



Letter To The Editor

Epidemiology of uveal melanomas in Germany

Joel M. Mor,¹  Alexander C. Rokohl,¹ Stefan Dahm,² Klaus Kraywinkel² and Ludwig M. Heindl^{1,3} 

¹Department of Ophthalmology, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; ²Robert-Koch-Institute, Berlin, Germany; ³Center for Integrated Oncology (CIO), Aachen-Bonn-Cologne-Duesseldorf, Cologne, Germany

doi: 10.1111/aos.15010

Editor,

Data regarding the epidemiology of uveal melanoma in Europe are predominantly based on twentieth century registry data from 16 European states from 1983 to 1994 (Vidal et al. 1995; Bergman et al. 2002; Virgili et al. 2007; Koomen et al. 2010). For this period, the EURO CARE group found a north-south gradient in age-standardized incidence rates, ranging from <0.2/100 000 in southern Europe to >0.8/100 000 in Scandinavia (Virgili et al. 2007). In Germany, the incidence rate was 0.4-0.5/100 000. However, these numbers are solely based on data from a single cancer registry, representing only 1 of 16 federal counties (Saarland) (Virgili et al. 2007). The 5-year survival rate of patients with uveal melanoma in Europe in the years 1983-2002 was 69% (Virgili et al. 2008; Mallone et al. 2012). Ever since, the data basis for epidemiologic analyses of oncologic diseases in Germany has substantially improved with a nationwide recording of all cancer patients since 2009. Although one cannot assume complete registration in every federal state yet, the system now permits a differentiated evaluation of epidemiologic data even for rare tumours.

Here, we report recent incidence and survival data of uveal melanoma in Germany, based on the entirety of all German population based cancer registries, which in turn report to the

German Centre for Cancer registry data for nationwide analysis. We included all primary melanomas of the choroid, ciliary body and iris (singular cases with the ICD-10 localization code C69.2 (retina) were interpreted as choroidal melanomas with transretinal spread), and melanomas of unspecified location or overlapping lesions of eye and adnexa (Virgili et al. 2007; Virgili et al. 2008). With regard to localization codes C69.3 (choroid) and C69.4 (ciliary body), we counted malignant tumours with unspecified histopathology as melanomas, because other entities are extremely rare in these locations. Inclusion criteria were comparable to those chosen by the EURO CARE group to allow comparability (Virgili et al. 2007).

Time trend analyses from 1996 to 2015 were performed using Joinpoint regression models (Joinpoint Regression Program, version 4.6.0.0.; 2018; National Cancer Institute). Incidence rates were age-standardized using the old European standard population. To determine 5-year survival rates, the observed survival at 5 years after the initial diagnosis was divided by the expected survival during this period, applying the Ederer II method based on mortality tables from the Federal Statistical Office. The period survival approach was applied in order to estimate survival rates. This approach utilizes the data of all patients who were alive in the period of interest (2013-2015) and were healthy before 2008. For these analyses, data from 12 federal counties were included. The calculations were performed using R^{*} (version 3.6.1), R-package, periodR^{*} (version 1.0-6).

From 2013 to 2015, 1828 uveal melanomas were registered (948 male, 880 female). The majority were choroidal melanomas (83%), followed by ciliary body and iris melanomas (13%), and melanomas of unspecified locations (4%). Four cases had the localization, retina (C69.2), making up 0.2%. 73% of melanomas were verified with histopathology.

The age-standardized incidence was 0.51/100 000 with a median age of 67 years at the time of diagnosis, confirming EURO CARE and US findings (Virgili et al. 2007; Aronow et al. 2018). The incidence was 0.75/100 000 in the newly formed states (former Eastern

Germany) and 0.44/100 000 in the Old Federal States (former Western Germany). The gender specific incidence rates were 0.56/100 000 for men and 0.46/100 000 for women.

The majority of tumours occurred in patients above 65 years. In regions with adequate cancer registry data since 1996 (newly formed German states, Berlin, Hamburg, Saarland, administrative region of Münster), 20 year time trend analyses revealed a non-significant mean annual increase of 0.9% (95%-CI: -0.8-2.7) and 1.1% (95%-CI: -0.6-2.7) for men and women respectively.

