

Outcomes for the young healthy nasopharyngeal carcinoma patients with radiation induced sarcoma – A retrospective study

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Introduction

Nasopharyngeal carcinoma (NPC) is endemic in southern part of China. Radiation therapy is the primary treatment for NPC. As there is a large group of long-term survivors followed up in our clinic, we have the privilege to study long-term complications of radiation therapy, including radiation-induced sarcoma (RIS).

Objective

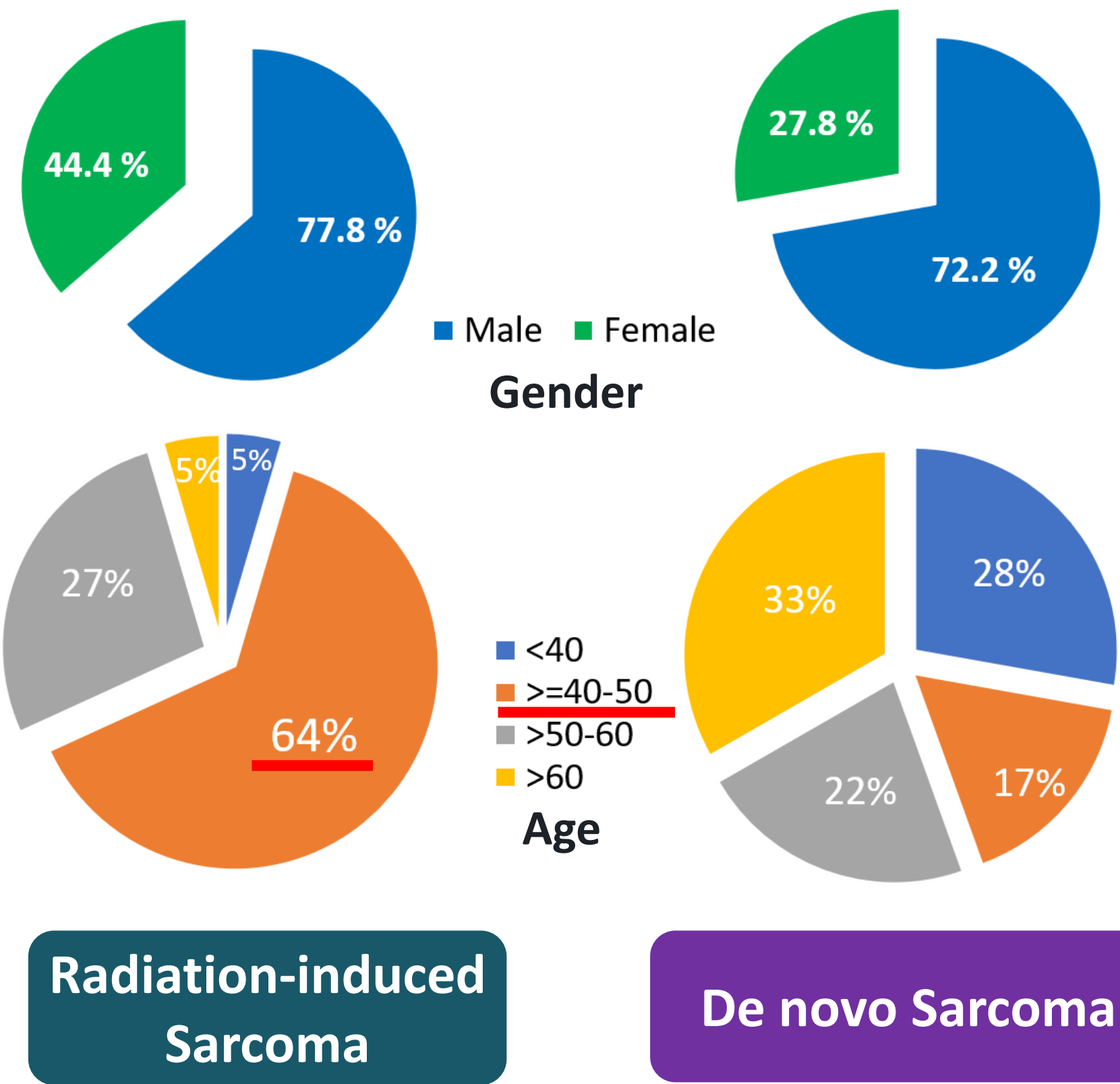
To study clinical presentations and outcomes, and pathological features, of RIS for NPC survivors. Comparisons to De novo sarcoma subjects were made.

