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Incidence and types of canine tumours in Croatia

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ABSTRACT

Neoplastic diseases are among the leading health concerns in medicine. As such, epidemiological studies considering canine tumours are beneficial in understanding the patterns of tumour occurrence. The aim of this study was to analyze data on the occurrence of canine tumours in Croatia. From 1 January 2006 to 31 December 2009, a total of 1568 tumours were diagnosed after routine biopsy submission or necropsy. The WHO classification was used for designating tumour type. Most tumours (59.1%) were malignant, 35.4% were benign, while the remainder (5.29%) were treated as not specified. Tumours originated from the skin and subcutis (45.73%), mammary gland (21.75%) and genital system (7.97%). The most common specific tumour types diagnosed were mammary tubulopapillary carcinoma (7.14%), mast cell tumour (4.91%) and fibrosarcoma (4.91%). Differences in tumour occurrence in dog populations from inland and coastal areas were negligible in all but mammary tubulopapillary carcinoma (6.37% in inland; 11.54% in coastal areas). Using data from the Croatian national registry of vaccinated dogs, the crude incidence of tumours was calculated only for the Zagreb area. Expressed as the number of tumours per 100,000 dogs per year, the incidence was 1504 for all tumours, 532 for benign and 790 for malignant tumours. The overall frequencies of dominant tumour types and the crude incidence of canine tumours in the Zagreb area are comparable to other investigations.

Key words: dog, tumour, incidence, types, Croatia

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Introduction

Neoplastic diseases are among the most common causes of death in dogs. As such, the need for detailed understanding of the etiology, pathogenesis, treatment, prognosis and epidemiology of canine tumours is evident. These issues have been widely addressed in the literature (CULLEN et al., 2002; BRATULIĆ et al., 1996; GRABAREVIĆ et al., 2009a). However, recent reports on the incidence of various tumour types are not abundant, especially regarding geographic differences. Several previous animal tumour registries are now inactive, e.g.: California Animal Neoplasm Registry (DORN et al., 1968a), Purdue Comparative Oncology Program (BRØNDEN et al., 2007), and Cancer Registry and Surveillance System for Companion Animals, Cornell (PAGE, R. L. (2004): Summary of Cancer Surveillance and Registry Project from the Cornell University College of Veterinary Medicine, http://envirocancer. cornell.edu/research/animalreg/summarycompanion.pdf [accesed 5 June 2010].). Registries still active today include: Veterinary Medical Database (VMDB, 2010. The Veterinary Medical Database, http://www.vmdb.org/[accessed 5 June 2010]), VetCancer Registry (VetCancer Registry, 2006, http://www.vetcancerregistry.com [accessed 5 June 2010]), Norwegian Canine Cancer Registry (GAMLEM et al., 2008), Danish Veterinary Cancer Registry (BRØNDEN et al., 2010), Animal Tumour Registry of the Vicenza and Venice Provinces of the Veneto Region (VASCELLARI et al., 2009), and Animal Tumour Registry of Genoa (MERLO et al., 2008).

One of the primary objectives of these registries is to obtain an incidence rate of tumours per year per 100,000 dogs. In order to obtain this figure, it is necessary to know the exact population of dogs in the study area. Unlike in human practice, this is virtually impossible in veterinary medicine, and therefore projections or estimations are usually used. Alternatively, to draw conclusions about tumour incidence in the population as a whole, some investigators used limited, yet well defined population of insured dogs, and published data of age structure of the whole population (DOBSON et al., 2002). The general benefit from such epidemiological studies is not only aimed at better understanding of canine tumour epidemiology, but also toward detecting and understanding environmental hazards in developing these diseases when comparing dogs with humans (O'BRIEN et al., 2000; KNAPP et al., 2000). Different approaches in analyzing data about canine tumour incidence are also possible. For example, RICHARDS et al. (2001) gathered data on canine biopsies (neoplastic and non-neoplastic) and then drew conclusions from the standpoint of the diagnostic histopathology service. The primary aim of this study was to compile and present data on dog tumours diagnosed in the Republic of Croatia during 2006-2009 and to compare these data with the literature. The secondary goal was to estimate the total incidence of canine tumours per year per dog in the Zagreb area.

