



Background

DOTA-TOC/TATE provides superior sensitivity for detection of bone metastases from neuroendocrine tumors (NETs) compared to conventional imaging. We aimed to evaluate the prevalence, detection, and complications of bone metastases among NET patients with DOTA-TOC/TATE imaging.

Methods

We conducted a retrospective review of DOTA-TOC/TATE scans performed on NET patients between 2014-2017. Patients were stratified into two cohorts: 1) with bone metastases and 2) without bone metastases based on review of DOTA-imaging and DOTA-imaging reports. Patient characteristics, clinicopathologic data, and skeletal related events (SREs) were abstracted.

Exclusion Criteria

1. Patients with secondary malignancy
2. Patients without records available for chart review
3. Patients with paragangliomas or pheochromocytomas

Statistical Methods

Wilcoxon rank sum or Pearson chi-squared tests were used to compare patient characteristics and clinicopathologic data between the two cohorts. Statistical significance was declared at $p < 0.05$.

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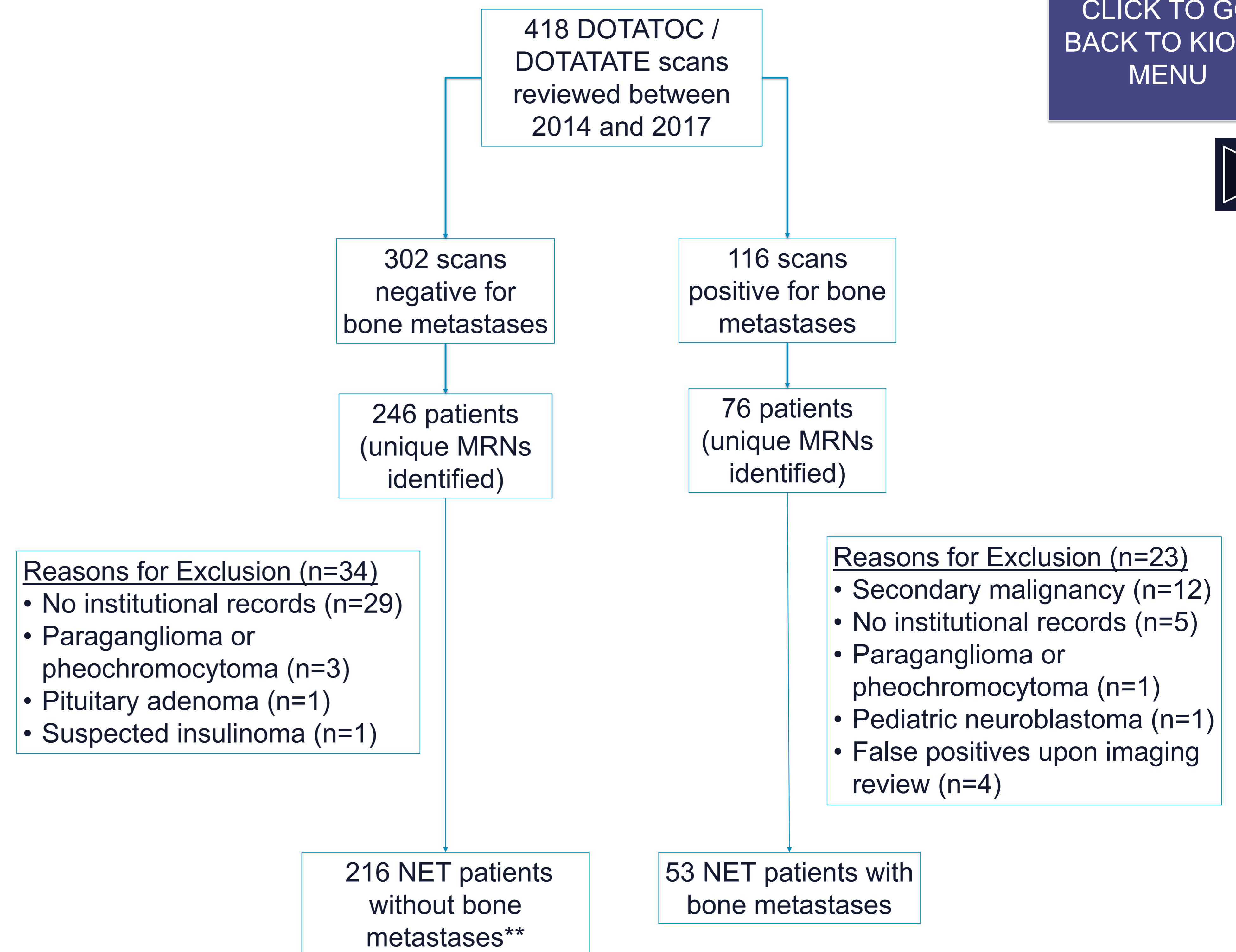