Methods

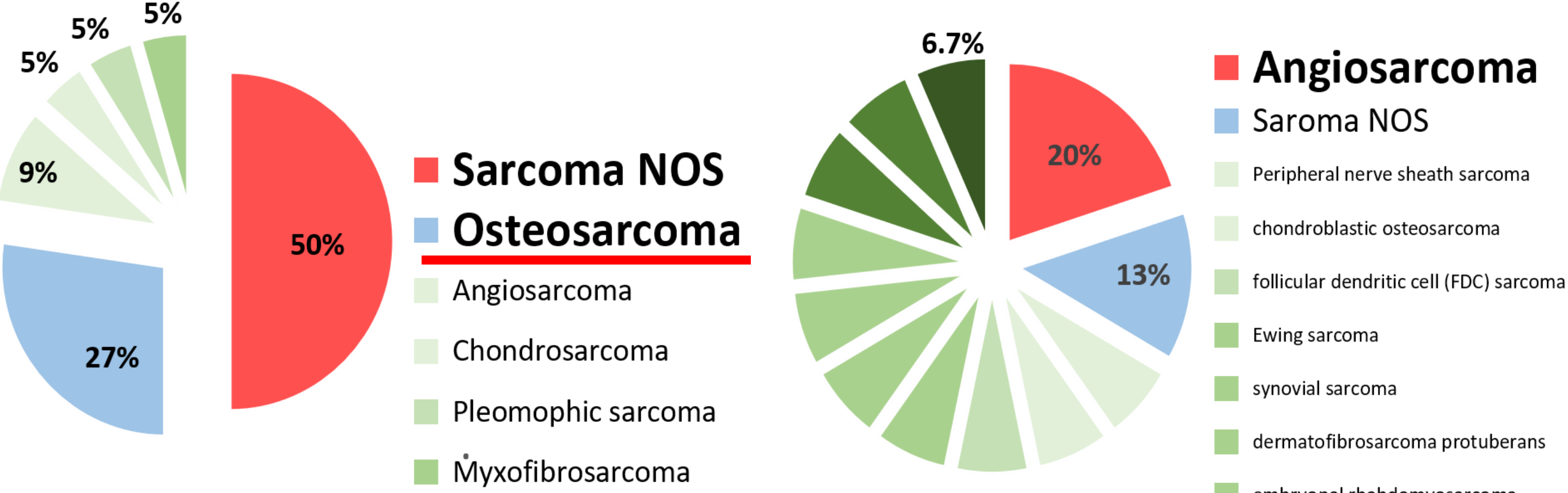
This is a retrospective study. Patients with head & neck sarcoma managed in the Department of Otorhinolaryngology, Head and Neck Surgery, of Prince of Wales Hospital in Hong Kong, from 2009 to 2019, were recruited. They were either with radiation induced sarcoma (with history of NPC with radiation therapy received) or De novo sarcoma (with no history of NPC or radiation therapy). Pediatric patients or those with inadequate clinical information were excluded. Sarcoma regarded as “radiation-induced” must fulfill all the following criteria - 1. Tumor should occur within the previously irradiated field. 2. There must be a histological proof of sarcoma and the pathology was different from the primary histology. 3. The tumor should arise at least 3 years after the irradiation. There were 22 subjects with radiation induced sarcoma (RIS) and 18 subjects with De novo sarcoma.

