

IS LOCAL RECURRENCE IN EXTREMITY SARCOMA JUST A LOCAL RECURRENCE, OR DOES IT IMPACT THE OVERALL AND CANCER SPECIFIC SURVIVAL; NESTED CASE CONTROL STUDY FROM A SARCOMA REFERRAL CENTER.



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Background

- Extremity sarcoma is typically treated with a limb-sparing resection with improved functional outcomes compared to amputation. However, this can lead to close margins and an increased rate of local recurrence (LR).
- LR has been associated with decreased overall survival in many studies, but it remains unclear if the relationship is causal or simply representative of aggressive tumor biology.
- If LR precedes disseminated disease, this raises the question of whether the LR could have been the cause of the subsequent metastasis.
- Objectives of the study were to report the proportion of LR in isolation, LR with prior or concurrent metastasis, and LR with subsequent metastasis (LRSM) to determine if LR can be seen as an isolated and separate oncologic event, or if LR could be the source of disease dissemination.

Methods

- Investigators identified patients who developed LR from an ongoing prospective cohort of bone and soft tissue sarcoma patients.
- Cases were patients who developed LR with subsequent metastasis (LRSM).
- We compared this group with 3 different groups; 1) LR in isolation, 2) LR with synchronous metastases and 3) patients who developed metastases without LR.
- We excluded all patients who neither had LR nor metastases.
- Non-parametric analysis was used followed by overall and cancer specific survival analysis at 1, 2 and 5 years.
- Results were reported in-line with the criteria of Strengthening The Reporting of Cohort Studies in Surgery (STROCSS).

Figure 1: Patients' participation status flowchart.