The relative 5-year survival was 73.7% (95% CI 71.2%-76.2%; Table 1). For choroidal melanomas, the results were higher than for ciliary body melanomas with 76.2% (95% CI 74.4-78.0%) and 63.3% (95% CI 58.0%-68.6%) respectively. Melanomas in other locations (C69.2, C69.8, C69.9) had a relative 5-year survival of 58.5% (95% CI 55.8%-61.2%). Between 1996 and 2015, we found a small increase in incidence rates of 1% per year, which was, however, not statistically significant in our analysis. Interestingly, Smidt-Nielsen et al. (2021) recently reported increased incidence of small uveal melanomas in the same time period in Denmark. It is

Table 1. Relative 5-year survival of uveal melanoma patients in Germany 2013-2015, by age groups and location, with 95% confidence intervals.

	Relative 5-year survival, by age groups, with 95% confidence intervals		
	Result	Confidence interval	
15-49 years	83.4%	80.5%	86.3%
50-59 years	76.0%	72.9%	79.1%
60-69 years	73.5%	70.8%	76.2%
70-79 years	69.6%	66.5%	72.7%
80 years and older	74.2%	66.9%	81.5%
Total	73.7%	71.2%	76.2%
By location			
Choroid	76.2%	74.4%	78.0%
Ciliary body and iris	63.3%	58.0%	68.6%
Retina, unspecified location, overlapping lesions of eye and adnexa	58.5%	55.8%	61.2%
By gender			
Males	72.9%	70.5%	75.3%
Females	76.0%	73.8%	78.2%

debatable whether this rise in incidence may be due to earlier detection.

In conclusion, the incidence and survival rates are similar to previously published data from other European and US American registries (Virgili et al. 2007; Aronow et al. 2018), even though there is likely still undercoverage of cases in certain federal states. Apart from that, the percentage of histologically verified melanomas is decreasing because of the increase in patients treated with globe sparing therapies (radiotherapy modalities), thus making undercoverage likely in those registries that heavily rely on pathology institutes as a main source of reporting. Possibly, this issue has also led to undercoverage in the EURO-CARE project, especially in northern Europe. An increase in incidence cannot be definitively shown with the data at hand (once again confirming EURO-CARE results), and the development does not seem to be comparable to that of cutaneous melanoma where markedly stronger increases in incidence have been reported.

References

- Aronow ME, Topham AK & Singh AD (2018): Uveal melanoma: 5-year update on incidence, treatment, and survival (SEER 1973–2013). *Ocul Oncol Pathol* **4**: 145–151.
- Bergman L, Seregard S, Nilsson B, Ringborg U, Lundell G & Ragnarsson-Olding B (2002): Incidence of uveal melanoma in Sweden from 1960 to 1998. *Invest Ophthalmol Vis Sci* **43**: 2579–2583.
- Koomen ER, de Vries E, van Kempen LC et al. (2010): Epidemiology of extracutaneous melanoma in the Netherlands. *Cancer Epidemiol Biomarkers Prev* **19**: 1453–1459.
- Mallone S, De Vries E, Guzzo M et al. (2012): Descriptive epidemiology of malignant mucosal and uveal melanomas and adnexal skin carcinomas in Europe. *Eur J Cancer* **48**: 1167–1175.
- Smidt-Nielsen I, Bagger M, Heegaard S, Andersen KK & Kiilgaard JF (2021): Posterior uveal melanoma incidence and survival by AJCC tumour size in a 70-year nationwide cohort. *Acta Ophthalmol*. Online ahead of print.
- Vidal JL, Bacin F, Albuissou E et al. (1995): “Melanoma 92”. epidemiological study of uveal melanoma in France. *J Fr Ophtalmol* **18**: 520–528.
- Virgili G, Gatta G, Ciccolallo L et al. (2007): Incidence of uveal melanoma in Europe. *Ophthalmology* **114**: 2309–2315.
- Virgili G, Gatta G, Ciccolallo L et al. (2008): Survival in patients with uveal melanoma in Europe. *Arch Ophthalmol* **126**: 1413–1418.

Received on February 5th, 2021.

Accepted on August 4th, 2021.

Correspondence

Dr. med. Joel M. Mor
Department of Ophthalmology, University
Hospital of Cologne
Kerpener Strasse 62-50924 Köln
Germany
Tel: +49 221 478 4300
Fax: Xxx
Email: joel.mor@uk-koeln.de

Conflict of interest: Joel M. Mor, Alexander C. Rokohl, Stefan Dahm, Klaus Kraywinkel and Ludwig M. Heindl confirm that there is no conflict of interest.

Ethical guidelines: This work is solely based on the evaluation of epidemiological registry data. There are no ethical conflicts.