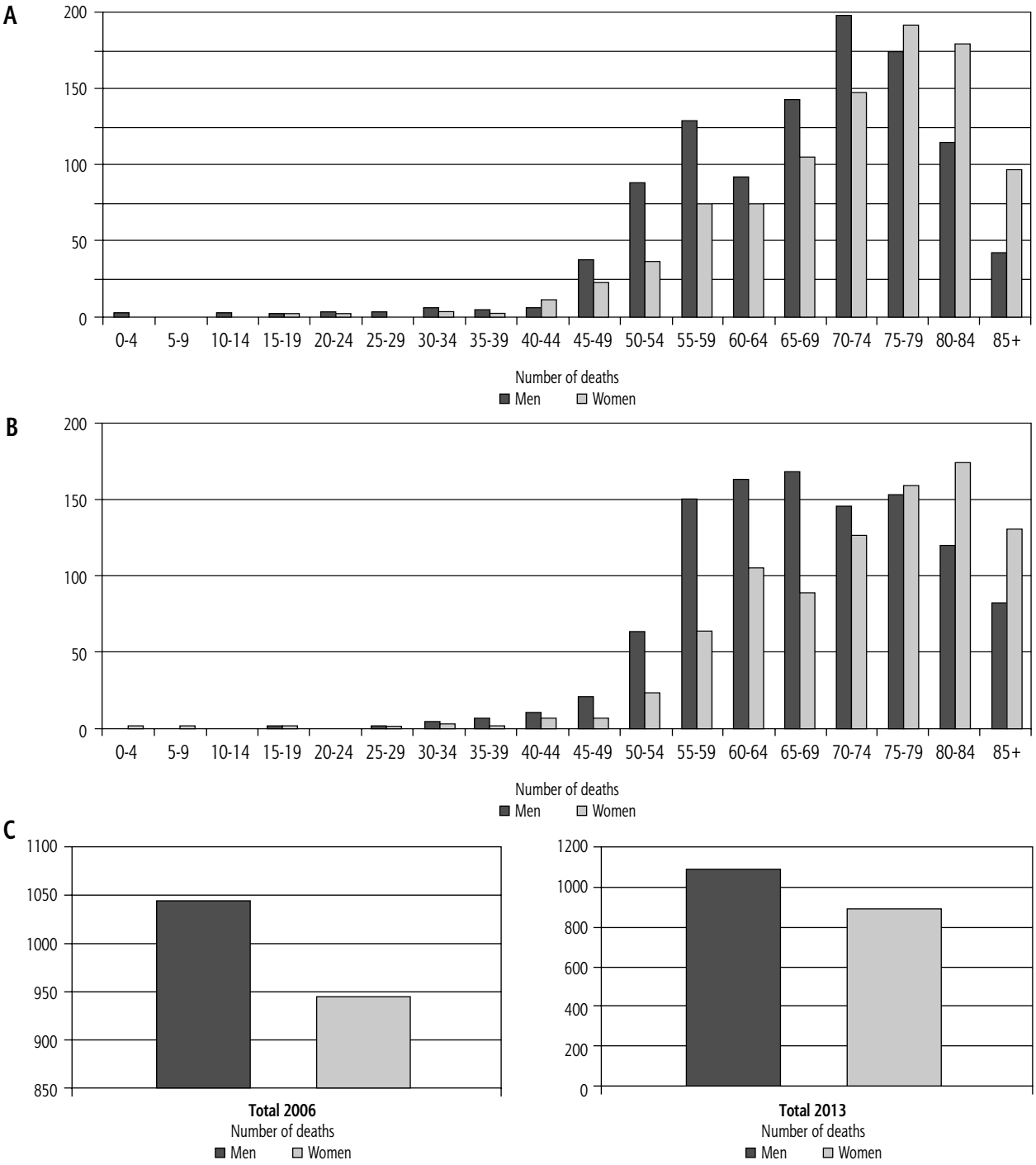


Fig. 8. Data from Polish Oncology Center (POC) – hepatocellular carcinoma mortality among men and women in 2006 **(A)** and 2013 **(B)** [11]; according to age. Total number of deaths **(C)**

Comparison of hepatocellular carcinoma incidence rates in men, 2006 vs. 2013

There was a significant decrease in incidence rate in men aged 45-49. There was a significant increase in incidence rate in men aged 60-64 (Table 2). All comparisons between 2006 and 2013 groups performed using χ^2 Pearson test.

