

Utility of Medical Therapy in Mandibular Osteoradionecrosis

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ABSTRACT

Background: Mandibular osteoradionecrosis (ORN) is a challenging problem for the head and neck surgeon. Most cases of ORN occur within the first three years following radiation therapy (RT). Traditional conservative management of ORN has included oral hygiene, analgesics, antibiotics, limited surgical debridement and hyperbaric oxygen therapy, while advanced cases have required resection and reconstruction, usually necessitating microvascular free tissue transfer. More recently, there has been evidence supporting the use of pentoxifylline and tocopherol (P&T) as components of conservative medical management. The purpose of this study is to evaluate the outcomes of patients based on their medical treatment.

Study Design: Retrospective cohort study

Methods: All patients with a diagnosis of mandibular ORN treated in head and neck oncology clinic at a tertiary care medical center over an 11-year period (2003-2014) were reviewed. During this time frame, the use of P&T was introduced into the medical management of patients with ORN. Treatment details, symptoms, and outcomes including pathologic fracture, progression of disease, need for debridement, and need for resection and major reconstruction were assessed.

Results: 48 patients met inclusion criteria. 43 patients (89.6%) were treated with antibiotics. 14 patients (29.2%) were treated with P&T. 17 (35.4%) patients presented with or progressed to pathologic fracture. 27 patients (56.3%) required a surgical procedure from minor debridement to resection with major reconstruction. 12 patients (27.9%) required mandibulectomy and reconstruction with microvascular free tissue transfer. Overall, progression of ORN was noted in 28 patients (58.3%). When assessed using standard Kaplan-Meier approach, there was no statistically significant difference between time to pathologic fracture or time to surgery for patients treated with or without P&T. However, despite not achieving statistical significance, a larger percentage of patients treated with P&T were noted to have disease progression (71.4% vs. 52.9% without P&T) and to have pathologic fractures (50.0% vs. 28.6% without P&T).

Conclusions: There was no significant benefit of the use of P&T in patients with mandibular ORN in terms of time to pathologic fracture or time to surgical intervention. However, there was an apparent selection bias towards the use of P&T in more advanced cases. Future studies should match cases based on presenting severity in order to obtain a more complete evaluation of the impact of P&T. Additionally, comorbid factors (e.g., radiation dose, diabetes) and patient behaviors (e.g., tobacco use, compliance with medical regimen) need to be assessed for their contribution to outcome.

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BACKGROUND

Mandibular osteoradionecrosis (ORN) is a challenging problem for the head and neck surgeon. Most cases of ORN occur within the first three years following radiation therapy (RT). Traditional conservative management of ORN has included oral hygiene, analgesics, antibiotics, limited surgical debridement and hyperbaric oxygen therapy, while advanced cases have required resection and reconstruction, usually necessitating microvascular free tissue transfer. More recently, there has been evidence supporting the use of pentoxifylline and tocopherol (P&T) as components of conservative medical management. The purpose of this study is to evaluate the outcomes of patients based on their medical treatment.¹

METHODS

All patients with a diagnosis of mandibular ORN treated in head and neck oncology clinic at a tertiary care medical center over an 11-year period (2003-2014) were reviewed. During this time frame, the use of P&T was introduced into the medical management of patients with ORN. Treatment details, symptoms, and outcomes including pathologic fracture, progression of disease, need for debridement, and need for resection and major reconstruction were assessed.