Materials and methods

A retrospective case control study was performed at the Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Zagreb in the period 2006-2009, using samples from canine biopsy and necropsy samples that proved to be neoplastic. Diagnoses were reached by experienced veterinary pathologists performing histopathologic evaluation of standard H&E stained microscopic slides. Where necessary, the final diagnosis was established using differential stains and immunohistochemistry methods. The variables set for the investigation were age, sex and breed of dog from which a tumour biopsy was taken, or from which the tumour was excised at the necropsy. Data on the anatomical site of the tumour and geographic location of the dog were also taken into account. The unit of the investigation was the single tumour (not the animal), so if several tumours were encountered on a particular animal, they were all approached separately. However, biologically identical tumours found on the same dog at different anatomical sites were treated as a single tumour. All 1568 tumours gathered during the study period were classified according to the World Health Organization International histological classification of tumours of domestic animals (http://www.afip.org/consultation/vetpath/who/whoclass.html). Statistical analyses of collected data were performed in Microsoft Office Excel. In order to evaluate the distribution of tumours, all cases were sort by sex, and in age groups of two years as follows: 0-1.99 years, 2-3.99 years, 4-5.99 years, etc. Finally, all tumours were also sorted by geographic location into two simplified groups: coastal and inland areas (the group coastal areas involved tumours of dogs living on the Croatian seacoast or within close range of the coast, using geographic barriers such as mountain chains as natural boundaries; the group inland involved all other cases). In order to estimate the total population of dogs in the Zagreb area (this included the City of Zagreb and Zagreb County), data obtained from the National Registry of Vaccinated Dogs were used.

Results

A total of 1568 tumours (817 in male dogs -52.1%; 751 in female dogs -47.9%) were diagnosed during the four year period. Of those, 930 (59.1%) cases were malignant, 555 (35.4%) were benign, and 83 (5.29%) were treated as not specified [meibomian gland epithelioma, hepatoid (perianal or circumanal) gland epithelioma, myxoma, sebaceous epithelioma, granulosa cell tumour, thecoma (theca cell tumour), interstitial (Leydig) cell tumour, seminoma, sertoli (sustentacular) cell tumour, cutaneous histiocytosis]. Among male dogs, the most frequently diagnosed neoplasms were tumours of the skin and subcutis (60.34%), genital system (11.26%) and oral cavity (5.63%). Among female dogs, tumours of the mammary gland (44.87%), skin and subcutis (29.83%), hemopoietic cells (4.39%), and genital tract (4.39%) were most dominant. Detailed information considering the

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Vet. arhiv 83 (1), 31-45, 2013

34

I.-C. Šoštarić-Zuckermann et al.: Canine tumours in Croatia

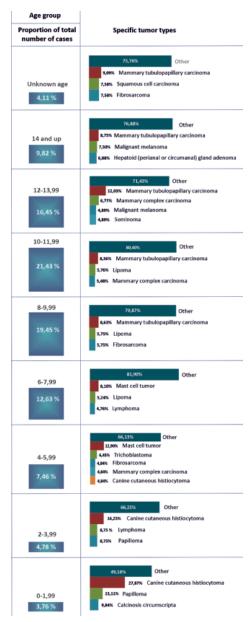


Fig. 1. Distribution of tumours by specific tumour type and body system by age group

Dog breed Proportion of total number of cases	Specific tumor types
Boxer 3,76 %	20,3455 Mast cell tumor 6,78% Fibrosarcoma 6,78% Fibromatous epulis of periodontal ligament origin
Golden Retriever 4,21 %	10,61% Mast cell tumor 7.58% Squamous cell carcinoma 6,00% Fibrosarcoma 4,55% Hepatold (perianal or circumanal) gland adenoma
Rottweiler 4,59 %	9,72% Malignant melanoma 0,33% Fibrosarcoma 6,84% Melanocytoma 5,56% Mammary tubulopapillary carcinoma
German Shepherd 5,87 %	10,87% Hemangiosarcoma 7,61% Squamous cell carcinoma 5,43% Fibrosarcoma 5,43% Calcinosis circumscripta
Cocker Spaniel 6,06 %	2,37% Mammary complex carcinoma 7,37% Mammary tubulopapillary carcinoma 6,32% Hemangiosarcoma 4,21% Trichoblastoma
Labrador Retriever 6,51 %	11,76% Mast cell tumor 10,78% Lipoma 4,99% Malignant melanoma 3,92% Mammary tubulopapillary carcinoma 2,96% Papilloma 2,95% Sebaceous adenoma
Poodle 6,63 %	17,315 Mammary tubulopapillary carcinom A,655 Mammary complex carcinoma 4,81% Hepatoid (perianal or circumanal) gland carcinoma 4,81% Hepatoid (perianal or circumanal) gland adenoma
Mongrel 21,11 %	4,16% Mammary tubulopapillary carcinoma 7,55% Lipoma 5,74% Fibrosarcoma 5,41% Mammary complex carcinoma 4,45% Hepatoid (perianal or circumanal) gland carcinoma 4,25% Hepatoid (perianal or circumanal) gland adenoma