Figure 1. Flow diagram detailing selection for patient chart review. **The 4 false positives identified upon review of imaging were added to the bone metastases negative cohort.



Results

- Between 2014-2017, 418 scans were performed. Among 269 unique patients, median age was 61 years (21-84), and most common primary sites were small bowel (53%) and pancreas (26%). Bone metastases were reported in 53 (20%) patients.

	Patients with bone metastases (n = 53)	Patients without bone metastases (n = 216)
Median Age (range)	61 (26,80)	62 (21, 84)
Sex		
Male	27 (51%)	106 (49%)
Female	26 (49%)	110 (51%)
Primary Tumor		
Pancreas	11 (21%)	59 (27%)
Small Bowel / Unknown	28 (53%)	117 (54%)
Other GI NET	8 (15%)	22 (10%)
Non-GI NET	6 (11%)	18 (8%)
Histologic Grade		
Ki-67 <3%	18 (34%)	106 (49%)
Ki-67 3-20%	29 (55%)	74 (34%)
Ki-67 >20%	4 (8%)	9 (4%)
Unknown	2 (4%)	27 (13%)

Table 1. Patient characteristics

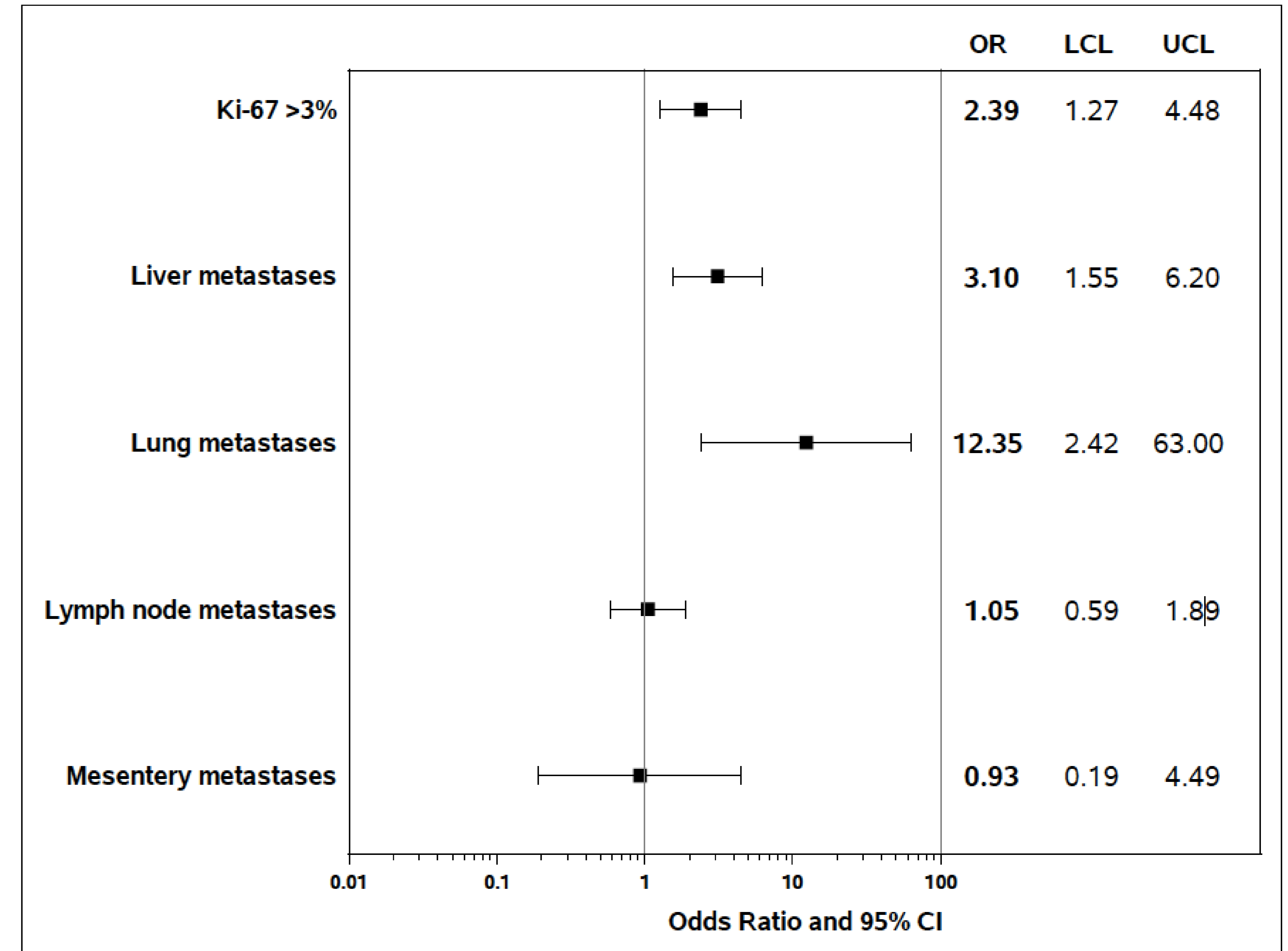
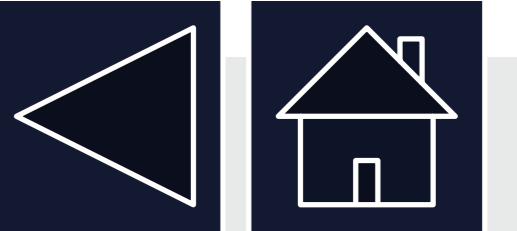