Comparison of hepatocellular carcinoma incidence rates between genders, 2006 vs. 2013

The change in incidence rate in men and women in 2006 vs. 2013 was statistically significant (Table 3). All comparisons between 2006 and 2013 group performed using χ^2 Pearson test.

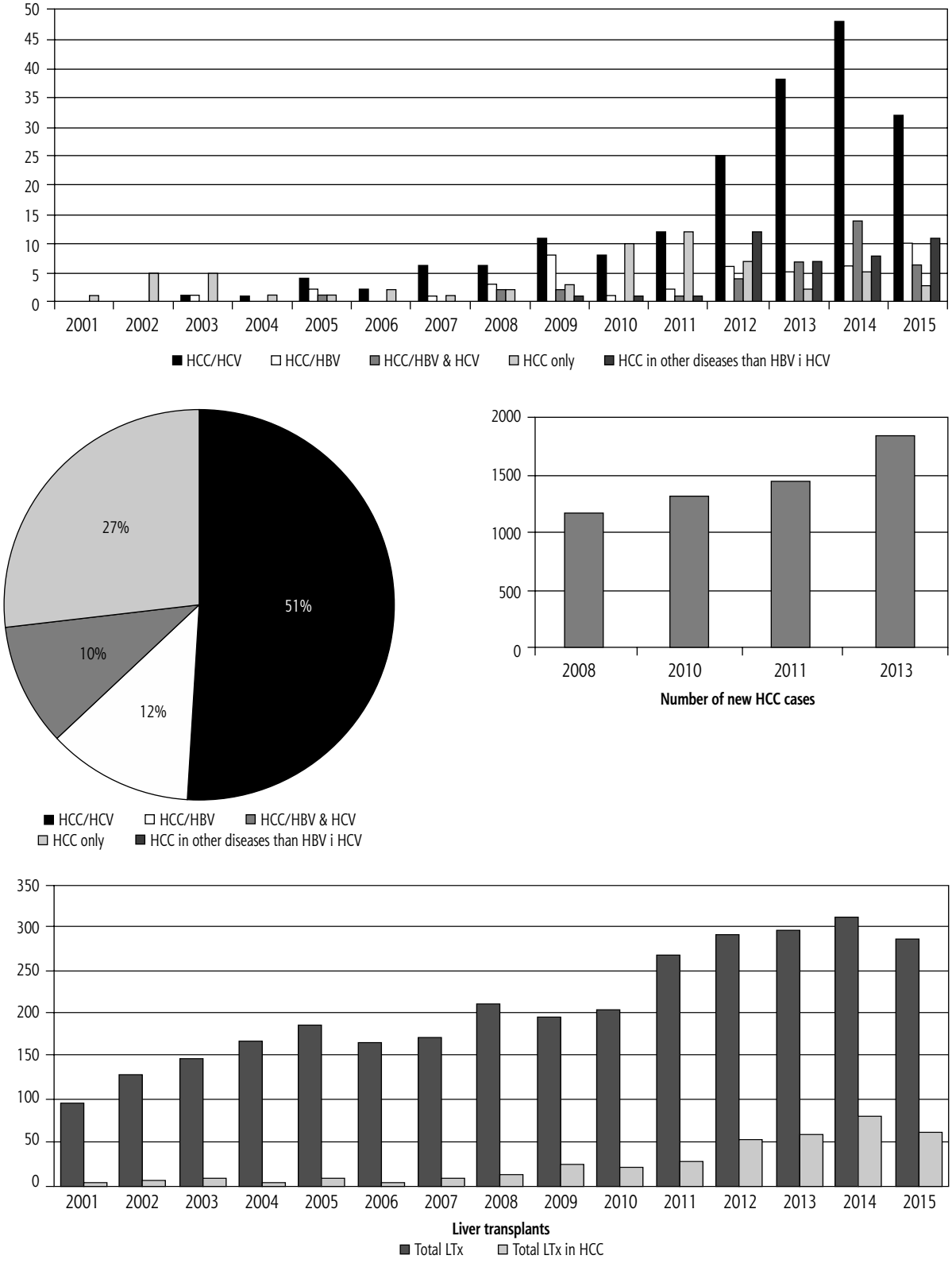
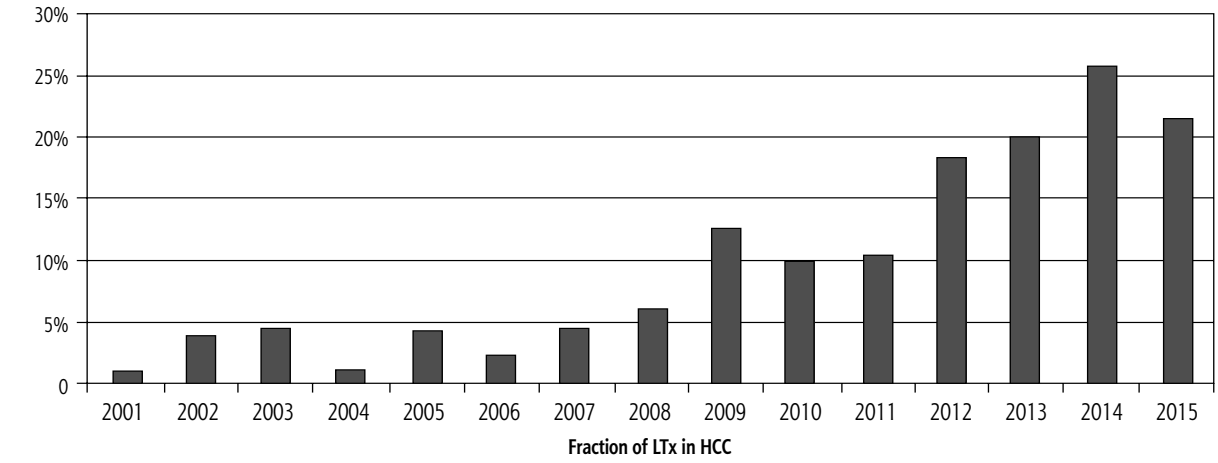


