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Incidence and survival of skin melanoma in Puglia: A comparison with the rest of Italy

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Abstract

Introduction: There is a wide heterogeneity in incidence, prevalence, mortality and survival of skin melanoma through the world and in Italy as well. In this study we investigated, for the first time, incidence, mortality and survival of skin melanoma in Puglia, comparing results with Italian data.
Materials and methods: We collected accurate information about clinical and pathological variables, and measured crude and age-adjusted incidence and mortality rates, and estimated relative and net survival according to Ederer II and Pohar-Perme methods, respectively. Incidence, mortality and survival were performed by district and for the whole Puglia region; internal and external comparisons were done.
Results: Age-adjusted incidence rates per 100,000 inhabitants in males were: Puglia 9.9 (95% confidence interval [CI] 9.1 to 10.8), AIRTUM Italy (AIRTUM pool) 12.0 (95% CI 11.6 to 12.4), Pool of Southern Italian registries (South pool) 7.1 (95% CI 6.6 to 7.6); in females: Puglia 9.7 (95% CI 8.9 to 10.6), AIRTUM pool 11.3 (95% CI 10.9 to 11.7), South pool 6.5 (95% CI 6.0 to 7.0). Age-standardized mortality rates per 100,000 inhabitants were in males and females in Puglia respectively 2.4 (95% CI 2.0 to 2.8) and 1.6 (95% CI 1.3 to 1.9). 5 years age-standardized relative survival was as follows: in males Puglia 81.4% (95% CI 77.0 to 85.0), Italy 81.6% (95% CI 80.4 to 82.8); in females Puglia 87.3% (95% CI 83.3 to 90.4), Italy 88.6% (95% CI 87.6 to 89.6).
Conclusions: Incidence of skin melanoma is higher in Puglia compared with the southern Italy pool and lower compared with the other three Italian macro-areas (central, north-western and north-eastern Italy),but there are not statistically significant differences. A North to South gradient of melanoma skin is showed also in Puglia, except for Bari district where incidence is higher probably due to greater availability of public and private diagnostic centres. Overall mortality and survival in Puglia are very close to Italian estimates. The highest mortality is registered in males in BAT district where also the lowest survival is observed.

KEY WORDS: melanoma, epidemiology; incidence; mortality; registries.

Riassunto

Introduzione: Il melanoma cutaneo presenta un'ampia eterogeneità di incidenza, prevalenza, mortalità e sopravvivenza, sia nel mondo che in Italia. In questo studio abbiamo indagato, per la prima volta, l'incidenza, la mortalità e la sopravvivenza del melanoma cutaneo in Puglia, confrontando i risultati con i dati Italiani.
Materiali e metodi: Abbiamo raccolto informazioni dettagliate su variabili cliniche e patologiche, calcolato i tassi di incidenza e di mortalità grezzi e standardizzati per età e stimato la sopravvivenza netta e relativa secondo i metodi Pohar-Perme ed Ederer II. L'incidenza, la mortalità e la sopravvivenza sono state calcolate per singola provincia e per l'intera regione; sono stati, inoltre, effettuati confronti interni ed esterni.
Risultati: I tassi di incidenza standardizzati per età, per 100.000 abitanti, nei maschi sono i seguenti: Puglia 9,9 (IC 95% 9,1 – 10,8), AIRTUM Italia (pool AIRTUM) 12,0 (IC 95% 11,6 – 12,4), Gruppo dei registri AIRTUM del Sud Italia (pool SUD) 7,1 (IC 95% 6,6 – 7,6); nelle femmine: Puglia 9,7 (IC 95% 8,9 – 10,6), pool AIRTUM 11.3 (IC 95% 10,9 – 11,7), pool SUD 6,5 (IC 95% 6,0 – 7,0). I tassi di mortalità standardizzati per età, per 100.000 abitanti, sono stati in Puglia nei maschi e nelle femmine pari, rispettivamente, a 2,4 (IC 95% 2,0 – 2,8) e 1,6 (IC 95% 1,3 – 1,9). La sopravvivenza relativa standardizzata a 5 anni è stata nei maschi: Puglia 81,4% (IC 95% 77,0 – 85,0), Italia 81,6% (IC 95% 80,4 – 82,8); nelle femmine: Puglia 87,3% (IC 95% 83,3 – 90,4), Italia 88,6% (IC 95% 87,6 – 89,6).
Conclusioni: L'incidenza del melanoma cutaneo in Puglia è più alta della restante parte del Sud Italia ed è più bassa rispetto alle restanti macroaree Italiane (Nord-Est, Nord-Ovest, Centro), con differenze non statisticamente significative. Un gradiente Nord-Sud del melanoma è evidente anche in Puglia, eccetto per la città di Bari dove si rileva un'incidenza più alta per una maggiore disponibilità territoriale di centri diagnostici pubblici e privati. La mortalità e la sopravvivenza complessive pugliesi sono paragonabili a quelle italiane.

