

The Clinical Implications of Betel (Areca) Nut Use on Oral Cavity Cancer

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Introduction

- Betel nut (BN), or Areca nut, comes from the seed of the Areca Palm fruit found mainly in South and Southeast Asia.
- BN is the primary ingredient of betel quid, a bite-sized morsel of areca nut, betel leaf, slaked lime, and spices.
- It is the 4th most common psychoactive substance after alcohol, nicotine, and caffeine, consumed by > 600 million across the world.
- BN use is associated with both precancerous and cancerous lesions – a notable precancerous finding is oral submucous fibrosis (OSMF). This leads to ulceration, xerostomia, trismus, and pain (Figure 1).
- BN is associated with a higher risk of oral squamous cell carcinoma (SCC), independent of tobacco use.
- The literature also suggests worse 5-year overall survival (OS) in BN users.

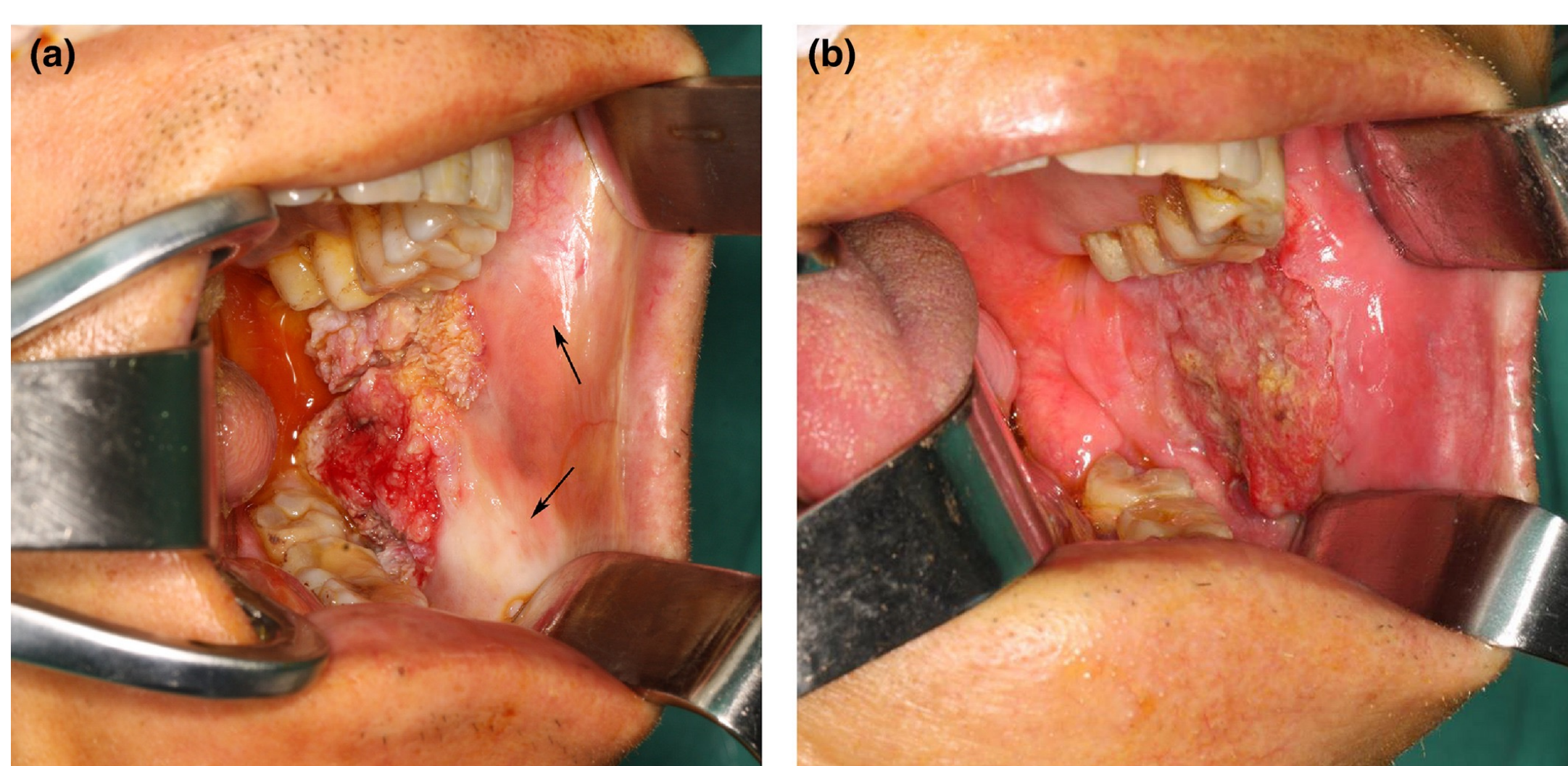


Figure 1. (a) The adjacent tissues in cases of BN-associated buccal mucosa SCC exhibit signs of OSMF (black arrows). (b) In contrast, the surrounding tissues in buccal mucosa SCC cases unrelated to BN chewing appear as normal mucosa (Yang et al., 2021).

Objective

- To investigate the clinical implications of BN use in our oral SCC patient population and to compare their treatment course and outcomes.