Fig. 2. Distribution of tumours by specific tumour type and body system by breed

Individual tumor type	Cases	%	Male	Female
Mammary tubulopapillary carcinoma	112	7.14	0	112
Mast cell tumor	77	4.91	44	33
Fibrosarcoma	77	4.91	43	34
Lipoma	74	4.71	33	41
Mammary complex carcinoma	73	4.66	2	71
Hepatoid (perianal or circumanal) gland carcinoma	52	3.32	47	5
Malignant melanoma	51	3.25	31	19
Lymphoma	49	3.13	26	23
Canine cutaneous histiocytoma	47	2.99	39	9
Hemangiosarcoma	47	2.99	34	13
Hepatoid (perianal or circumanal) gland adenoma	45	2.87	42	3
Squamous cell carcinoma	45	2.87	29	16

Table 2. Most common specific tumor types

Table 3. Comparison o	f tumors	from the	e inland	and from	the coasta	l region
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	Inland	Coastal region
General		
Total number of tumors	1334 (85.08%)	234 (14.92%)
Benign	474 (35.53%)	81 (34.62%)
Malignant	791 (59.3%)	139 (59.4%)
Not specified	69 (5.17%)	14 (5.98%)
Specific tumor types		
Mammary tubulopapillary carcinoma	85 (6.37%)	27 (11.54%)
Mast cell tumor	67 (5.02%)	10 (4.27%)
Fibrosarcoma	66 (4.95%)	11 (4.7%)
Lipoma	57 (4.27%)	17 (7.26%)
Mammary complex carcinoma	59 (4.42%)	14 (5.98%)
Hepatoid (perianal or circumanal) gland carcinoma	46 (3.45%)	6 (2.56%)
Malignant melanoma	45 (3.37%)	6 (2.56%)
Lymphoma	43 (3.22%)	6 (2.56%)
Canine cutaneous histiocytoma	41 (3.07%)	6 (2.56%)
Hemangiosarcoma	40 (3%)	7 (3%)
Hepatoid (perianal or circumanal) gland adenoma	42 (3.15%)	3 (1.28%)
Squamous cell carcinoma	40 (3%)	5 (2.14%)

Body system		
Skin and subcutis	613 (45.95%)	104 (44.44%)
Mammary gland	274 (20.54%)	67 (28.63%)
Genital	113 (8.47%)	12 (5.13%)
Hemopoietic	65 (4.87%)	8 (3.42%)
Oral cavity	58 (4.35%)	15 (6.41%)
Vascular	58 (4.35%)	6 (2.56%)
Endocrine and exocrine glands	41 (3. 07%)	1 (0.43%)
Bones and joints	30 (2.25%)	5 (2.14%)
Respiratory	26 (1.95%)	2 (0.85%)
Gastic and intestinal	15 (1.12%)	6 (2.56%)
Ocular and otic	15 (1.12%)	3 (1.28%)
Liver	12 (0.9%)	1 (0.43%)
Urinary	8 (0.6%)	3 (1.28%)
Others	6 (0.45%)	1 (0.43%)

Table 3. Comparison of tumors from the inland and from the coastal region (continued)

Table 4. Number of cases and calculated incidence rate of specific canine tumors in Zagreb area