TAKE-HOME MESSAGE

Incidence of skin melanoma in Puglia is higher when compared with the rest of southern Italy. This is the first study of incidence, mortality and survival of skin melanoma in Puglia, by district, and its results are suitable for policy makers in order to direct primary and secondary prevention of melanoma skin using foremost awareness-raising campaigns in schools and in medical surgeries.

Competing interests - none declared.

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INTRODUCTION

Skin melanoma is a malignancy rising from transformation of melanocytes. Incidence and prevalence of melanoma depend on genetic, phenotypic and environmental factors, survival mostly depends on early diagnosis and opportunistic screening; therefore incidence, prevalence, mortality and survival vary considerably world-wide. Incidence rates and prevalence are higher in populations where Caucasians predominate, and lower in countries where inhabitants have an Asian or an African origin [1–3]. It has been noticed that skin melanoma is the malignancy with the most impressive upward time-trend in incidence in western countries, however this increasing trend observed in last decades is believed to be mostly due to a higher diagnostic pressure. In Italy, it is characterized by an annual percentage change (APC) of about 3% [4]. Mortality and survival depends also by diagnostic skills and techniques and by reliable therapies: the prognosis of skin melanoma was actually worse in the past, however it improved largely in last years [5–7] and mortality trend is stable in women and slightly decreasing in men [4]. An important inverse correlation was found also between incidence of skin melanoma and latitude [8, 9], and indeed incidence decreases from North to South in the northern hemisphere and a similar gradient was retrieved in Italy [10]. In melanoma, a great role in improving the prognosis is related to primary and secondary prevention campaigns, the first based on the reduction of exposure to sun rays and the use of anti UV sunscreen and the second on the application of the A-B-C-D-E rule for auto-detection and the early diagnosis by expert dermatologists. Using data provided by the Cancer Registry of Puglia (RTP) we investigated incidence and survival of skin melanoma in this region of South Italy and we compared them with data from other Italian macroareas (North-East, North-West, Centre and South Italy) [11]. Before our study, few information was known about the incidence of melanoma in the Apulian population; information about survival derived all by clinical trials that are not population-based, instead as in our case. RTP is a regional population-based cancer registry, active since 2008 to ensure standardized and comparable data about oncological phenomena in a large Italian region characterized by a structural variability and high health migration. Puglia consists of six administrative districts (Foggia, Barletta-Andria-Trani - BAT, Bari, Brindisi, Taranto and Lecce) and in every district a Health Local Unit (HLU) exists. RTP has been instituted with a regional deliberative act and it has been structured to answer to the needs of homogeneity and comparability of data. RTP consists in an Operating Coordination Centre, located in the Cancer Research Institute in Bari, which supports six sections in each HLU. This kind of network allows an abiding interchange of knowledge and information between RTP researches but, at the same time, it ensures a local autonomy work and responsibility. Four of the six sections (BAT, Brindisi, Lecce and Taranto) are at the present time accredited by Italian Network of Cancer Registries (AIRTUM). Actually, the section of Bari does not include the whole district, but eight municipalities (Bari, regional and district capital city, Bitetto, Bitritto, Conversano, Modugno, Mola di Bari, Polignano a mare and Rutigliano) which cover 37% of the district population. In our study, we privileged the representativeness of the data of incidence across the whole region, so that all sections have participated with the incident cases of skin melanoma available, however data from not accredited sections have been subjected to quality controls similar to those required for AIRTUM accreditation to ensure comparability. Main aims of the study were to examine whether in Puglia it is found a north-south gradient in melanoma incidence and mortality, and which is the rank of Puglia in relation to the rest of South Italy and whether there are differences in survival in intra- and extra- regional comparisons.

