

Neel N Patel, Joseph Oliver Werenski¹, Marcos R Gonzalez, Marilee Ja Clunk², Meagan Rose McCadden, Alexis Virginia Richard, Ivan Chebib¹, Yin P Hung, Gunnlaugur P Nielsen, Santiago Andres Lozano Calderon³

INTRODUCTION: The percentage of tumor necrosis is a crucial prognostic factor in osteosarcoma. Many studies adopt a 90% cutoff based on osteoblastic osteosarcoma, but these findings are generalized to all conventional subtypes, including chondroblastic osteosarcoma. We sought to answer these questions: (1) Is tumor necrosis $\geq 90\%$ associated with better overall survival (OS) and disease-free survival (DFS) in osteoblastic and chondroblastic osteosarcoma? (2) Does the osteosarcoma subtype impact tumor necrosis? (3) Does the osteosarcoma subtype in “good” responders (tumor necrosis $\geq 90\%$) affect OS and DFS?

RESULTS: Patients with osteoblastic osteosarcoma and tumor necrosis $\geq 90\%$ had higher five- and ten-year OS and DFS compared to those with necrosis $< 90\%$. In chondroblastic osteosarcoma, a trend towards higher OS and DFS was seen in patients with tumor necrosis $\geq 90\%$; this, however, was not significant. Chondroblastic osteosarcoma was not a risk factor for either tumor necrosis $< 90\%$ ($p=0.89$) or tumor necrosis $< 70\%$ ($p=0.57$). However, patients with age ≥ 35 years had an increased 3.87- and 3.2-times higher risk of having a tumor necrosis $< 90\%$ and $< 70\%$, respectively. Size ≥ 7 cm was also a risk factor for being a "poor" responder, defined as tumor necrosis $< 90\%$ or $< 70\%$. Patients with osteosarcoma located in the tibia had a 64% lower risk of being "poor" responders, based on both necrosis $< 90\%$ and necrosis $< 70\%$. Patients with osteoblastic or chondroblastic osteosarcoma that were deemed "good" responders (tumor necrosis $\geq 90\%$) had similar OS and DFS at the five- and ten-year marks.

Figure 1. Flarechart of patient inclusion.

Figure 2. (A) Overall and (B) disease-free survival of patients with osteoblastic osteosarcoma; (C) overall and (D) disease-free survival of patients with chondroblastic osteosarcoma; (E) overall survival and (F) disease-free survival of good responders, defined as those with a tumor necrosis $\geq 90\%$.

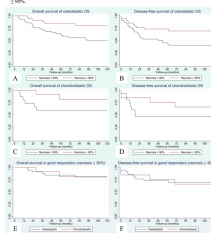


Table 3. Survival estimates for the entire cohort and based on categorical age.

		Overall survival			Event-free survival		
		Neoadjuvant (90%)	Neoadjuvant (90%)	<i>p</i>	Neoadjuvant (90%)	Neoadjuvant (90%)	<i>p</i>
Estrogen status	5-year	42.02 (40.79–75.46)	43.4 (40.4–80.3)	0.81	41 (31.6–57.4)	70.5 (55–82.4)	0.001
	10-year	37.5 (28.7–40.8)	39.1 (36.1–80.9)	0.090	48 (28–56)	72.2 (62–80)	0.001
Ovarianity	5-year	43.04 (40.9–76.2)	44.2 (40.1–80.1)	0.646	40 (29.9–54.8)	73.3 (56.9–82.5)	0.001
	10-year	40.9 (29.3–44.3)	42.6 (38.2–80.7)	0.81	40 (25.3–54.8)	70.9 (60–82.0)	0.001
Ovarianity at 5 years	5-year	36.7 (30–39)	33.3 (30.3–81.3)	0.152	39 (24.0–48.3)	73.3 (57–81.6)	0.001
	10-year	36.7 (30–39)	33.3 (30.3–81.3)	0.152	39 (24.0–48.3)	70.2 (62–80.8)	0.001

	Nurses < 80%		Nurses > 80%	
	HR (95% CI)	<i>p</i>	HR (95% CI)	<i>p</i>

	Neurotic < 80%	Neurotic > 50%
Age > 59	HR (95% CI)	p
Female	3.87 (1.51-10.1)	0.004
Psychological history	0.77 (0.52-1.15)	0.78
Physical history	0.96 (0.72-1.27)	0.85
Bone		
Tibia	0.56 (0.34-0.91)	0.02
Femur	0.48 (0.32-0.72)	0.03
Hip	0.52 (0.34-0.80)	0.003
Other	0.42 (0.16-1.17)	0.09
Type of fracture (baseline 1 limb only)		
Open	1.24 (0.33-4.71)	0.79
Simple	0.65 (0.24-1.76)	0.42
Simple + 7 cm	0.65 (0.24-1.76)	0.42
MI score (AUC: 0.64)		
MI	1.04 (0.26-4.1)	0.96
MI + fracture	0.56 (0.22-1.36)	0.02
MI + fracture + fracture	0.34 (0.15-0.77)	0.001
MI + fracture + fracture + fracture	0.19 (0.07-0.51)	0.001