

Survival of metastatic cancer and myeloma patients after diagnosis of Osteonecrosis of Jaws (ONJ). Potential impact on ONJ treatment strategies.

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Abstract

Survival of cancer and myeloma patients after diagnosis of medication-related Osteonecrosis of Jaws (ONJ) has not adequately been reported. ONJ is not rare in patients with bone metastatic cancer and myeloma patients, occurring mostly after prolonged treatment with antiresorptive drugs (zoledronic acid and other bisphosphonates, and/or denosumab). On the other hand, expected residual survival can influence the choice of ONJ treatment strategies (surgical versus conservative). We reviewed survival data after ONJ diagnosis time of 609 patients registered in the regional database of a cancer network in North-Western Italy (Rete Oncologica di Piemonte e Valle d'Aosta).

Main characteristics. Disease: metastatic breast cancer 43%; myeloma 24.1%; prostate cancer 19.2%; lung cancer 5.7.% renal cancer 3.2% other cancer types 4.8%. Sex: 237 M, 372 F. Median age 69 (32-90) years. Main treatment: 79.1% zoledronic acid, 4.8% denosumab; 16.1 % other drugs or drug sequences. Observed actuarial median survival after the registered ONJ diagnosis time was 29 (95% CI 26-35)

months for breast cancer patients, 31 (95% CI 28-43) months for myeloma patients, 19 (95% CI 15-26) months for prostate cancer patients, 11 (95% CI 5-19) months for lung cancer patients, 30 (95% CI 13-57) months for renal cancer patients, 53 (95% CI 17-84) months for other cancer patients.

Two, three and four-year actuarial survival were respectively: 57.6%, 42.2%, 33.9% for breast cancer patients, 64.6%, 44.9%, 36% for myeloma patients, 42.7%, 27.3%, 19.6% for prostate patients; 28.5%, 14.3%, 11.4% for lung cancer patients; 57.8%, 36.8%, 26.3% for renal cancer patients; 62%, 58.6%, 58.6% for others cancer types.

In conclusion, expected survival after ONJ diagnosis is not really short (less than one year) in most of ONJ patients. Our data do not support generalized exclusion of jawbone surgery in ONJ patients due to expected short survival.

Background: There are few literature data about survival of cancer and myeloma patients after diagnosis of Osteonecrosis of Jaws (ONJ) related to antiresorptive treatment (bisphosphonates or denosumab), with/without biological agents ([1] [2] [3] [4] [5]). Osteonecrosis of Jaws (ONJ) is not rare in patients with bone metastatic cancer and myeloma patients, occurring after prolonged antiresorptive treatment: most of cases are registered after 12-36 months of treatment, even if with a large range (cases observed after few months and other after more than ten years). Furthermore, the expected residual survival after ONJ diagnosis can influence the choice of ONJ treatment strategies: many authors exclude surgery on the base of a supposed short expected survival and for fear of a worsened quality of life and/or impaired ability to tolerate surgery. Some guidelines recommend surgery exclusively for advanced ONJ ([6], [7]), whereas other authors and groups recommend surgery even in early stages of ONJ, to give a better quality of life for patients' residual life time ([8], [9], [10], [11][12]). We analyzed the survival after ONJ diagnosis time in cancer and myeloma patients of a large regional ONJ database ([13], [14])

Materials and Methods: Reports of ONJ patients were retrospectively collected and cross-checked from medical oncology, haematology, and oral care Units of North-Western Italy (Rete Oncologica di Piemonte e Valle d'Aosta), over a 16-year timespan - January 1st, 2003- December 31st, 2018. The following data was collected: M/F ratio, mean age/age range at diagnosis of MRONJ, type of cancer, type of drug - zoledronate, denosumab, others - and date of death, whenever occurred. Kaplan-Meier curves were formulated for survival analysis within each subset of cancer patients, with the aims of acquiring the actuarial median survival, expressed in months, after ONJ diagnosis, as well as the two, three and four-years actuarial survival curves.

Results Data from 609 patients (237 M, 372 F) were acquired. Median age at diagnosis of MRONJ was of 69 (32-90) years, with 127 (20.8%) under 60 years old, 211 (34.7%) of 60-70 years old, 271 (44.5%) over 70 years old.

Underlying diseases were breast cancer (262/609, 43%), multiple myeloma (147/609, 24.1%), prostate (117/609, 19.1%) lung cancer (35/609, 5.7%), renal cancer (19/609, 3.2%), other types of cancer (29/609,

4.8%).

Sex distribution for each cancer was as follows: breast cancer 6 M, 256 F; prostate cancer: 117 M; multiple myeloma: 64 M, 83 F; lung cancer: 18 M, 17 F; renal cancer 15 M 4 F; other cancers: 17 M, 12 F.

Age at ONJ diagnosis for each cancer was as follows: breast cancer 69 ± 9.1 (range 32-90) years; prostate cancer 71 ± 5.9 (age range 54-86) years; myeloma 72 ± 7.4 (range 47-89) years; lung cancer 66 ± 7.6 (range: 49-80) years; renal cancer 62 ± 6.3 (age range 46-73) years; others 69 ± 9.6 (range 40-85) years.