MATERIALS AND METHODS

We included all incident cases of invasive skin melanoma diagnosed in Puglia in 2006 – 2008 (since the Bari district is partially

subjected to oncological recording, 80% of the regional population is covered). Age-adjusted incidence rates obtained by direct standardization (DSR) using European population were calculated and they were compared with Italian data provided by AIRTUM [11]. We collected the following pathological and clinical biological variables: TNM and stage at diagnosis, morphology, Clark level, Breslow depth, skin site, phase of growth, cell type, histotype, vascular invasion, ulceration, regression, residual nevus, number of mitotic figures. A simplified staging according to the rules of summary staging provided by the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute by United States, was carried out: localized if the tumour is limited to the site of origin, regional if only regional lymph nodes are involved and distant if distant metastasis have occurred [12]. In a second step we analysed mortality data for skin melanoma, provided by Italian National Institute of Statistics (ISTAT) for the whole regional area [13]. We calculated age-adjusted incidence rates obtained by direct standardization (DSR) using European population for each district and we compared them with Apulian data overall. In a third step, survival of skin melanoma in Puglia, by district, was evaluated both in terms of relative survival according to Ederer II method [14], and in terms of net survival according to Pohar-Perme's method [15, 16]. Survival was evaluated for the cases with histological confirmation and more than 15 years old. Therefore, age-standardized relative survival, stage standardized relative survival and net survival curves have been realized and 5-years survival has been compared across Apulian districts and with data of the AIRTUM pool of Italian cancer registries. However, since the values are very similar and only the reference data with the relative survival are currently available for comparison, only relative survival is shown. Differences in incidence, mortality and survival among areas were considered statistically significant when their confidence intervals were not overlapped.

RESULTS

Incidence

1134 cases of skin melanoma were registered in Puglia in the 2006-2008 period, with equally distribution between genders (51.3% females and 48.7% males). The most represented districts were Bari and Foggia (Table 1); BAT shows the lower median age at diagnosis while Lecce and Brindisi show the higher (Table 1). Trunk, followed by legs, was the most frequent site group of melanoma skin in Apulian region (Table 2). Histologic confirmation was present in 1,113 cases (98%). Information about one of the most important prognostic factor as Breslow depth was available in 99% of cases (Table 2). The most frequent morphology was the superficial spreading, followed by nodular morphology (Table 2). Information for summary staging was available in 81% of cases and stage distribution was variable by district (Table 3). Age standardized rates by gender and by area are shown as follows: Males (Fig. 1): Bari (BA) 17.4 (95% confidence interval [CI] 11.9 to 17.4), Barletta-Andria-Trani (BT) 10.8 (95% CI 8.4 to 13.8), Brindisi (BR) 8.8 (95% CI 6.6 to 11.4), Foggia (FG) 11.1 (95% CI 9.2 to 13.4), Lecce (LE) 5.8 (95% CI 4.6 to 7.2), Taranto (TA) 10.6 (95% CI 8.7 to 12.8), Puglia 9.9 (95% CI 9.1 to 10.8), AIRTUM Italy (AIRTUM pool) 12.0 (95% CI 11.6 to 12.4), Pool of Southern Italian registries (South pool) 7.1 (95% CI 6.6 to 7.6). Females (Fig. 1): BA 14.4 (95% CI 11.9 to 17.2), BAT 8.7 (95% CI 6.6 to 11.4), BR 8.2 (95% CI 6.3 to 10.7), FG 10.1 (95% CI 8.3 to 12.4), LE 7.9 (95% CI 6.5 to 9.5), TA 9.7 (95% CI 7.9 to 11.9), Puglia 9.7 (95% CI 8.9 to 10.6), AIRTUM pool 11.3 (95% CI 10.9 to 11.7), South pool 6.5 (95% CI 6.0 to 7.0). Moreover, a subgroup analysis on the young population was performed; we explored incidence in < 40 years old population and we found a difference in rates between sexes, mostly in the last two years available; in particular, age standardized incidence in young males in 2006, 2007 and 2008 was respectively 1.5, 1.1, 2.1 (per

100,000 inhabitants) while in young females was 1.4, 2.7, 3.1 (per 100,000 inhabitants).