Fig. 9. Poltransplant data regarding hepatocellular carcinoma (HCC) treatment with liver transplantation (LTx) in Poland concords with the tendencies noted by European Liver Registry (ELTR)



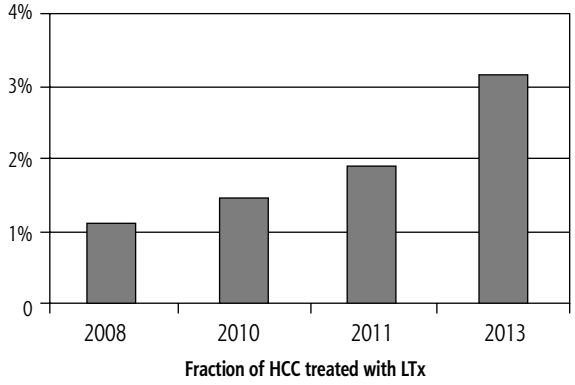


Fig. 9. Cont.

Comparison of hepatocellular carcinoma mortality between in women, 2006 vs. 2013

There was a significant decrease in mortality at age 45-49 and 75-79. There was a significant increase in mortality at age 60-64 and 85+ (Table 4). All comparisons between 2006 and 2013 group performed using χ^2 Pearson test.

Comparison of hepatocellular carcinoma mortality between in men, 2006 vs. 2013

There was a significant decrease in mortality at age 45-49 and 70-74. There was a significant increase in mortality at age 60-64 and 85+ (Table 5). All comparison between 2006 and 2013 group performed using χ^2 Pearson test.

Comparison of hepatocellular carcinoma mortality between genders, 2006 vs. 2013

No statistically significant differences were found (Table 6). All comparison between 2006 and 2013 group performed using χ^2 Pearson test.

Treatment of hepatocellular carcinoma with liver transplantation

HCC treatment with liver transplantation (LTx)was associated with early recurrence at first. In spite of the above-mentioned reservation, nowadays LTx has become a standard method of treatment, presenting the best prognosis. It is strongly associated with the introduction of Milan criteria introduced in 1996 by Mazzaferro.

Poltransplant data regarding HCC treatment with LTx in Poland concords with the tendencies noted by European Liver Registry (ELTR).

In 2001, the percentage of liver transplantation in treatment of HCC was equal to 1.1, while in 2015 it exceeded 21% and was even 25.8% a year before. Although the number of liver transplants in the HCC group increased, the total number of transplants is still trifling. In 2013, transplanted patients with HCC constituted a group of only 3.2% of the new cases.

Discussion

Data regarding the HCC incidence rate are divergent. Statistics presented by POC showed even a slight

Table 1.

Age group	Incidence rate		χ^2	*p**
	2006	2013		
0-4	5	5	–	–
5-9	0	1	–	–
10-14	0	1	–	–
15-19	2	0	–	–
20-24	2	2	–	–
25-29	6	2	2.00	0.157
30-34	9	0	9.00	0.003
35-39	7	15	2.91	0.088
40-44	5	8	0.69	0.405
45-49	22	15	1.32	0.250
50-54	43	28	3.17	0.075
55-59	67	58	0.65	0.421
60-64	57	92	8.22	0.004
65-69	72	81	0.53	0.467
70-74	81	90	0.47	0.491
75-79	98	114	1.37	0.242
80-84	111	91	1.98	0.159
85+	66	65	0.01	0.930
Total	653	668	0.17	0.680

**Nonparametric χ^2 Pearson test*

Table 2.

Age group	Incidence rate		χ^2	*p**	OR**
	2006	2013			
0-4	4	7	0.82	0.366	
5-9	0	0	–	–	
10-14	0	1	–	–	
15-19	1	3	1.00	0.317	
20-24	6	3	1.00	0.317	
25-29	2	3	0.20	0.654	
30-34	5	3	0.50	0.480	
35-39	7	9	0.25	0.617	
40-44	13	12	0.04	0.841	
45-49	37	16	8.32	0.004	0.43
50-54	77	63	1.40	0.237	
55-59	93	121	3.66	0.056	
60-64	78	146	20.64	< 0.001	1.87
65-69	131	128	0.03	0.852	
70-74	141	115	2.64	0.104	
75-79	118	111	0.21	0.644	
80-84	63	63	–	–	
85+	24	33	1.42	0.233	
Total	800	847	0.84	0.630	

**Nonparametric χ^2 Pearson test.*
***Odds ratio (OR > 1 increase in risk, OR < 1 decrease in risk)*

Table 3.

Age group	Incidence rate 2006		Incidence rate 2013		χ^2	*p**	Φ-Yule
	Men	Women	Men	Women			
0-4	4	5	7	5	0.40	0.5283	0.019
5-9	0	0	0	1	–	–	–
10-14	0	0	1	1	–	–	–
15-19	1	2	3	0	3.00	0.0833	0.500
20-24	6	2	3	2	1.03	0.3105	0.086
25-29	2	6	3	2	1.59	0.2070	0.123
30-34	5	9	3	0	4.10	0.0429	0.241
35-39	7	7	9	15	0.57	0.4516	0.015
40-44	13	5	12	8	0.63	0.4278	0.017
45-49	37	22	16	15	1.03	0.3092	0.011
50-54	77	43	63	28	0.59	0.4407	0.003
55-59	93	67	121	58	3.26	0.0711	0.010
60-64	78	57	146	92	0.46	0.4991	0.001
65-69	131	72	128	81	0.48	0.4898	0.001
70-74	141	81	115	90	2.44	0.1182	0.006
75-79	118	98	111	114	1.24	0.2658	0.003
80-84	63	111	63	91	0.76	0.3822	0.002
85+	24	66	33	65	1.09	0.2964	0.006
Total	800	653	837	668	0.09	0.7610	0.000

**Nonparametric χ^2 Pearson test*

Table 4.