Distribution of main treatment administered was as follows: 79.1% zoledronic acid, 4.8% denosumab; 16.1% other drugs or drug sequences.

Observed actuarial median survival after ONJ diagnosis was as follows:

- breast cancer 29 (95% CI: 26-35) months (Fig 1);
- prostate cancers: 19 (95% CI: 15-26) months (Fig 2);
- multiple myeloma 31 (95% CI: 28-43) months (Fig 3);
- lung cancer 11 (95% CI: 5-19) months;
- renal cancer 30 (95% CI: 13-57) months;
- others: 53 (95% CI: 17-84) months.

From the actuarial survival curves the following survival rates at 2,3,4 years emerged, respectively: breast cancer : 57.6%, 42.2%, 33.9%; myeloma: 64.6%, 44.9%, 36%; prostate cancer : 42.7%, 27.3%, 19.6%; lung cancer : 28.5%, 14.3%, 11.4%; renal cancer : 57.8%, 36.8%, 26.3%; other cancers: 62%, 58.6%, 58.6%.

Conclusions. : Survival of cancer and myeloma patients after ONJ diagnosis is not short as one could expect on the basis of literature data. Consequently, exclusion of surgical treatment of ONJ disease due to patient expected short survival seems not to be warranted.

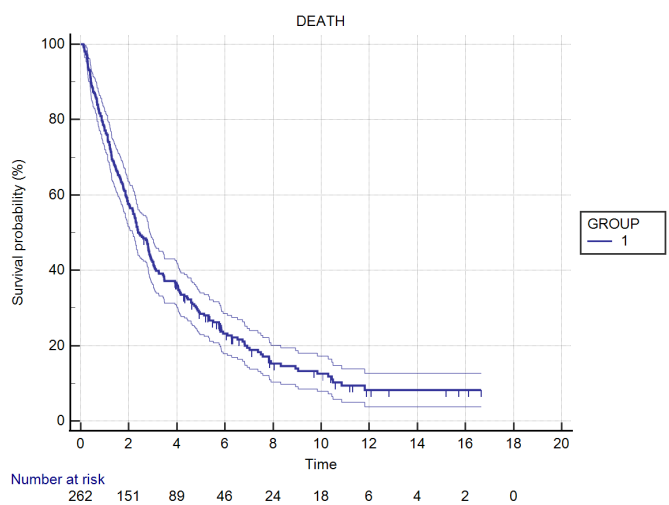


Figure 1 - Breast cancer patients actuarial survival

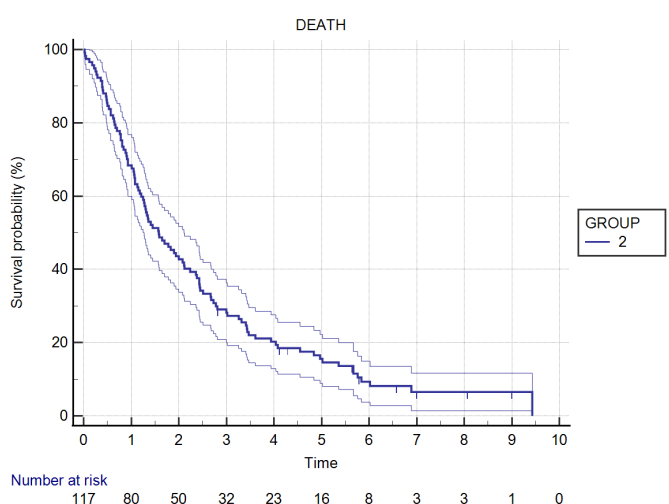


Figure 2 - Prostate cancer patients actuarial survival

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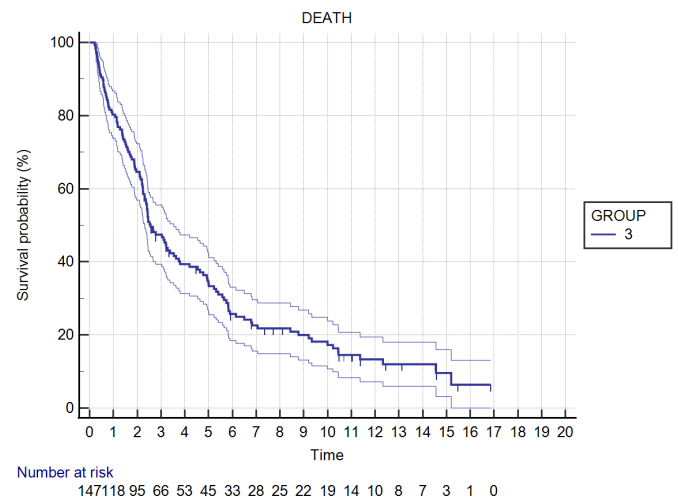


Figure 3 - Myeloma patients actuarial survival

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