Mortality

303 deaths for skin melanoma occurred in Puglia in the 2006-2008 period. Age standardized rates by gender and by area are shown in Figure 2. Males: Bari (BA) 2.2 (95% CI 1.6 to 3.0), BAT (BT) 3.3 (95% CI 2.3 to 5.1), Brindisi (BR) 2.2 (95% CI 1.2 to 3.6), Foggia (FG) 2.5 (95% CI 1.3 to 3.7), Lecce (LE) 2.2 (95% CI 1.5 to 3.2), Taranto (TA) 2.8 (95% CI 1.9 to 4), Puglia 2.4 (95% CI 2 to 2.8), Southern Italy 1.99 (95% CI 1.89 to 2.08), Italy 2.53 (95% CI 2.47 to 2.59). Females: BA 2.1 (95% CI 1.5 to 2.8), BAT 1.8 (95% CI 0.9 to 3.2), BR 1.0 (95% CI 0.5 to 2.1), FG 1.6 (95% CI 0.9 to 2.6), LE 1.1 (95% CI 0.6 to 1.7), TA 1.4 (95% CI 0.8 to 2.3), Puglia 1.6 (95% CI 1.3 to 1.9), Southern Italy 1.33 (95% CI 1.25-1.41), Italy 1.48 (95% CI 1.43-1.52).

Survival

We analysed the 5 years age-standardized relative survival by gender, which as regard to males was in Puglia 81.4% (95% CI 77.0 to 85.0), and in Italy 81.6% (95% CI 80.4 to 82.8); for females it was in Puglia 87.3% (95% CI 83.3 to 90.4), in Italy 88.6% (95% CI 87.6 to 89.6). Relative survival in Puglia by SEER stage, adjusted for age was as follows: localized 96.2% (95% CI 92.1 to 98.2), regional 53.2% (95% CI 43.7 to 61.9), distant 10.9% (95% CI 3.7 to 22.5), unknown 80.0% (95% CI 72.5 to 85.6%). There was considerable heterogeneity in the age-standardized relative survival for the different districts of Puglia. Males (Fig. 3): BA 86.2% (95% CI 74.7 to 92.7), BT 70.5% (95% CI 54.5 to 81.7), BR 80.7% (95% CI 66.4 to 89.4), FG 83.0% (95% CI 72.7 to 89.7), LE 82.5% (95% CI 68.7 to 90.6), TA 85.2% (95% CI 74.9 to 91.5). Females (Fig. 4): BA 90.4% (95% CI 78.3 to 95.9), BT 82.2% (95% CI 63.8 to 91.8), BR 79.8% (95% CI 64.9 to 88.8), FG 91.9% (95% CI 82.5 to 96.3), LE 85.6% (95% CI 76.1 to 91.5), TA 91.0% (95% CI 75.9 to 96.9).

Table 1. Province distribution and age of skin melanoma cases in the Apulian region.

			Age		
Province	**Frequency**	**%**	**median**	**Avg**	**std. dev.**
BA	240	21.1	57.5	56.7	16.1
BT	126	11.1	53.5	53.9	17.5
BR	125	11.0	59.0	58.5	16.5
FG	235	20.7	57.0	56.4	17.7
LE	198	17.5	59.0	57.3	16.6
TA	210	18.5	56.5	55.7	18.0
Total	1134	100.0			

Table 2. Distribution of site group, Breslow depth and morphologies of skin melanoma cases in the Apulian region.

Site group	**Frequency**	**%**
Trunk	434	38.3
Legs	287	25.3
Arms	206	18.2
Head	109	9.6
Neck	9	0.8
Unknown	89	7.9
Total	1134	100
Breslow depth	**Frequency**	**%**
<= 1 mm	484	43.0
1.01 – 2.00 mm	193	17.2
2.01 – 4.00 mm	161	14.3
> 4.00 mm	129	11.5
Unknown	158	14.0
Total	1125	100.0
Morphologies	**Frequency**	**%**
Superficial spreading	444	39.9
Nodular	164	14.7
Skin melanoma, NAS	145	13.0
Lentigo maligna	22	2.0
Acral lentiginous	9	0.8
Others	329	29.6
Total	1113	100.0

Table 2. Distribution stage of skin melanoma cases stage by Apulian district, cases with histological confirmation.