	Number of cases	Incidence rate (/100000 dogs/year)
	76	99.9
Mast cell tumor	64	84.1
Fibrosarcoma	56	73.6
Lipoma	52	68.3
Mammary complex carcinoma	49	64.4
Malignant melanoma	41	53.9
Hepatoid (perianal or circumanal) gland carcinoma	37	48.6
Hemangiosarcoma	37	48.6
Lymphoma	36	47.3
Hepatoid (perianal or circumanal) gland adenoma	36	47.3
Squamous cell carcinoma	35	46
Canine cutaneous histiocytoma	32	42

frequency of tumours in a particular body system and distribution in given body systems according to malignancy and gender is presented in Table 1. Mammary tubulopapillary carcinoma (112 cases) was the single most common diagnosis made, followed by mast cell tumour and fibrosarcoma (each with 77 cases). Detailed figures on the most common individual tumour types are presented in Table 2. When considering distribution of specific tumours in various age groups, the incidence of canine cutaneous histiocytoma was highest in the youngest age groups, mast cell tumour was most common in middle-aged dogs, while in (female) dogs older than 8 years, mammary tubulopapillary carcinoma was clearly the most common specific tumour type. Precise data concerning the latter is given in Fig. 1. Omitting mongrel dogs (21.11%) as a particular breed, the most common breed in this study was the Poodle (miniature, standard and giant combined; 6.63%), followed by Labrador Retriever (6.51%), Cocker Spaniel (6.06%), German Shepherd (5.87%), Rottweiler (4.59%), Golden Retriever (4.21%) and Boxer (3.76%). In all these breeds, the most common organ system affected with tumours was the skin and subcutis, with the exception of the Poodle in which the most tumours originated from the mammary gland. The distribution of specific tumour types in the most common breeds are shown in Fig. 2. In order to detect differences between population of dogs from coastal areas and the inland, tumours were sorted into these two distinct geographical areas and the data compared (Table 3). According to the data of the Croatian National Registry of Vaccinated Dogs, there was an annual average of 76,112.5 vaccinated dogs in the Zagreb area in the period 2006-2009. The total number of tumours in the Zagreb area was 1145 (73.02% of the total), of which 405 were benign, 602 were malignant, and 58 treated as not specified. Taking that into account, an estimation of the overall crude incidence of tumours in the Zagreb area can be made (expressed as the number of tumours per 100,000 dogs per year): 1504 -all tumours, 532 -benign tumours and 790 -malignant tumours. Incidences were also calculated for the most frequent specific tumour types in the Zagreb area, and are presented in Table 4.

Discussion

The results of this study reveal few interesting aspects (and problems) regarding canine tumour types and incidence. A total of 1568 canine tumours reported during a four year period in Croatia is not a large sample when compared with the 2509 tumours reported during the three-year study by VASCELLARI et al. (2009), 14,401 during an eight-year study by GAMLEM et al. (2008), or 6743 tumours collected during the 18 year study by MERLO et al. (2008). In the mentioned studies the authors offered a free of charge histopathological analysis of tumour samples, while that was not the case in our study. Therefore, one reason for the relatively small number of samples was the cost of histopathological analysis. Another reason for relatively sparse tumour submission may lie in the fact that there is still a need, at least in some rural parts of the country, to promote the importance of histopathologic diagnosis of tumours among practitioners.

When looking at total numbers, the ratio of 59.1% malignant and 35.4% benign tumours is generally comparable with other reports (BRØNDEN et al., 2007), although our figures show a somewhat higher portion of malignant tumours. This could be explained by the fact that most owners do not treat slow-growing neoplasm or small tumours of their pets. The sex ratio in our study (52.1% male, 47.9% female dogs) is nearly equally distributed. The body systems mostly affected were, as expected, skin/subcutis (45.73%) and mammary gland (21.75%), followed by genital system (7.97%). A similar proportion of tumours by body system (site) has been reported by other authors (40.8% skin/subcutis, 34.8% mammary gland, and 7.2% genital (VASCELLARI et al., 2009); 51% skin/subcutis, 30% mammary gland, and 3.9% genital (GAMLEM et al., 2008). It is widely accepted that the perceived frequencies of tumours in these body systems tend to be greater as owners and veterinarians are more likely to detect a neoplasm in these organs than in more concealed internal organs (e.g. liver or lungs). Smaller differences in the proportion of tumours by body system could be the result of different environmental influences or customs regarding spaying of animals between the Croatian dog populations and those from other studies.