Age group	Deaths		χ^2	*p**	OR**
	2006	2013			
0-4	0	1	–	–	
5-9	0	1	–	–	
10-14	0	0	–	–	
15-19	1	1	–	–	
20-24	2	0	–	–	
25-29	0	1	–	–	
30-34	3	3	–	–	
35-39	2	1	–	–	
40-44	11	7	0.89	0.346	
45-49	22	7	7.76	0.006	0.32
50-54	36	23	2.86	0.091	
55-59	74	63	0.88	0.347	
60-64	74	105	5.37	0.021	1.42
65-69	104	89	1.17	0.280	
70-74	148	126	1.77	0.184	
75-79	192	159	13.70	< 0.001	0.83
80-84	179	174	0.07	0.790	
85+	97	130	4.80	0.029	1.34
Total	945	891	1.59	0.208	

**Nonparametric χ^2 Pearson test*
***Odds ratio (OR > 1 increase in risk, OR < 1 decrease in risk)*

Table 5.

Age group	Deaths		χ^2	*p**	OR**
	2006	2013			
0-4	1	0	–	–	
5-9	0	0	–	–	
10-14	1	0	–	–	
15-19	1	1	–	–	
20-24	3	0	–	–	
25-29	3	1	1.00	0.317	
30-34	6	4	0.40	0.527	
35-39	5	6	0.09	0.763	
40-44	6	11	1.47	0.225	
45-49	37	21	4.41	0.036	0.57
50-54	88	64	3.79	0.052	
55-59	129	150	1.58	0.209	
60-64	92	163	19.70	< 0.001	1.77
65-69	143	168	2.01	0.156	
70-74	198	145	8.19	0.004	0.73
75-79	175	153	1.48	0.224	
80-84	115	120	0.11	0.744	
85+	42	82	12.90	< 0.001	1.95
Total	1045	1089	0.91	0.341	

**Nonparametric χ^2 Pearson test*
***Odds ratio (OR > 1 increase in risk, OR < 1 decrease in risk)*

Table 6.

Age group	Deaths 2006		Deaths 2013		χ^2	*p**	Φ-Yule
	Men	Women	Men	Women			
0-4	1	0	0	1	–	–	–
5-9	0	0	0	1	–	–	–
10-14	1	0	0	0	–	–	–
15-19	1	1	1	1	–	–	–
20-24	3	2	0	0	–	–	–
25-29	3	0	1	1	1.88	0.1709	0.375
30-34	6	3	4	3	0.15	0.6963	0.010
35-39	5	2	6	1	0.42	0.5148	0.030
40-44	6	11	11	7	2.33	0.1267	0.067
45-49	37	22	21	7	1.29	0.2560	0.015
50-54	88	36	64	23	0.17	0.6792	0.001
55-59	129	74	150	63	2.22	0.1358	0.005
60-64	92	74	163	105	1.23	0.2668	0.003
65-69	143	104	168	89	2.98	0.0844	0.006
70-74	198	148	145	126	0.85	0.3560	0.001
75-79	175	192	153	159	0.12	0.7248	0.000
80-84	115	179	120	174	0.18	0.6738	0.000
85+	42	97	82	130	2.63	0.1047	0.008
Total	1045	945	1089	891	2.47	0.1160	0.001