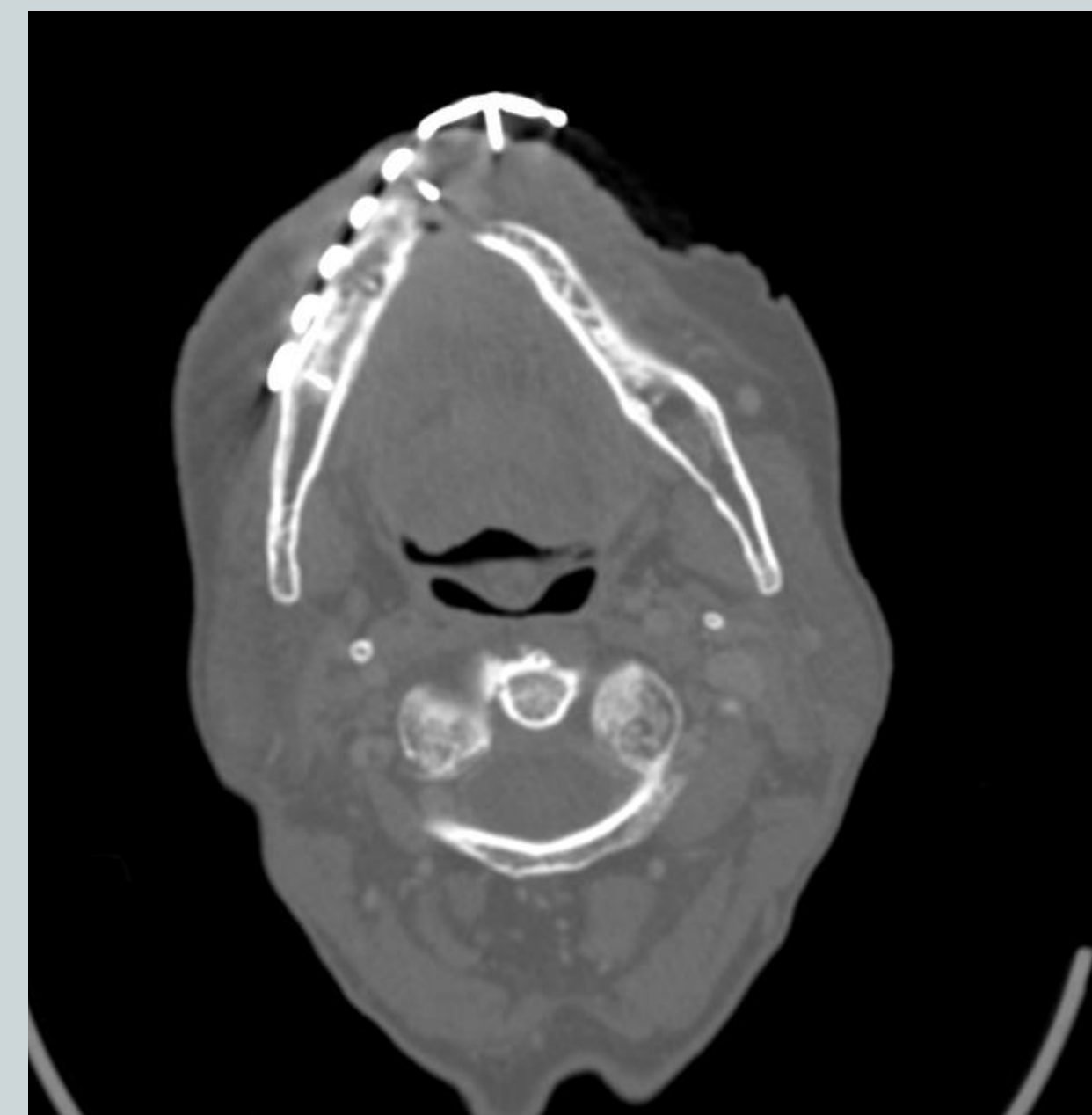


Figure 1. Axial CT study patient demonstrating pathologic parasymphyseal fracture and hardware extrusion.