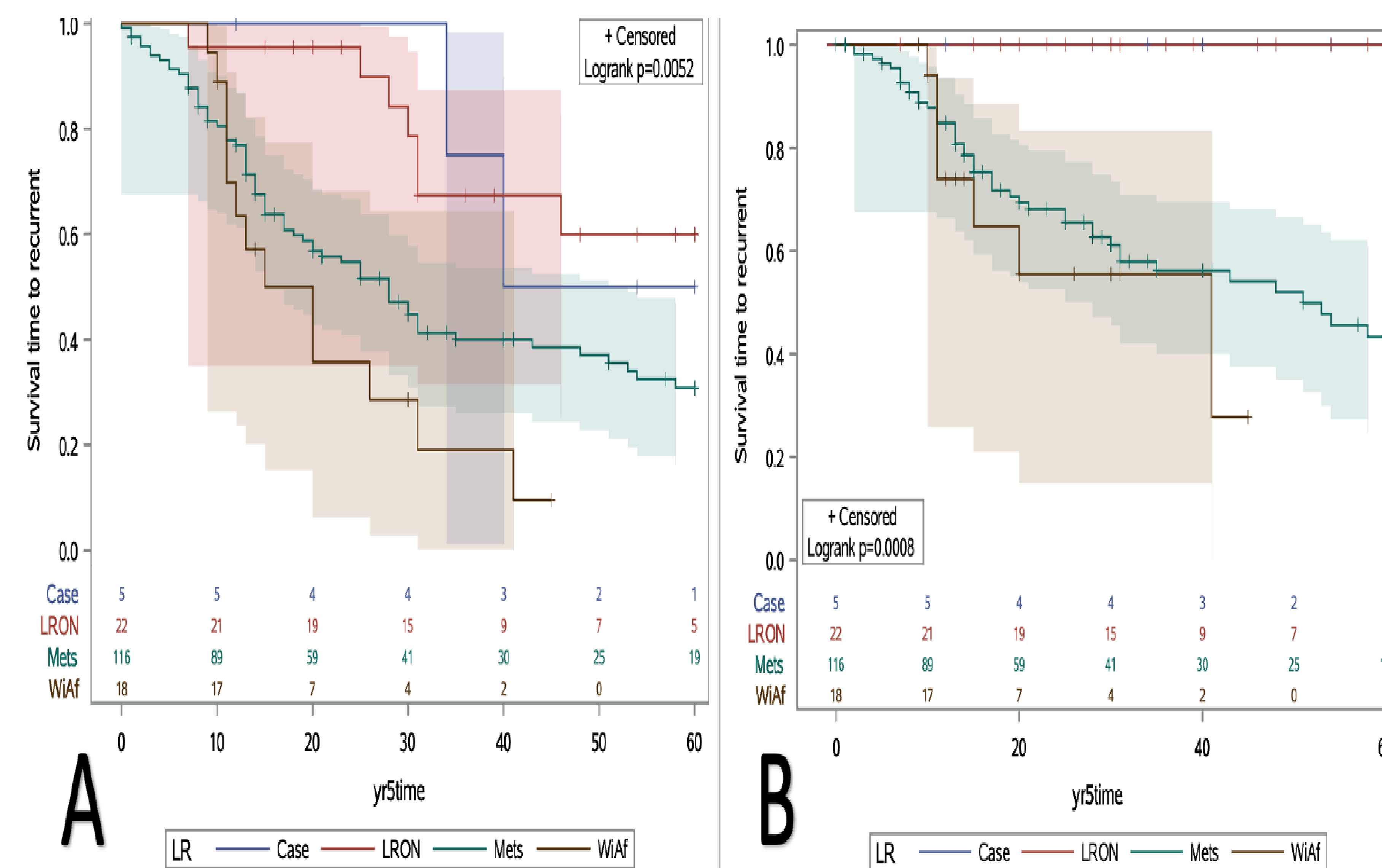
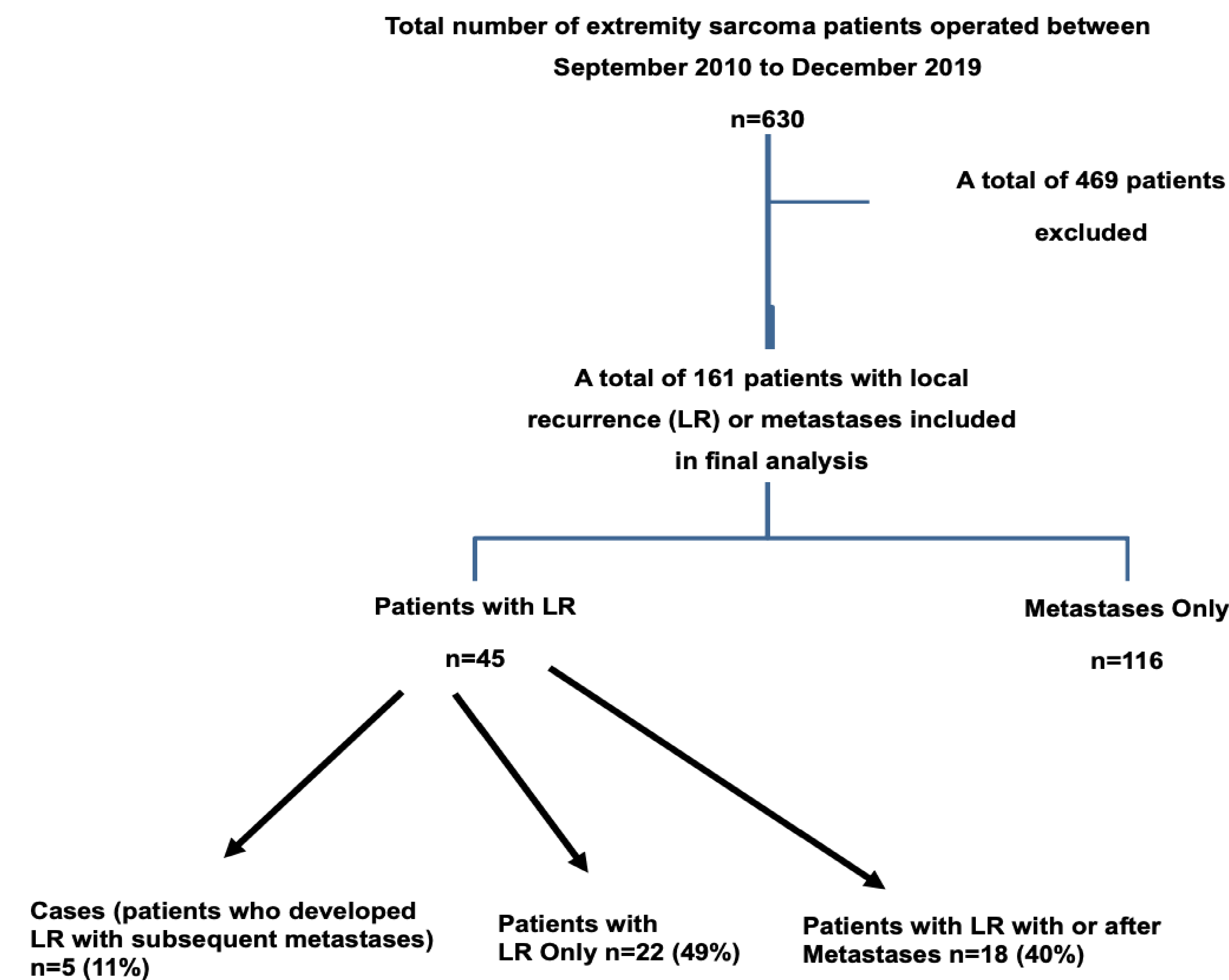