	Stage (%)				
District	**Local**	**Regional**	**Distant**	**Unknown**	**Total**
BA	71.3	11.7	2.9	14.2	100.0
BT	60.3	15.1	7.1	17.5	100.0
BR	48.4	13.7	8.9	29.0	100.0
FG	69.7	10.3	2.1	18.0	100.0
LE	57.1	6.1	5.6	31.3	100.0
TA	61.0	16.2	3.8	19.1	100.0
Total	62.8	11.8	4.5	20.9	100.0

Figure 1. Incidence rates of skin melanoma by Apulian district, per 100,000 inhabitants, males and females and comparison with Italy.

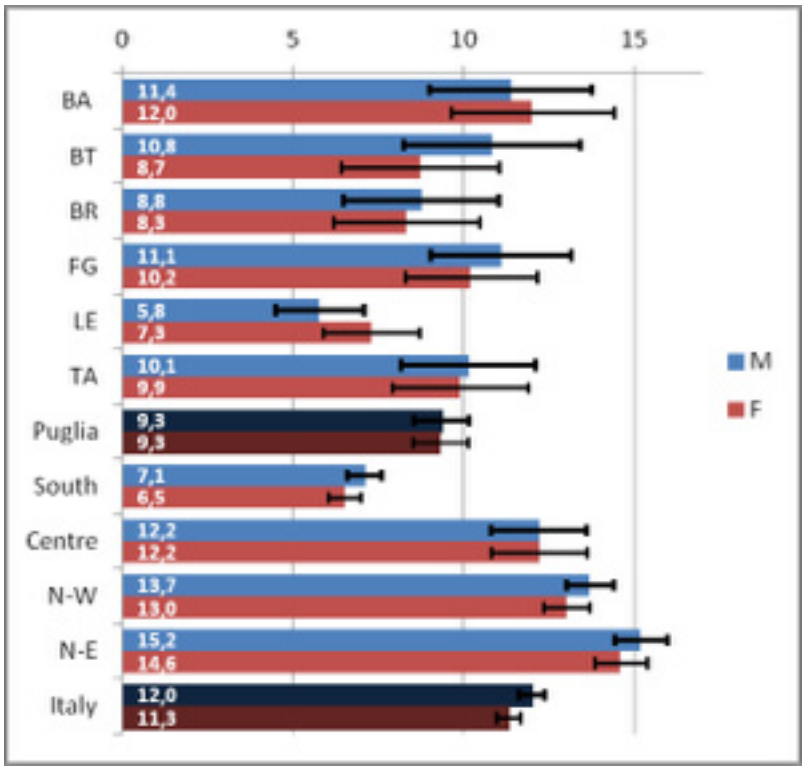


Figure 2. Mortality rates of skin melanoma by Apulian district per 100,000 inhabitants, males and females and comparison with Italy.

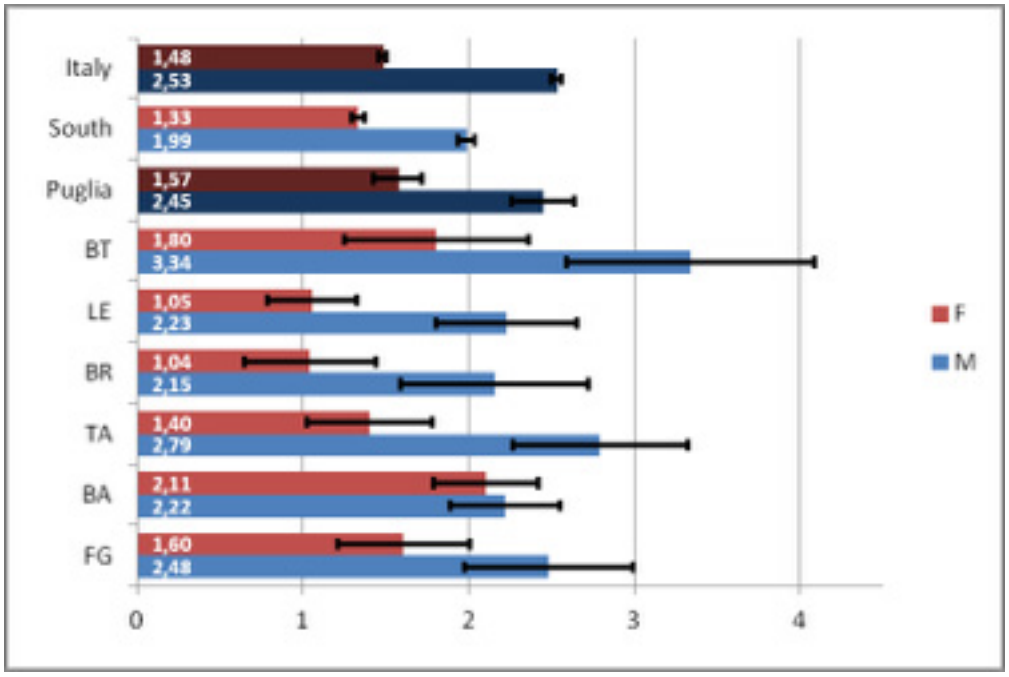


Figure 3. Relative survival of skin melanoma (EDERER II method) by Apulian district: Males.