Results and Discussions

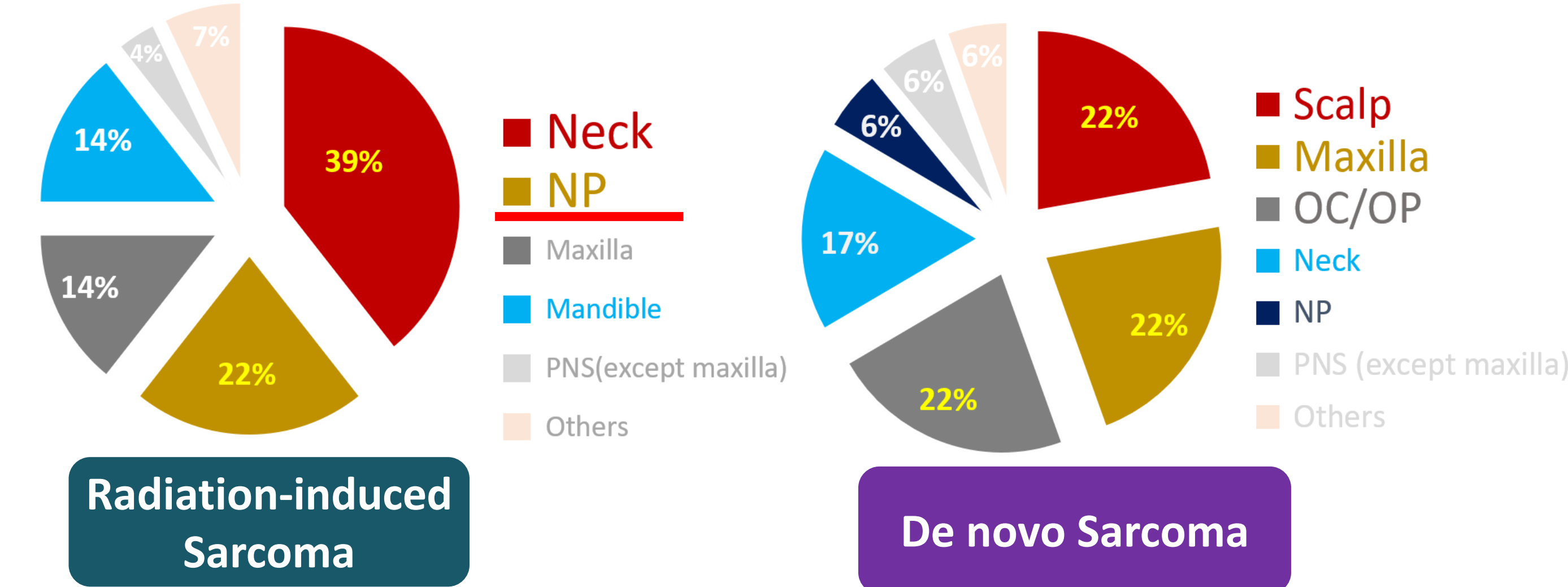
Demographics (Fig1,2)



Histological Subtypes (Fig3)



Tumor locations (Fig4)



TNM-stage - Each subject was staged according to American Joint Committee on Cancer (AJCC) 8th edition. RIS usually presented **late** compared to De novo sarcoma – often at an **advanced T-stage at presentation**. (72% with T4a/b and 14% with T3). This could be due to neck fibrosis after radiation therapy, which may make small neck tumors less easily identifiable early. Preferential locations of the tumor could also be a reason. For example, angiosarcoma in the De novo group often presented on skin/scalp, which was more superficial and easily identifiable at their early stages. It was **uncommon** for both RIS and De novo sarcoma to have **neck lymph nodes** involvement - only 20% had N1 disease for both groups. **None** of the subjects have **distant metastasis** at presentation.

Treatment modality (Fig6) - Most subjects received surgery. Subjects not receiving surgery were mostly due to inoperable disease. For RIS operated patients, two-third received just **surgery alone with no adjuvant therapy**. This is because after previous radiotherapy, there was often **limited room for re-irradiation**, which might cause severe radiation related complications. In contrast, all the operated patients in De novo group also received neoadjuvant / adjuvant therapy. This may explain the differences in disease survival and recurrence between two groups.

Overall survival (OS) - RIS group had a significantly **worse overall survival (OS)** than De novo group (Fig7). We further stratified each group into operated & non-operated subgroups. (Fig8) Both non-operated subgroups had similarly poor survival. Most subjects died within two years. And their operated counterparts had significantly better OS. These show that **surgery is the main stay of treatment** modality to give significant survival benefit for both groups.

Disease Recurrence - For subjects with **recurrence**, almost 90% in radiation group happened **locally**. In contrast, de novo sarcoma group had more distal recurrence. This could be that more subjects were able to receive adjuvant radiotherapy for primary disease site in De novo group.