Figure 2. Odds ratios of bone metastases in relation to histologic grade or other metastases. NETs with Ki-67≥3% were more likely to have bone metastases than NETs with Ki-67<3% (p=0.01). Patients with bone metastases were more likely to have liver (p<0.01), lung, (p<0.01) or peritoneal (P=0.02) metastases than those without bone metastases.



Results (continued)

- Among 53 patients with bone metastases, 22 (42%) did not have bone metastases reported on conventional prior imaging. Median time between DOTA-TOC/TATE and prior imaging was 92 days (28-205).
- At the time of bone metastases diagnosis, there was no difference in occurrence of SREs between patients with bone metastases identified on conventional imaging compared to those with bone metastases identified on DOTA-imaging (p=0.27).
- Of 15 patients with SREs (28%), 13 (87%) presented with pain, 4 (27%) with pathologic fracture, 2 (13%) with cord compression, and 1 (7%) with hypercalcemia. Of 15 patients with SREs, 14 (93%) patients received surgery or radiation.

Conclusion

Bone metastases occur in a significant portion of NET patients and are associated with higher Ki-67 and with the presence of liver, lung, or peritoneal metastases. Given the substantial symptomatic burden of bone metastases in patients with NETs, further studies on bone health agents to guide clinical management are needed.

	Ki-67 <3% (n=18)	Ki-67 3-20% (n=29)	Ki-67 > 20% (n=4)	Total (n=51)	p-value
SRE present	6 (33%)	6 (21%)	3 (75%)	15 (29%)	0.07
Bone Pain	5 (28%)	5 (17%)	3 (75%)	13 (25%)	0.04
Pathologic Fracture	2 (11%)	2 (7%)	0	4 (8%)	0.73
Cord Compression	0	0	2 (50%)	2 (4%)	<0.01
Hypercalcemia	0	1 (3%)	0	1 (2%)	0.68
Requiring surgery or radiation	4 (22%)	7 (24%)	3 (75%)	14 (27%)	0.08
> 1 SRE	3 (17%)	4 (14%)	2 (50%)	9 (18%)	0.20

Table 2. Skeletal Related Events (SREs) any time in patients with bone metastases by histologic grade. Patient with NETs with Ki-67 >20% were more likely to suffer from bone pain than those with NETs <20% (p=0.04).