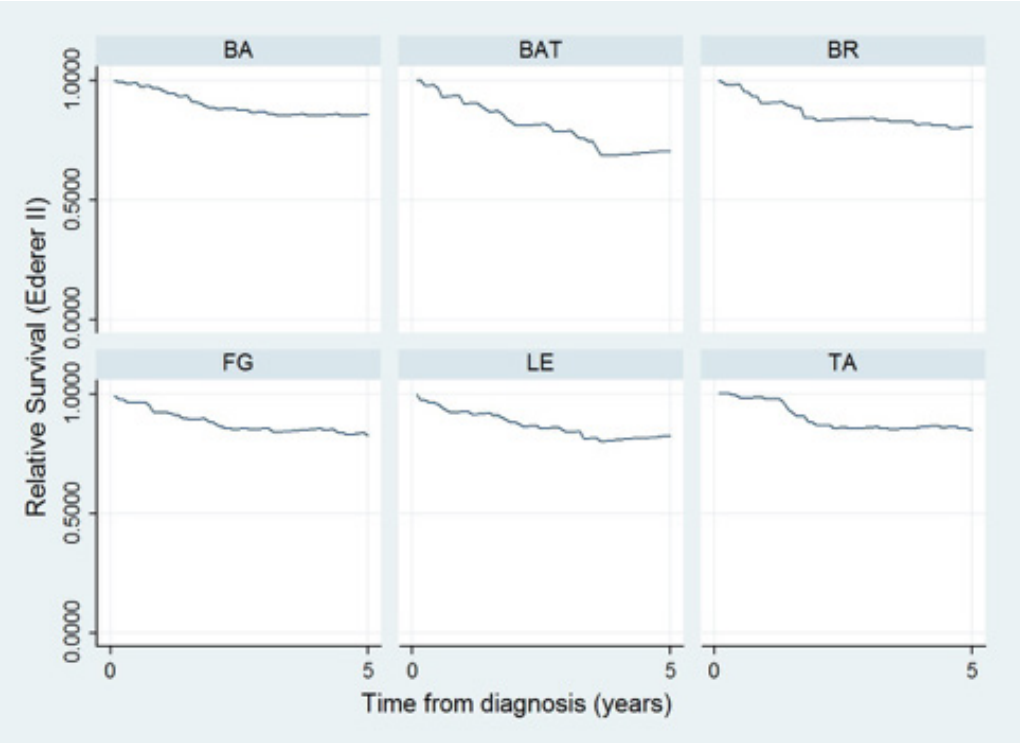
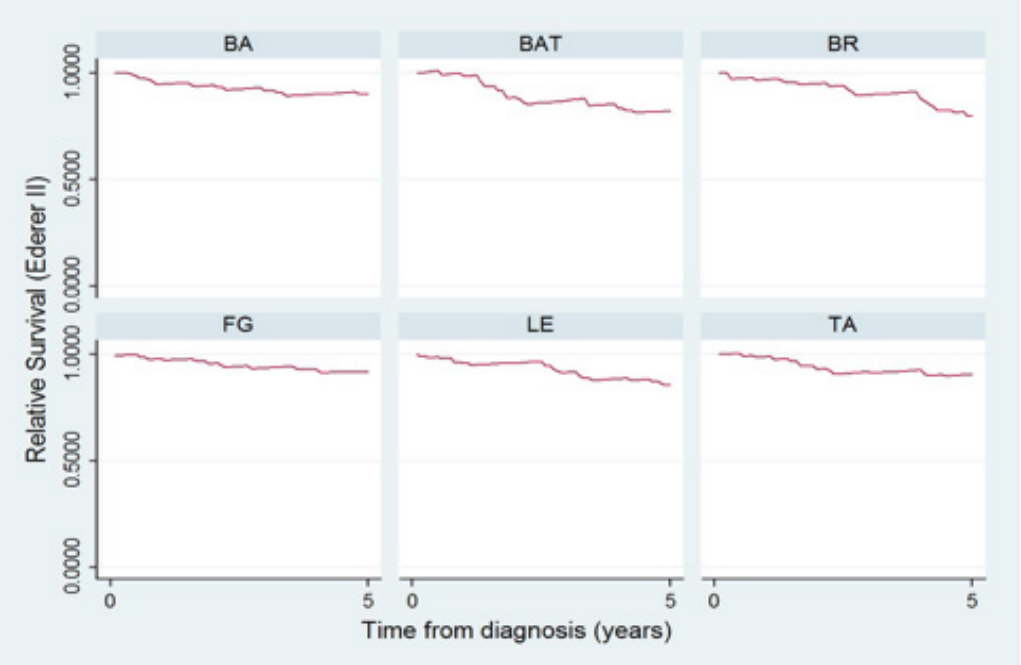