Methods

- A retrospective chart review was conducted at our institution. Subjects of interest were patients who underwent surgical treatment for SCC of the buccal mucosa, alveolar ridge, or retromolar trigone from January 1, 2010 to March 1, 2023. Patient and tumor characteristics as well as treatment type and outcome data were collected. Statistical analysis was performed using R studio.

References

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Results

- BN use was associated with earlier cancer onset and male predilection.
- In our population, it was seen exclusively in patients from India or labeled as other.
- These patients had significantly less tobacco intake, although it is unclear if their BN chewing preparations contained tobacco, since this is common practice in India (Table 1).

Table 1. Demographics and History

	Betel Nut Use (n=26)	No Betel Nut Use (n= 139)	p-value
Age (y), Mean +/- SD	57.6 +/- 8.4	69.6 +/- 12	<0.01
Gender			<0.01
Male	23	75	
Female	3	64	
Race/Ethnicity, n			<0.01
White	0	112	
Black	0	6	
Hispanic	0	9	
Indian	16	2	
Other	10	10	
Tobacco, n			<0.01
None	18	49	
<10 PY	2	11	
>10 PY	2	65	
Unknown	4	14	
Alcohol, n			0.45
None	14	53	
Social	4	21	
Heavy	8	62	
Unknown	0	3	