It was expected that mammary tubulopapillary carcinoma would be the most common specific diagnosis, since simple carcinomas are described as the most common malignant mammary tumours (MISDORP, 2002). Mast cell tumours (4.91% of total tumours) and fibrosarcomas (4.91% of total tumours) shared the position of second most common, which is comparable to results of BRØNDEN et al. (2010), whose results differed from ours only in that lymphomas were the third most frequent malignant tumour. Concerning occurrence of mast cell tumours in Croatia, it is important to mention that a previous study by GRABAREVIĆ et al. (2009b) found a proportion of 6.5% of these tumours in years 2002 to 2006. This decline from 6.5% to 4.9% is probably too small to interpret it as an indication of decreasing occurrence of mast cell tumours), canine cutaneous histiocytoma (2.99% of total tumours) and hepatoid (perianal or circumanal) gland adenoma (2.87% of total tumours) were most common, which is again comparable to results of BRØNDEN et al. (2010).

The distribution of tumours by age group shows a known pattern in which canine cutaneous histiocytoma predominate in the youngest age groups, mast cell tumour is the most common tumour in middle-aged dogs, while mammary tubulopapillary carcinoma is most common in older age groups in females. A similar distribution, although not expressed in such a specific tumour diagnosis, is presented by GAMLEM et al. (2008).

The distribution of tumours by breed showed breed predispositions. Of all specific tumour types, mast cell tumours (as most common) constituted 20.33% in Boxers, 11.76% in Labrador Retrievers and 10.6% in Golden Retrievers which is in accordance with

other data (GOLDSCHMIDT and HENDRICK, 2002). The most common specific tumour type in German Shepherd was hemangiosarcoma (10.87%), which is also described in the literature (GOLDSCHMIDT and HENDRICK, 2002). The high incidence of mammary tubulopapillary carcinoma in Poodles (17.3%) was unexpected, and should be the subject of further study.

Comparison of population of dogs from the inland (I) and coastal areas (C) showed no relevant differences. However, some minor but interesting differences were noted. Firstly, it is clearly evident that number of C samples is much smaller than the number of I samples. The reason for this is that the majority of samples originated from the Zagreb area or nearby areas, and many veterinary practitioners from the coastal areas do not submit their samples due to shipment costs and the lack of custom of doing so. Comparing proportions of specific tumour types between C and I shows that the proportion of mammary tubulopapillary carcinoma in C samples (11.54%) is almost twice that of I samples (6.37%). Moreover, a difference in proportion of mammary tumours (both, malignant and benign) is also noted (28.63% in C, 20.54% in I). Environmental factors could pose at least a part of the answer. Slight, but evident differences between C and I populations were noted in the following specific tumour types: lipoma (C 7.26%, I 4.27%), hepatoid (perianal or circumanal) gland adenoma (C 1.28%, I 3.15%), and tumours of the genital system (C 5.13%, I 8.47%).

The majority of studies considering the incidence of canine tumours express the incidence as the number of tumours per 100,000 dogs per year. This incidence in the Zagreb area is 1504 for all tumours, 532 for benign tumours and 790 for malignant ones. It would be incorrect to include all of Croatia in this calculation, since 73.02% of all tumours came from the Zagreb area, so crude incidence rates were calculated only for the Zagreb area using data from the National Registry of Vaccinated Dogs. However, due to the incompleteness of data in the registry, it was not possible to obtain more detailed information considering sex, age or breed of vaccinated dogs. It should be mentioned that this population of vaccinated dogs should not be treated as very precise, since not all owners vaccinate their dogs (despite being required by the law). Any undiagnosed or misdiagnosed tumours also contributed to incorrect overall incidence of tumours. It is difficult to compare these frequencies with those of other studies (due to the different estimation models of populations and different histological classification), however it is logical to do so. Our total of 1504 neoplasms per 100,000 dogs per year might seem to be a plausible figure when compared with the results of other studies eg. 2671 (DOBSON et al., 2002), and 1134 (DORN et al., 1968b). On the other hand, some reports from Italy, focusing more on mere cancers, showed a much lower incidence of these tumours than present here; namely, MERLO et al. (2008), found an incidence of cancers of 99.3 in male dogs, and 272.1 in female dogs, while VASCELLARI et al. (2009), found an incidence of