Figure 3. Relative survival of skin melanoma (EDERER II method) by Apulian district: Females.



CONCLUSIONS

Incidence of skin melanoma in Puglia is higher than in the southern Italy pool and lower than in the other three Italian macro-areas, without statistically significant differences. Therefore, this study adds an important element to the knowledge of geographical distribution of skin melanoma incidence in Italy, where a North to South gradient was already described. In Puglia itself a similar gradient can be observed, since the district with the lowest incidence is Lecce, which is the southernmost; Bari district shows the highest incidence, perhaps because it is a metropolitan area, where the opportunistic screening is more common and where there is a greater availability of public and private diagnostic centres; these data will be examined in further detail in order to interpret the ways of access to early diagnosis in Bari district in comparison to the other ones. This study is also an important example of the cooperation among the different sections of the RTP and results are characterized by high accuracy and good level of detail since cancer registry data represent the best approximation to the true cancer incidence in a population. The major limitations of the study were the short time period (three years) needed to ensure coverage of the entire region, and the time gap which depends on the complexity of accurate and complete cancer registration in a large region. However, for some districts more recent data (until 2012) and longer time periods (up to seven years) are already available. It would be also important to improve the capacity of staging in particular for the 'N' (lymph nodes) and 'M' (distant metastasis) of the TNM classification, information that is needed in order to carry out reliable prognostic assessment and survival estimates. Mortality of skin melanoma reflects mainly the earliness or lateness of diagnosis, rather than the incidence. High age-adjusted rates in BAT district, followed by Taranto in males are probably related to late diagnosis and advanced stages; in females high mortality rates in Bari, followed by BAT need further investigations. 5-years survival for melanoma in Puglia does not show a statistically significant difference from that of the whole AIRTUM pool, but it is higher than survival in the pool of southern registries. The heterogeneity in the estimated survival for the different districts of Puglia can be attributed to a different propensity to early detection; this interpretation is also supported by the different distribution of stage in the six districts. It is possible that the availability of specialized structures for the early diagnosis of melanoma, not equally distributed in the region, may affect early diagnosis and consequently survival.

Finally, our analysis is the first about incidence and survival of skin melanoma in a whole southern Italian region through cancer registry data and it can suggest hypotheses to be investigated with analytical studies. Moreover, we demonstrated an increment of incidence in young people, especially in women, as showed in literature; this result can be considered as a starting point for future research, using incidence data for a longer period of time. The cancer registry data have an inherently descriptive nature and allow ecological comparisons among different areas. It would be interesting to investigate in addition to the most well-known risk factors to which the greatest attributable risk is recognized, such as phenotype and solar exposure, other risk factors, primarily of a chemical nature, such as polychlorinated biphenyls [17], pesticides [18], dioxins [19]. However, to reach this objective it is needed on the one hand the achievement of many years of incidence, on the other the implementation of case-control studies to collect information about occupational, environmental and recreational risk factors.

Finally, data from this study are especially suitable for policy makers, public health managers, dermatologists, general practitioners, ordinary citizens in order to address inequalities of attention and access to diagnosis and treatment of skin melanoma; data should be also used for awareness-raising campaigns in schools, medical clinics, in order to improve primary and secondary prevention of this disease.