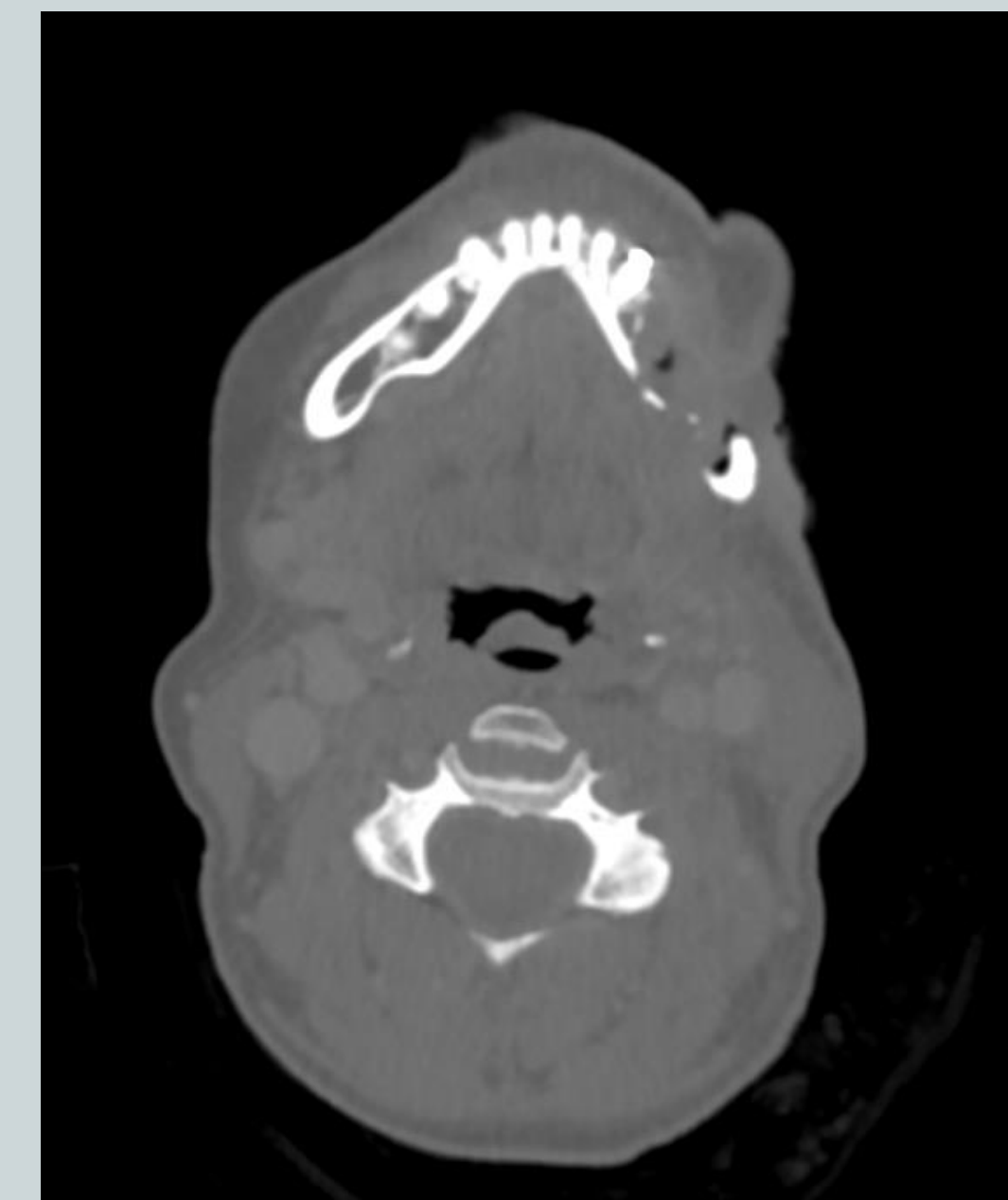


Figure 2. Axial CT of study patient demonstrating fragmentation and bony erosion of the left mandibular body with situlous tracts extending to the skin surface overlying the area of ORN.

RESULTS

48 patients met inclusion criteria. Using the staging system described by He et al², there were 10 patients with Stage I ORN, 16 patients with Stage II, and 17 patients with Stage III ORN. 43 patients (89.6%) were treated with antibiotics. 14 patients (29.2%) were treated with P&T. Patients with higher stage disease tended to be treated with P&T more frequently (Figure 3). 17 (35.4%) patients presented with or progressed to pathologic fracture. 27 patients (56.3%) required a surgical procedure from minor debridement to resection with major reconstruction. 12 patients (27.9%) required mandibulectomy and reconstruction with microvascular free tissue transfer (ie major surgery). Overall, progression of ORN was noted in 28 patients (58.3%). When assessed using standard Kaplan-Meier approach, there was no statistically significant difference between time to pathologic fracture or time to surgery for patients treated with or without P&T. However, despite not achieving statistical significance, a larger percentage of patients treated with P&T were noted to have disease progression (71.4% vs. 52.9% without P&T) and to have pathologic fractures (50.0% vs. 28.6% without P&T).