Prognostic factors of radiation induced sarcoma for NPC survivors

Univariate analysis was performed for several parameters to identify possible relationship to survival outcomes.

Receiving Surgery (Fig9) There was significant OS benefit for subjects receiving surgery than those who did not. Their 2-year overall survival was 60% and 5-year was still above 40%. In contrast, all non-operated subjects passed away within 2 years.

Clear resection margin (Fig10) There was significant OS benefit if clear resection margin could be achieved. For those with clear resection margin, the mean OS was 34.5 months. Those with close/involved margin, the mean overall survival was 19.2 months.

Limitation - The sample size for the study is small. It is difficult to perform more subgroup/multivariate analysis. Further collaboration with other centres with similar group of patients is necessary to give more significant results.

Conclusion

Radiation induced sarcoma for NPC survivors has different clinical, histological and prognostic profiles compared to De novo sarcoma. Surgery with clear resection margin is the treatment option to result in overall survival benefit.

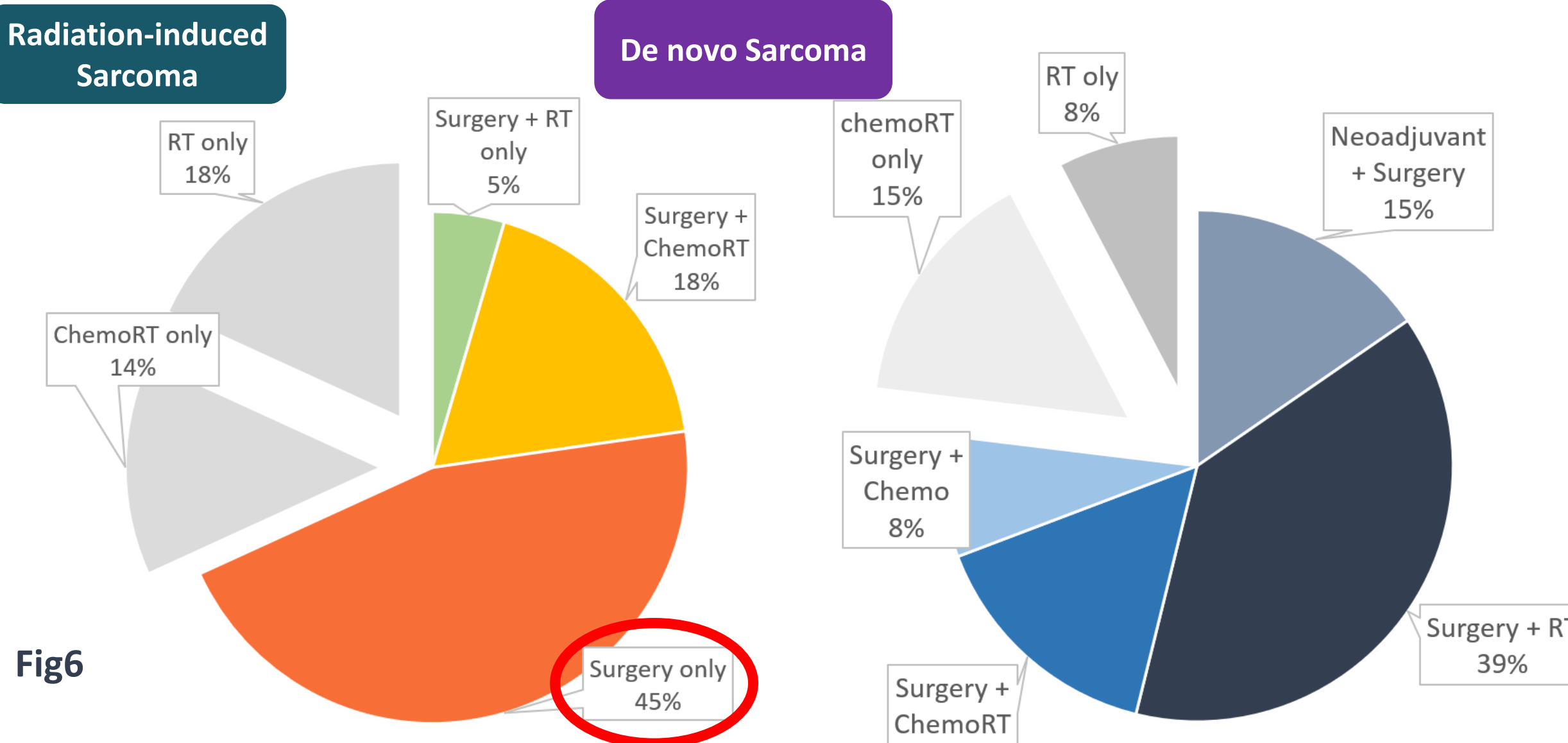
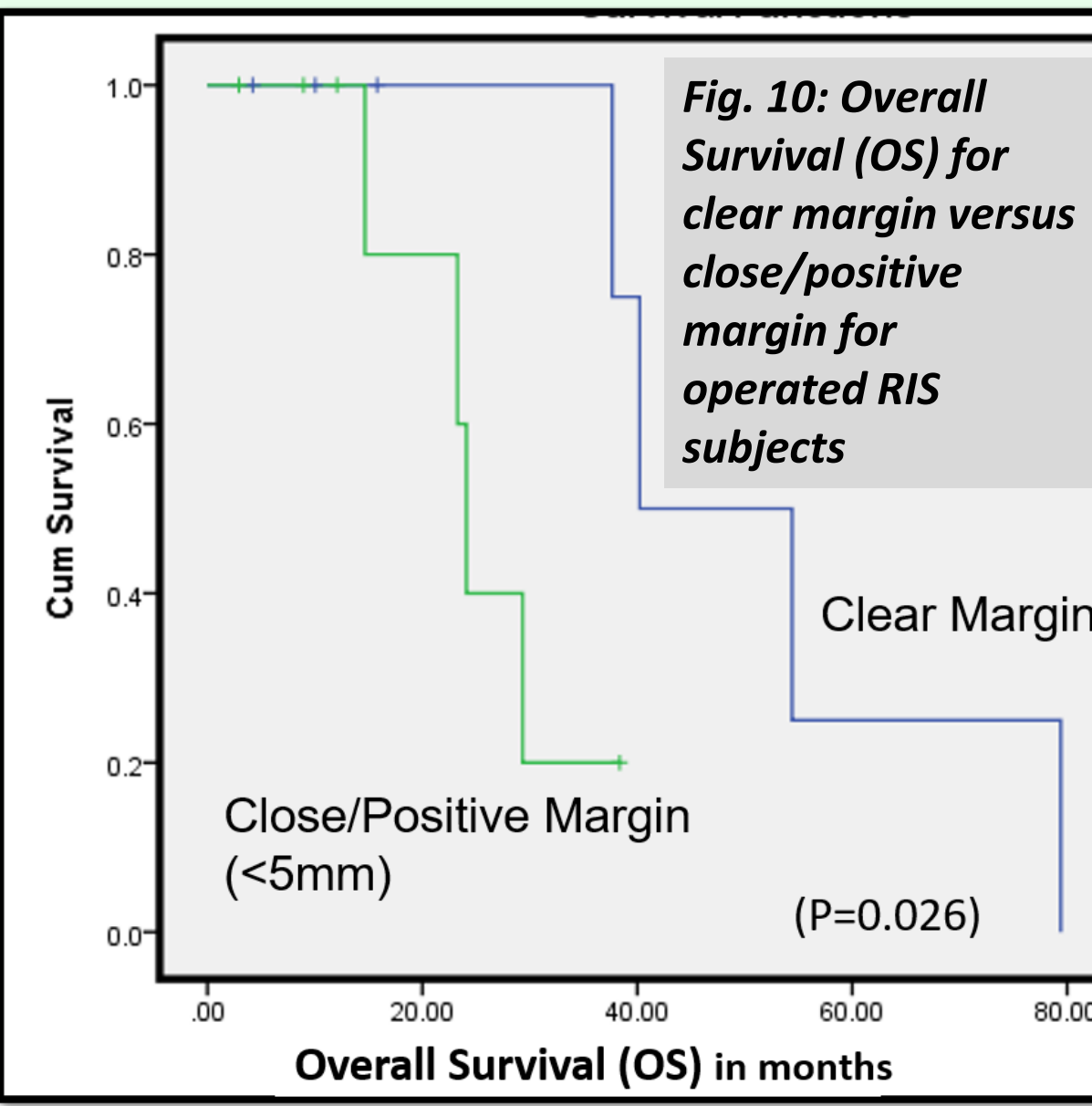
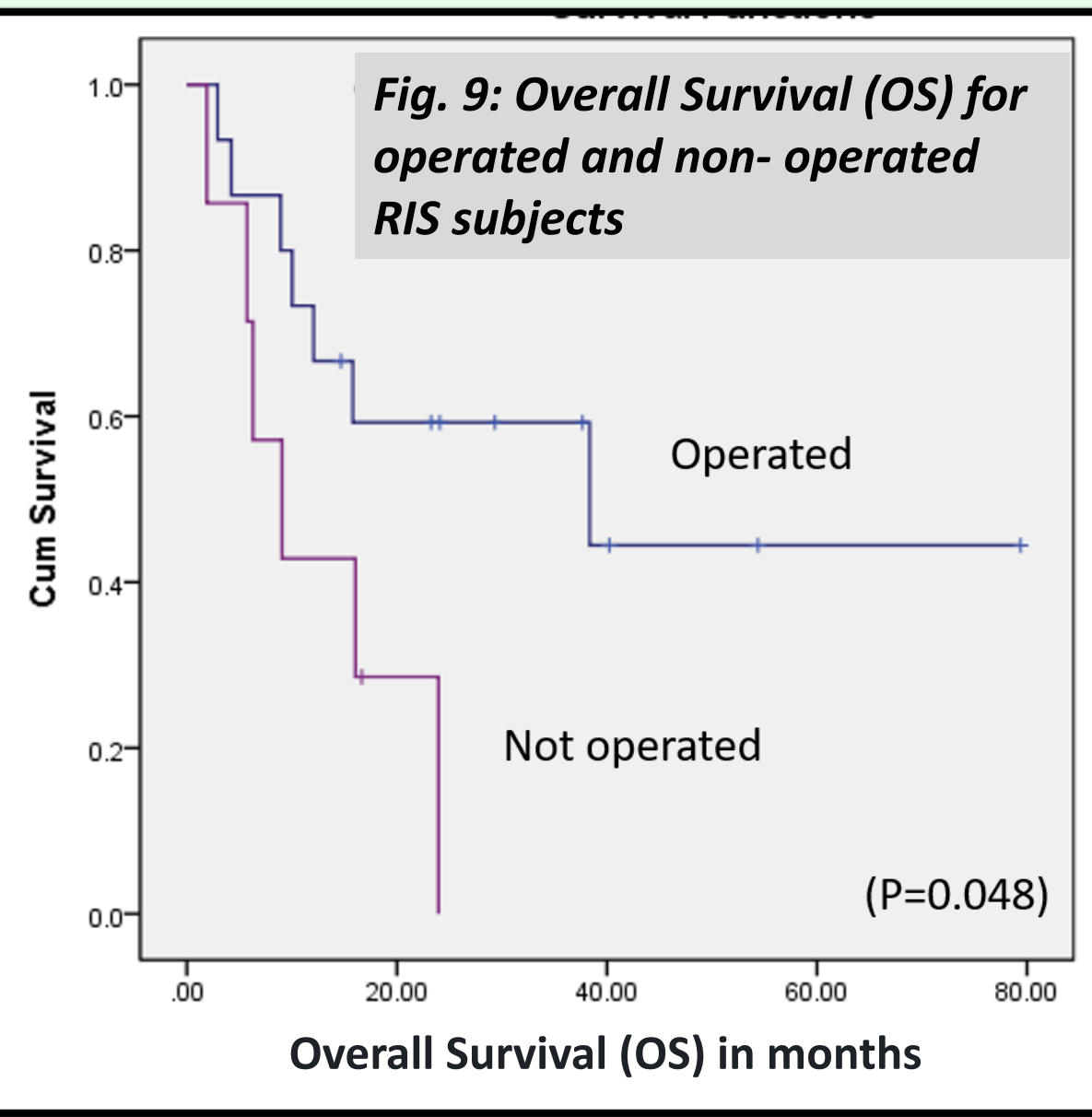
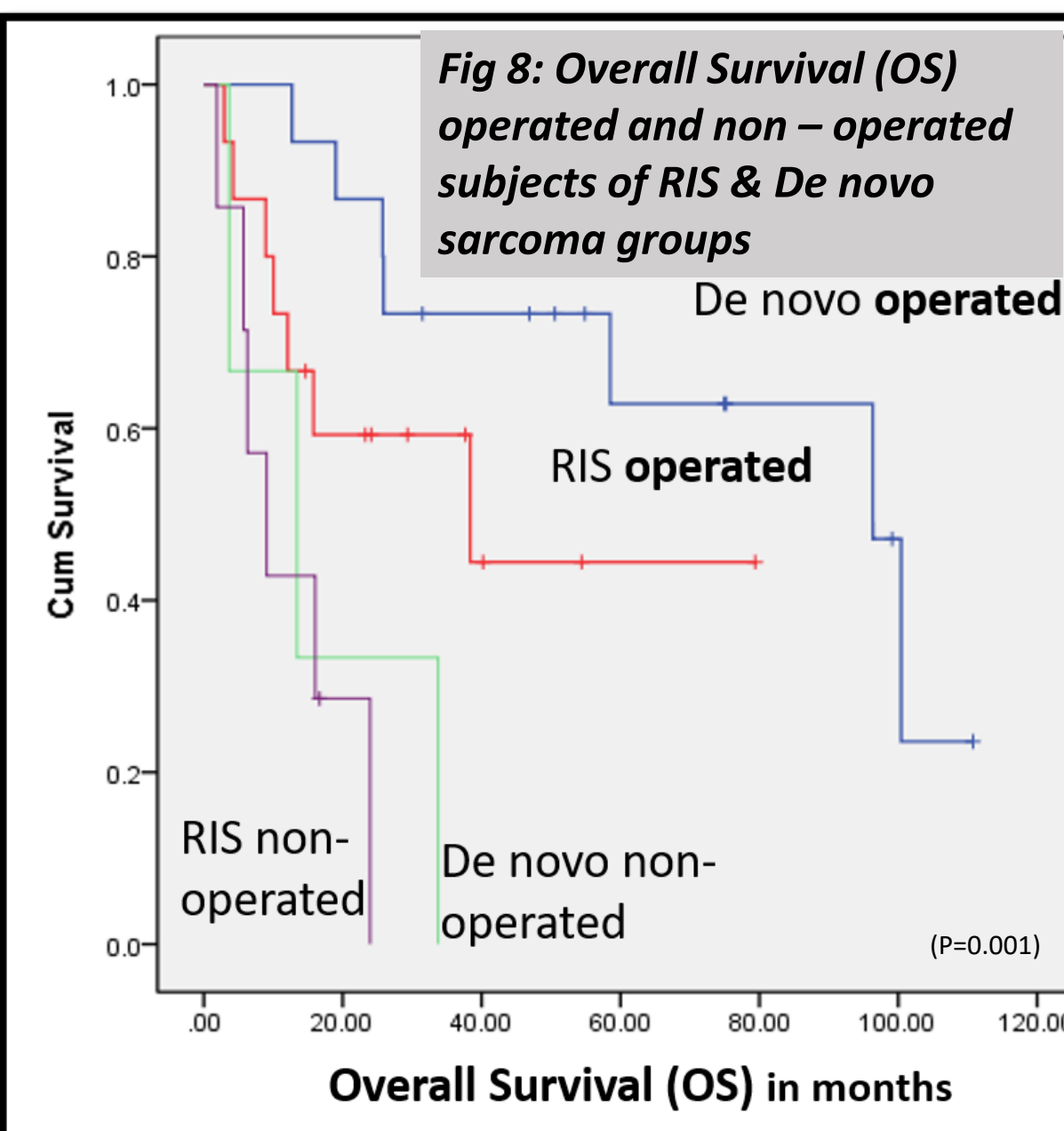
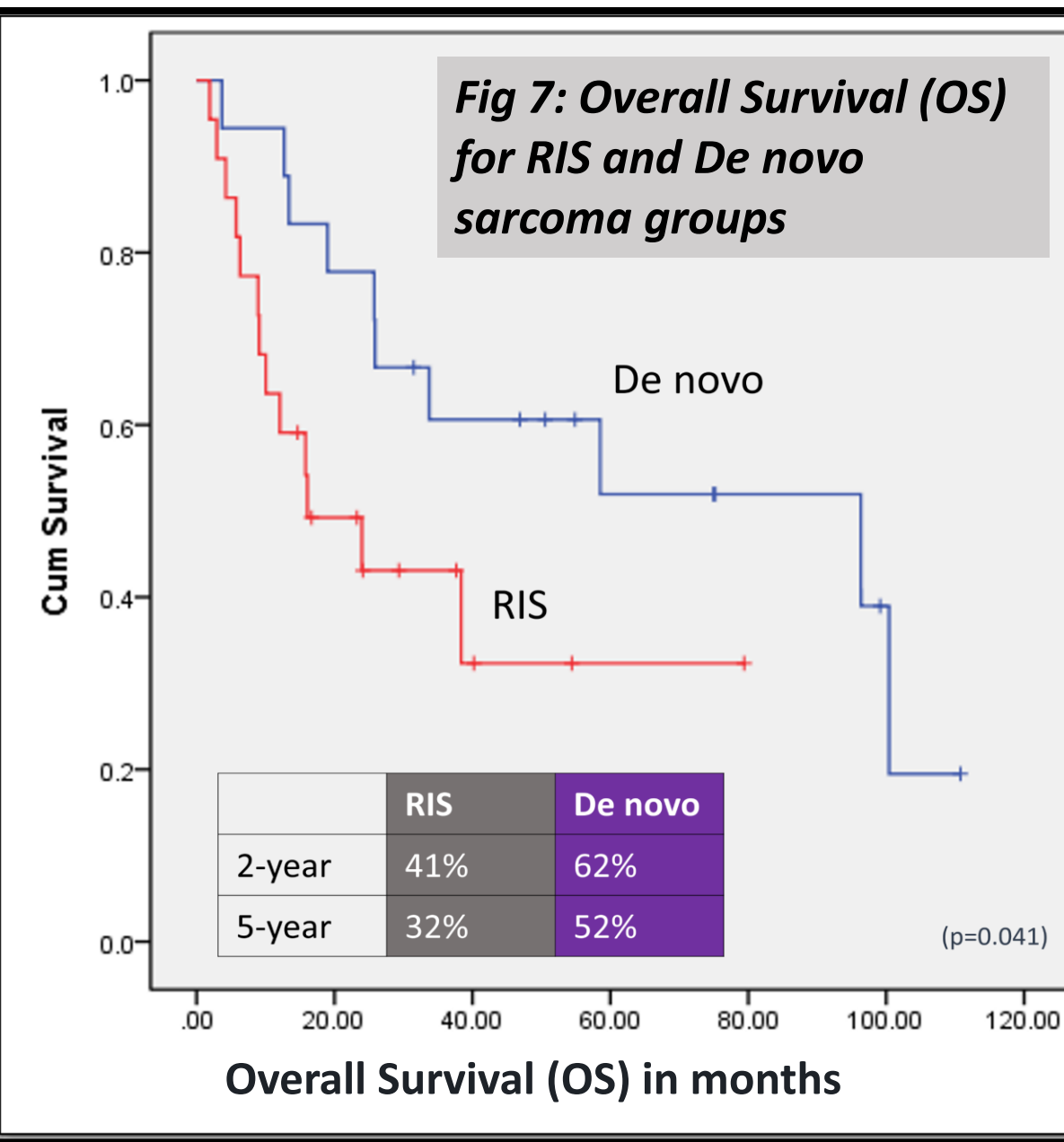


Fig6



Selected reference

1. Cha C, Antonescu CR, Quan ML, Maru S, Brennan MF. Long-term results with resection of radiation-induced soft tissue sarcomas. Ann Surg. 2004;239:903–909
2. Murray EM, Werner D, Greeff EA, Taylor DA. Postradiation sarcomas: 20 cases and a literature review. Int J Radiat Oncol Biol Phys. 1999;45:951–961