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References

1. WHO-IARC. Pathology and genetics of tumours of the skin [Internet]. Lyon: IARC Press; 2006 [cited 2016 Oct 15]. Available from: http://www.iarc.fr/en/publications/pdfs-online/pat-gen/bb6/.
2. Bulliard JL, De Weck D, Fisch T, Bordoni A, Levi F. Detailed site distribution of melanoma and sunlight exposure: aetiological patterns from a Swiss series. Ann Onc. 2007;18(4):789–794. doi: 10.1093/annonc/mdl490.
3. Osterlind A, Hou-Jensen K, MAller Jensen O. Incidence of cutaneous malignant melanoma in Denmark 1978-1982. Anatomic site distribution, histologic types, and comparison with non-melanoma skin cancer. Br J Cancer. 1988;58(3):385-391.
4. AIOM, CCM, ARTUM. I numeri del cancro in Italia 2015 [Internet]. Brescia: Intermedia editore; 2015 [cited 2016 Oct 15]. Available from: http://www.registri-tumori.it/PDF/AIOM2015/I_numeri_del_cancro_2015.pdf. Italian.
5. AIRTUM Working Group, CCM. Survival of cancer patients in Italy. Italian cancer figures. Report 2011. Epidemiol Prev. 2011;35(5-6) Suppl 3.
6. AIRTUM Working Group. I tumori in Italia. Rapporto 2007. Sopravvivenza. Epidemiol Prev. 2007;31(1-2) Suppl 1.
7. Rutherford MG, Ironmonger L, Ormiston-Smith N, Abel GA, Greenberg DC, Lyratzopoulos G, et al. Estimating the potential survival gains by eliminating socioeconomic and sex inequalities in stage at diagnosis of melanoma. Br J Cancer. 2015;112:S116–S123.
8. Erdey E, Torres SM. A new understanding in the epidemiology of melanoma. Expert Rev Anticancer Ther. 2010 November;10(11):1811–1823. doi:10.1586/era.10.170.
9. Chang Y, Barrett JH, Bishop DT, Armstrong BK, Bataille V, Bergman W, et al. Sun exposure and melanoma risk at different latitudes: a pooled analysis of 5700 cases and 7216 controls. Int J Epidemiol. 2009;38:814–830. doi:10.1093/ije/dyp166.
10. Crocetti E, Buzzoni C, Chiarugi A, Nardini P, Pimpinelli N. Relationship between latitude and melanoma in Italy. ISRN Oncol. Volume 2012 (2012), Article ID 864680, 5 pages. doi:10.5402/2012/864680.
11. ITACAN. AIRTUM Database online [Internet]. Milano: Airtum; 2016 [cited 2016 Oct 15]. Available from: http://www.registri-tumori.it/cms/it/bancadati.
12. SEER Training Modules [Internet] Washington, DC: US Department of Health & Human Services. National Institute of Health. National Cancer Institute [cited 2016 Oct 15]. Available from: http://training.seer.cancer.gov/ss2k/staging/review.html.

13. ISTAT [Internet]. Rome: ISTAT; 2016 [cited 2016 Oct 15]. Available from: http://www.istat.it/it/. Italian.

14. Cho H, Howlader N, Mariotto AB, Cronin KA. Estimating relative survival for cancer patients from the SEER Program using expected rates based on Ederer I versus Ederer II method. Surveillance Research Program, NCI, Technical Report #2011-01 [Internet] [cited 2016 Oct 15]. Available from: https://surveillance.cancer.gov/reports/tech2011.01.pdf.

15. Hakulinen T, Seppa K, Lambert PC. Choosing the net survival method for cancer survival estimation. Eur J Cancer. 2011;47:2202–2210.

16. Perme MP, Stare J, Estève J. On estimation in relative survival. Biometrics. 2012;68:113-120.

17. Pirastu R, Ricci P, Comba P, Bianchi F, Biggeri A, Conti S, et al. SENTIERI Project: discussion and conclusions. Epidemiol Prev. 2014 Mar-Apr;38(2 Suppl 1):125-33.

18. Fortes C, Mastroeni S, Melchi F, Pilla MA, Alotto M, Antonelli G, et al. The association between residential pesticide use and cutaneous melanoma. Eur J Cancer. 2007 Apr;43(6):1066-1075.

19. Akhtar FZ, Garabrant DH, Ketchum NS, Michalek JE. Cancer in US Air Force veterans of the Vietnam War. J Occup Environ Med. 2004 Feb;46(2):123-136.