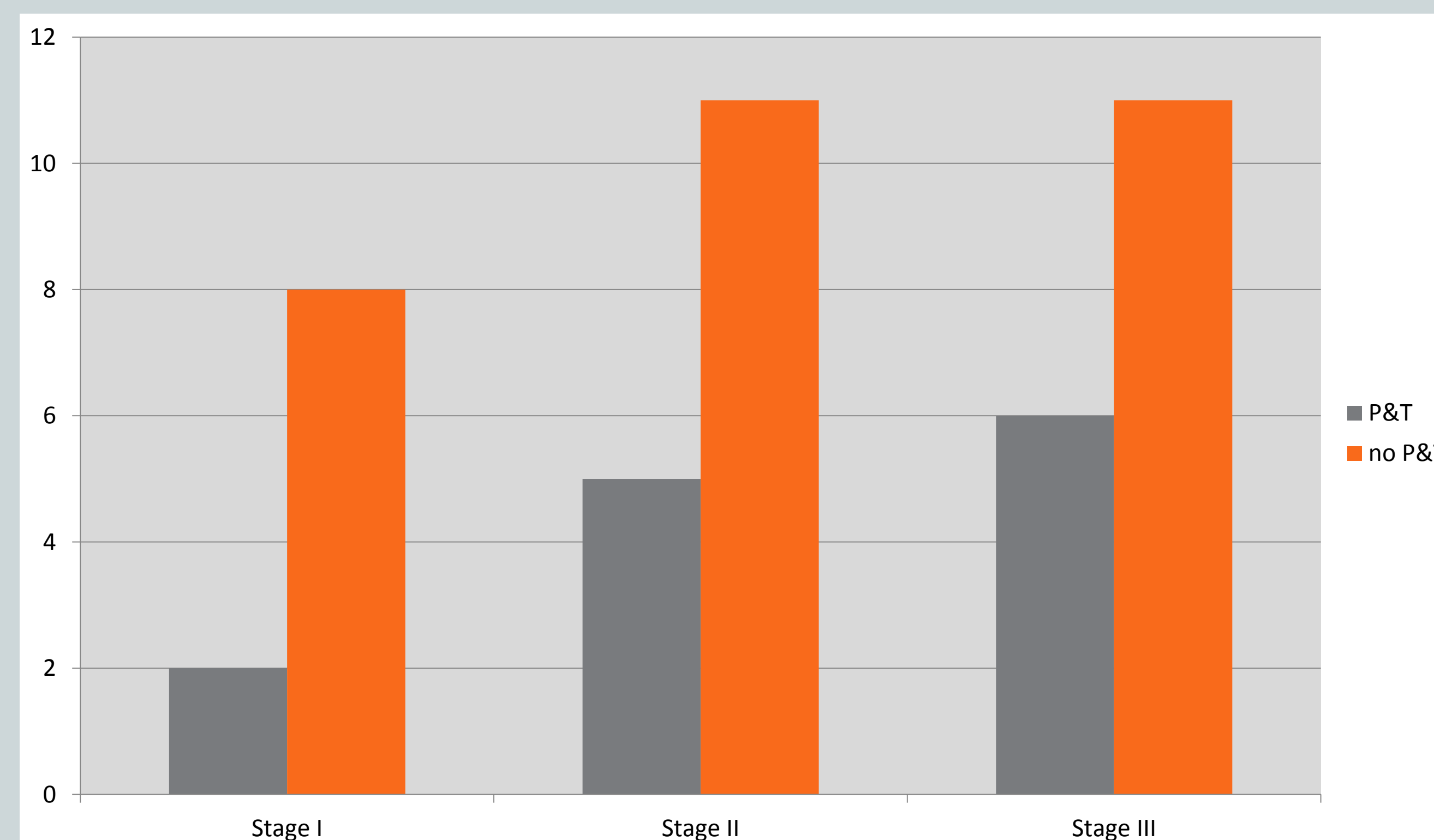


Figure 3. Number of patients who did or did not receive pentoxifylline and tocopherol based on stage of ORN.