282.2 for all tumours, and 143 for cancers. The incidence of mammary tubullopapillary carcinoma (99.9) and mammary complex carcinoma (64.4) is within the expected range when considering that an estimated annual incidence rate of all malignant mammary tumours is around 198 (MISDORP, 2002), but on the other hand seems quite high when compared to DOBSON et al. (2002), who reported an overall incidence of 205 tumours for all mammary tumours (benign and malignant), and only 32 and 18 for mammary carcinoma and adenocarcinoma, respectively. The incidence of mast cell tumour (84.1) is considerably lower than the approximation (126) by DOBSON et al. (2002). The same observation can be made for lipomas (68.3 in our study, versus 317 in DOBSON et al., 2002), and for lymphomas (47.3 in our study, versus 107 in DOBSON et al., 2002). One reason might be the fact that age-standardized incidence rates were expressed in mentioned study, which was not the case in our study. Namely, in our study, it is evident that most tumours came from older animals which tend to have more tumours, while DOBSON et al. (2002) projected data from a group of insured dogs (these tend to be younger, and therefore have less tumours) to an overall population of UK dogs (also tend to be younger than the population of dogs diagnosed with tumours in our study). However, these differences could mean a true difference in the incidence ratio of mentioned tumours, which might be under influence of environmental factors or breed structure difference in dogs from the UK and Croatia.

Until now, there was not a study similar to this one considering canine tumours in Croatia. There were, however, a conference report dealing with this issue (SOSTARIC-ZUCKERMANN et al., 2010), reports considering specific tumour types (GRABAREVIĆ et al., 2009a; GRABAREVIĆ et al., 2009b; GUDAN KURILJ et al., 2011) and individual case reports considering uncommon neoplasias in dogs (GUDAN KURILJ et al., 2012; BECK et al., 2011). Therefore, this study provides an important (first) step in better visualization and understanding of occurrence of canine tumours in Croatia. Most of the incidences of tumours are comparable with those from other studies. However, the results and comparison with other studies indicate the need to conduct subsequent studies, and the need for establishment of a computer based registry of tumours in domestic animals in Croatia.

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SAŽETAK

Neoplastične bolesti prednjače po svom značenju u zdravstvu. S obzirom na to epidemiološka istraživanja tumora u pasa korisna su u razumijevanju pravilnosti pojavljivanja tumora. Cilj ovog istraživanja bio je analizirati podatke o pojavnosti tumora u pasa u Hrvatskoj. U razdoblju od 1. siječnja 2006. do 31. prosinca 2009. dijagnosticirano je ukupno 1568 tumora, bilo da se radilo o rutinski dostavljenim biopsijama ili materijalu izuzetih s razudbi. Za određivanje tipa tumora koristilo se klasifikacijom Svjetske zdravstvene organizacije. Većina tumora (59,1%) bila je zloćudna, 35,4% tumora bilo je dobroćudno, dok su se ostali (5,29%) smatrali neodređenima. Tumori su potjecali iz kože i potkožja (45,73%), mliječne žlijezde (21,75%) i spolnoga sustava (7,97%). Najčešći specifični tipovi tumora koji su dijagnosticirani bili su tubulopapilarni karcinom mliječne žlijezde (7,14%), mastocitom i fibrosarkom (4,91%). Razlike u pojavnosti tumora u populaciji pasa kopnene te primorske Hrvatske bile su zanemarive za sve organske sustave, osim kod tumora mliječne žlijezde (20,54% kopnena Hrvatska, 28,63% primorska Hrvatska), te pojedinačno kod tubulopapilarnog karcinoma mliječne

žlijezde (6,37% kopnena Hrvatska; 11,54% primorska Hrvatska). Koristeći se podatcima iz Hrvatskoga nacionalnog registra cijepljenih pasa, izračunata je gruba pojavnost tumora u pasa na području grada Zagreba. Izračena kao broj tumora na 100 000 pasa po godini, incidencija je iznosila 1504 za sve tumore, 532 za dobroćudne tumore te 790 za zloćudne tumore. Sveukupna učestalost dominantnih tipova tumora te gruba incidencija tumora u pasa na području grada Zagreba usporediva je s onom iz drugih istraživanja.

Ključne riječi: pas, tumor, pojavnost, tipovi, Hrvatska