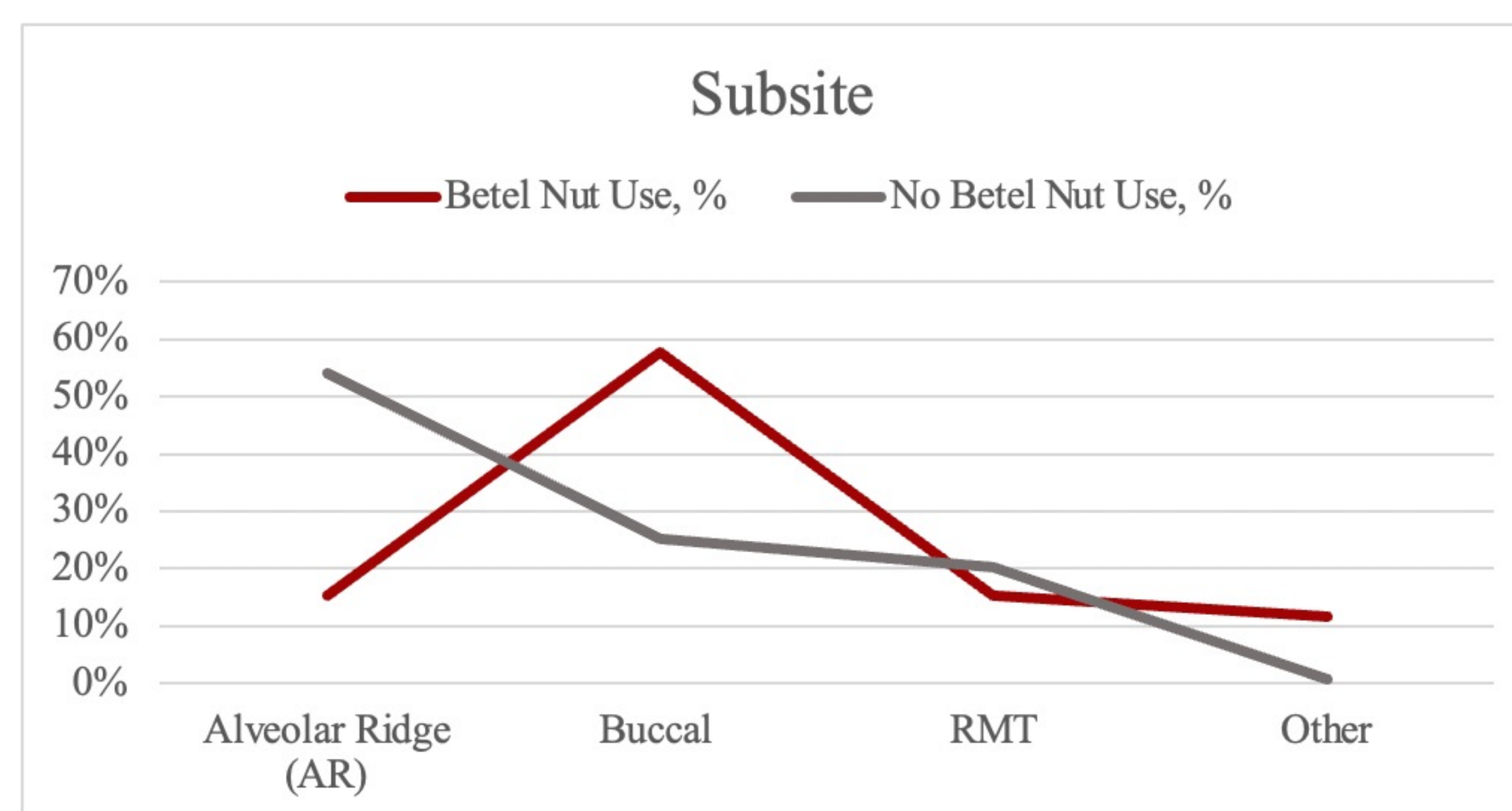


Figure 2. Subsite percentage, p < 0.01

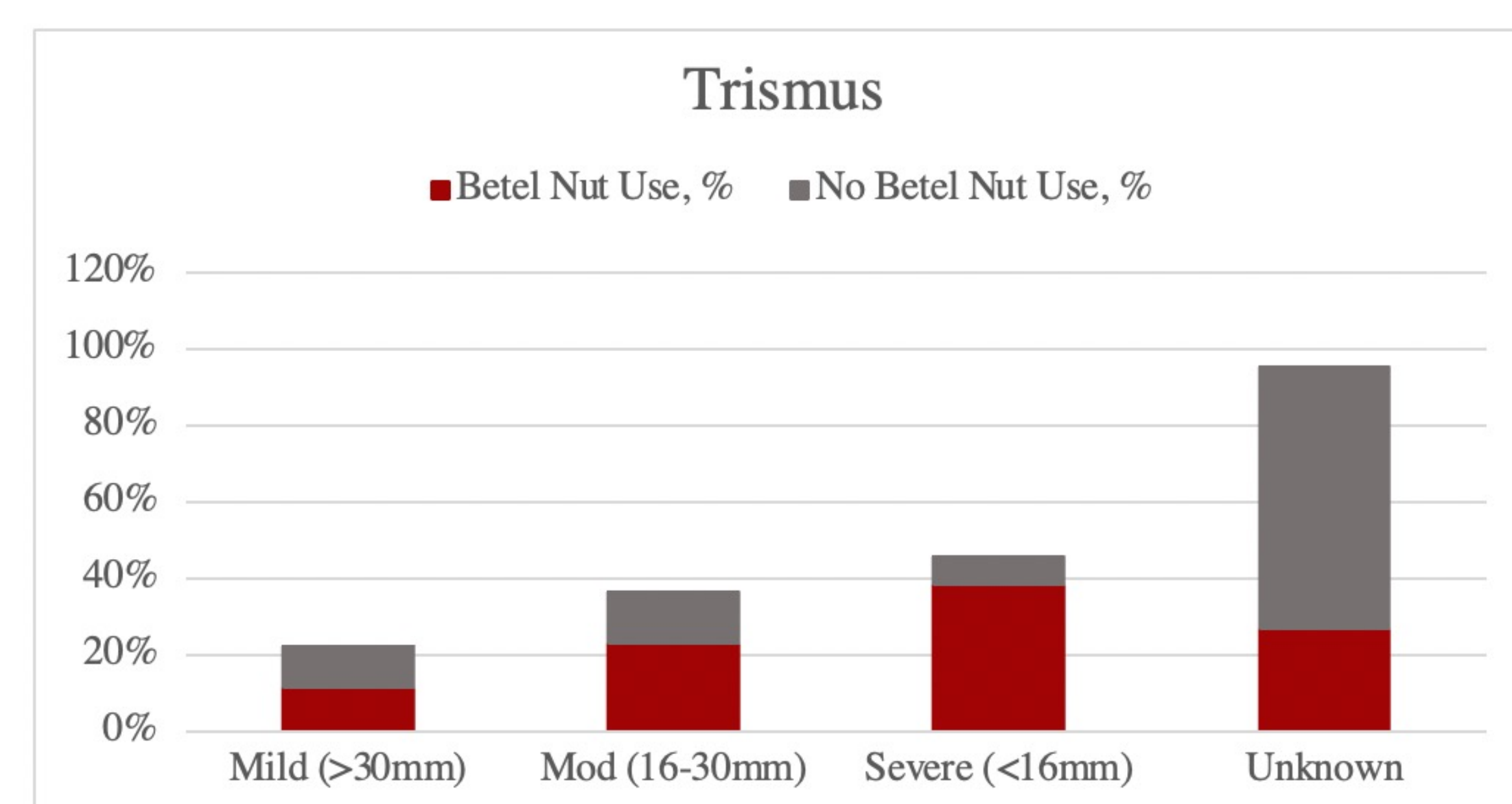


Figure 3. Trismus percentage, p < 0.01

- We compared adverse pathological features (positive nodes, margins, PNI, LVI, ECE, and histological grade) and found no significant difference between betel nut and non-betel nut users.

Table 2. Surgical Treatment

	Betel Nut Use (n=26)	No Betel Nut Use (n= 139)	p-value
Mandibulectomy, n			0.02
None	9	20	
Marginal	5	35	
Composite	12	84	
Flap, n			0.62
None	5	35	
Forearm	8	40	
Fibula	6	45	
Other	7	30	
Skin Graft, n			1.0
None	9	48	
STSG	16	88	
FTSG	1	4	
Neck Dissection, n			1.0
None	4	21	
Unilateral	15	94	
Bilateral	7	24	
Skin Excision, n			0.05
No	22	133	
Yes	4	6	
PEG Tube, n			0.04
No	4	51	
Yes	22	88	
PEG Dependence, n			0.43
Removed <1 y	8	30	
Present at 1 y	8	22	
Present at 5 y	0	3	
Unknown	2	33	
Time to PO, n			0.03
<30 d	11	84	
>30 d	15	43	
Unknown	0	12	
Length of Hospital Stay (d), Mean +/- SD	7.7 +/- 5.4	6.5 +/- 4.2	0.32
Disposition, n			0.32
Home	21	96	
SNF	4	36	
LTACH	1	2	
Other	0	5	

- There was a significant difference in patients receiving a mandibulectomy, favoring the non-BN group – this was likely due to the skewed number of patients with AR primary (Table 2).