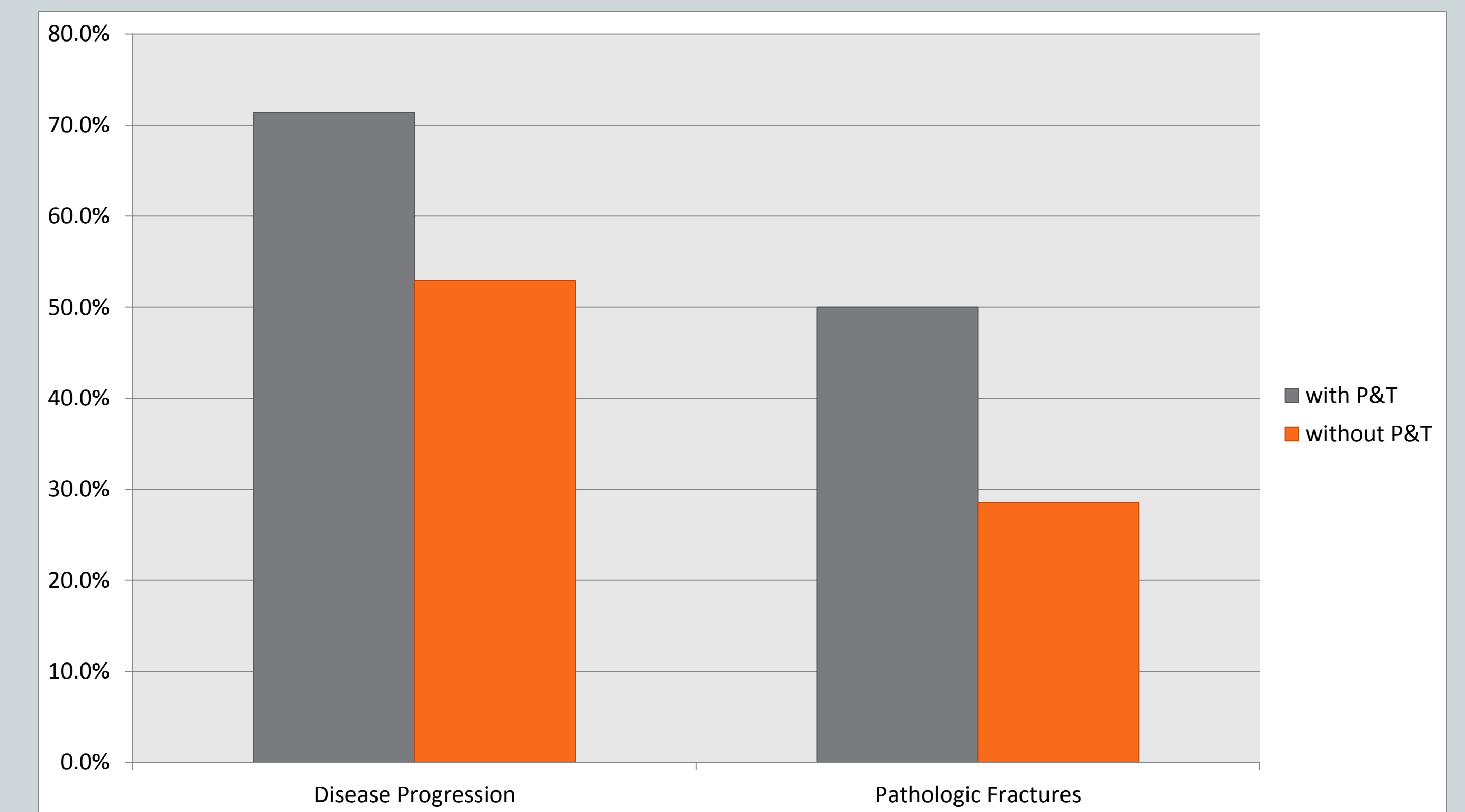


Figure 4. Percentage of patients with disease progression and pathologic fractures with and without the use of pentoxifylline and tocopherol.