Figure 2: A. Overall 5 years-survival between the 4 groups. **B.** Cancer-specific 5 years-survival.

LR= Local Recurrence; Case= (LR with subsequent Mets), LRON= LR Only, Mets= Metastases only group, WiAF= LR with synchronous Mets.

Results & Discussion

- From the overall cohort of 630 bone and soft tissue sarcoma patients treated between September 2010 to December 2019, 161 patients met the inclusion criteria with overall incidence of LR in 45 (7%) patients (Figure 1). Out of the 161 patients, 5 (3%) developed LRSM, 22 (14%) had LR in isolation, 18 (11%) had LR with prior or synchronous metastases, and 116 (72%) patients developed metastases without LR. When comparing the cases (LRSM) to controls (LR in isolation), cases were younger 49 ± 22 Vs 67 ± 27 years. Moreover, cases developed metastases after a median of 12.5(4-19) months. Bone sarcoma patients were more likely to develop LRSM than soft tissue sarcoma (OR 8.5 [95% CI 1.3-58.8]). Surgical margin, tumor grade and radiotherapy were not associated with the LRSM.
- At 5 years follow-up, the mean \pm SD of time to death in months in the 4 groups were 39.5 ± 2.6 for the LR in isolation group, 38 ± 1.8 for the LRSM, 31.9 ± 2.1 for those who developed metastases without LR and 21.3 ± 3.1 for the LR with synchronous metastases group. The 2 and 5 years overall and cancer-specific survival were highest for the LR in isolation group followed by the LRSM patients while worst for the patients who had LR with synchronous metastases with p value of <0.01 (Figure 2).
- At subgroup analysis, there was no significant difference in overall survival between the LRSM and LR in isolation group at 1, 2 and 5 years with p values of 0.6, 0.6 and 1.0, respectively.

Conclusion

- Developing LR with subsequent metastases is very rare, not related to the surgical margin and not associated with worse survival as compared to LR in isolation. In 11% of cases, the LR preceded disseminated disease and raises the question of whether the LR could have been the cause of the subsequent metastasis. The answer to this question has implications regarding surgical margins, borderline limb salvageable presentations, functional preservation, and the use of radiation. We recommend further studies with a larger sample size to determine the factors associated with such an outcome.