- When removing patients with AR SCC from both groups, there was no significant difference in patients receiving a mandibulectomy.

Table 3. Additional Features and Outcomes

	Betel Nut Use (n=26)	No Betel Nut Use (n= 139)	p-value
Adjuvant Therapy, n			0.27
None	7	56	
XRT	12	56	
ChemoRT	5	20	
Other/Unknown	2	7	
Persistence/Recurrence, n			0.05
None	15	108	
Local	8	20	
Regional	2	4	
Distant	3	4	
Unknown	0	3	
Additional Treatment, n			0.03
None	14	107	
Surgery	8	13	
Nonsurgical	6	16	
Other/Unknown	0	5	
Additional Primaries, n			0.7
No	25	126	
Yes	1	10	
5y OS, n			1.0
Alive	5	37	
Dead	3	25	
Unknown	18	77	

- There was no difference in number of additional primaries or 5y OS.
- However, many of the BN patients were treated within the last few years, and thus have insufficient long-term data.

Conclusion

- BN use is ubiquitous in certain populations around the world and has been demonstrated to be an independent risk factor for oral SCC.
- Our research suggest that patients who use betel nut have a more aggressive clinical course with earlier onset, demonstrating consistencies with the literature.
- Limitations to our research include the quality of the data and the length of follow-up.