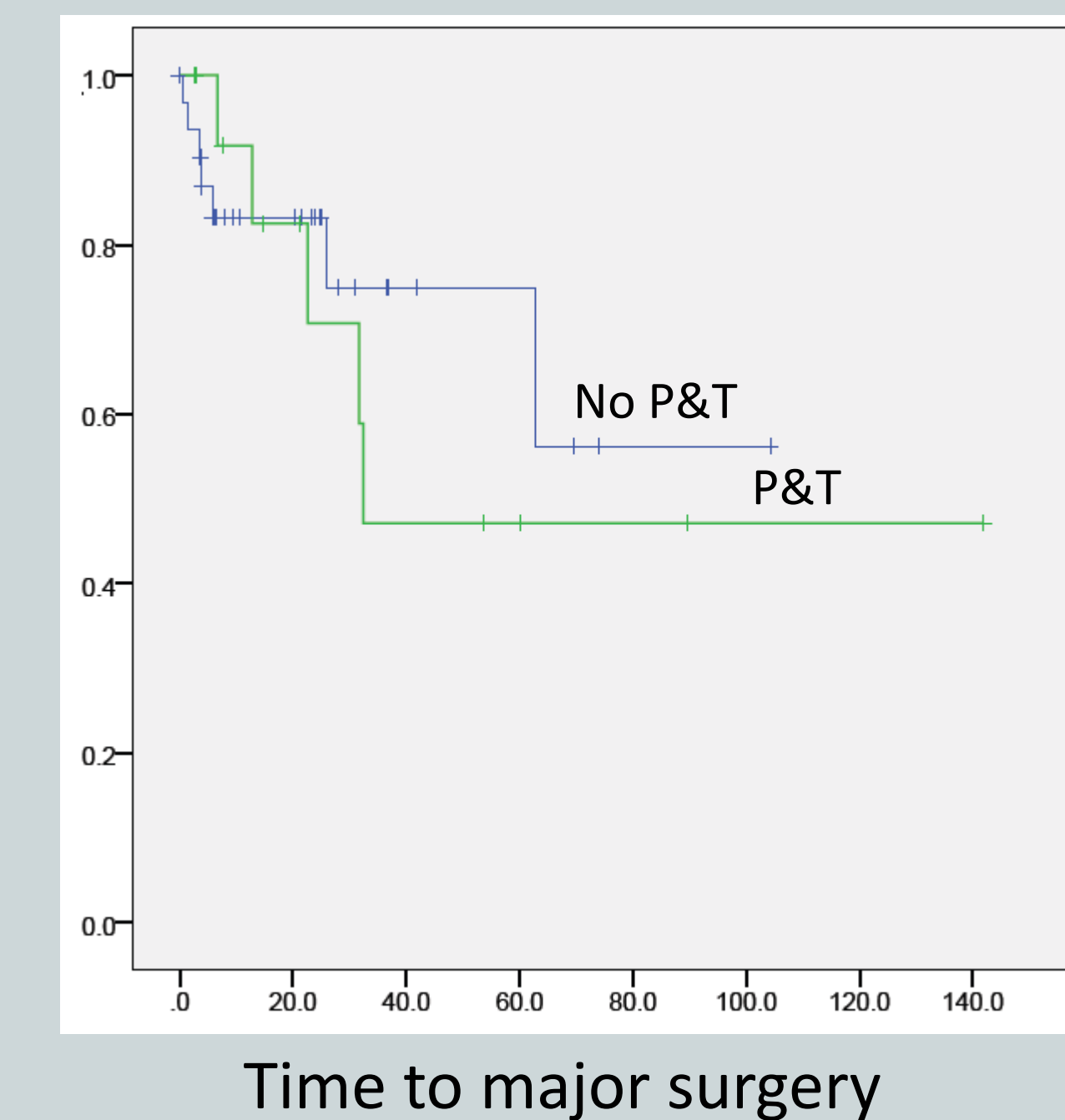


Figure 5. Time to major surgery for patients treated with and without P&T (p=0.65).

DISCUSSION

Osteoradionecrosis is a late sequelae of radiation-induced fibroatrophic process that results from high dose radiotherapy leading to irreversible tissue death and bone exposure. ORN can occur in up to 20% of patients with head and neck cancer treated with radiotherapy. The mechanism of ORN has been proposed as the dysregulation of wound healing with increased free radical production, fibroblast proliferation, and apoptosis. Conservative treatment of ORN includes long-term antibiotics, local wound care and debridement, as well as hyperbaric oxygen therapy. With progression of disease, resection of the affected mandible and reconstruction may be required. Even after reconstructive surgery, ORN can recur in up to 25% of cases.³

Pentoxifylline improves tissue blood perfusion and oxygenation, and has been used to treat vascular, liver, cardiac, and kidney disease. Tocopherol has been shown to have antioxidant properties, cause inhibition of platelet aggregation and production of nitric oxide in endothelial cells and of superoxide in neutrophils and macrophages. The combination of pentoxifylline and tocopherol have been shown to be an overall effective conservative treatment of mandibular ORN in certain patients.^{4,5}

CONCLUSIONS

There was no significant benefit of the use of P&T in patients with mandibular ORN in terms of time to pathologic fracture or time to surgical intervention. However, there was an apparent selection bias towards the use of P&T in more advanced cases. Future studies should match cases based on presenting severity in order to obtain a more complete evaluation of the impact of P&T. Additionally, comorbid factors (e.g., radiation dose, diabetes) and patient behaviors (e.g., tobacco use, compliance with medical regimen) need to be assessed for their contribution to outcome.

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