**Nonparametric χ^2 Pearson test*

decrease in incidence rate throughout 2006-2011. During that time the aggregated crude mortality rate decreased from 3.8 to 3.6 (Table 2). According to POC, the other standardized and crude incidence rates in that period, regarding both men and women, are stable or in slight decline (Table 5). That seems uncanny considering the fact that various world sources confirm a constant increase [12, 18, 25-28]. In Poland's closest neighbor, Germany, the HCC incidence rate has increased by 50% during the last 30 years [7]. Similarly, in the US the incidence rate increased by 4% during the last 10 years. Even more surprisingly, standardized and crude mortality rates did not rise, as against world tendencies [1, 2]. Are we living in a country with an overall lowered HCC incidence rate, or are the statistical data inaccurate? The mortality ratio, represented by the quotient of mortality to incidence rate, in all other cases smaller than 1, in the case of data presented by POC ranges between 1.36 and 1.42, exceeding even that in some counties (Table 4). World mortality rates are close to the incidence rate, but their ratio hardly reaches 1 [1]. In the case of POC reports it has been established that such a situation is most likely due to underreporting of new HCC cases (only 70% of new cases reported) [20]. Habior, after analysis of these data, reached the same conclusion [29].

Statistical data presented by NFZ appear more credible in that matter. Firstly, they showed that the overall incidence rate over the years 2008-2011 increased from 3.09 to 3.8 per 100 000 population, reaching in 2013 4.9/100 000. Similarly, the absolute number of new cases grew (Table 1). Secondly, those data are based on financial records submitted by hospitals for a refund, and hence are meticulously checked. Likewise in POC data, the mortality ratio was slightly higher than 1 and there has been a significant difference in the number of cases reported yearly in certain counties (Tables 1 and 2), according to both POC and NFZ. It leads to the conclusion that the data gathering process for HCC incidence was somehow faulty. Although the presented discrepancy can be attributed to defective reporting, the differences of incidence rate in certain counties is hard to explain. The highest calculated incidence rate based on NFZ data concerned the counties Mazowieckie and Pomorskie, and the lowest concerned Świętokrzyskie and Podkarpackie. Calculated rates based on POC data remained different. Counties of high incidence rate were Dolnośląskie and Warmińsko-mazurskie, the lowest Opolskie (in 2010) and Lubelskie (in 2011) (Table 2). According to Polish papers there are no significant regional differences in main HCC etiologic factor occurrence – HCV/HBV infection [30]. This proves undeniably that faulty data gathering techniques are at work. But this can be explained in a more trivial way too. Perhaps patients with diagnosed HCC are referred from certain geographical regions to more experienced centers located in Mazowieckie and Pomorskie counties and the system registers the place of their treatment, not residence. The most agreeable find is that the incidence rate is highest in older men. It concurs with observations made by other authors around the world [1, 2, 7, 8, 12]. Increased cancer risk in men occurs after 50 with a peak at 75-84 years of age. It is less intensified in women and shifted toward later age with a maximum at age over 80. Likewise, HCC mortality is highest in men after 50 with a peak after 80. Such high mortality in advanced age is correlated with other disease morbidity typical for that age [1, 7]. Nevertheless, increased HCC incidence rates after age 45 should be taken into account while developing prophylactic screening strategies. Currently, such screening is not implemented on a wide scale and only performed by selected, more "aware" centers.

Herein noted significantly lower incidence rates (2006-2013) in men and women at age 30-49 can be attributed to higher awareness of the population regarding proper screening and better efficacy of HCC treatment.

The increased incidence rate among men aged 60-64 goes hand in hand with higher mortality in both men and women and is in line with European trends. Those may be only incidental though and require further confirmation in the years to come.

Conclusions

The occurrence of HCC in Poland is at the average European level and is similarly rising. The incidence rate is underestimated. It is due to faulty epidemiology data collection techniques. The highest risk group comprises men over the age of 50 with concomitant liver cirrhosis. The most common HCC etiology is HCV infection.

The percentage of liver transplantation secondary to HCC increases every year. When properly following the Milan criteria, this method offers the best possible HCC treatment modality.

Disclosure

Authors report no conflict of interest.

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