Aspirin Use and Tumor Control Following Vestibular Schwannoma Resection: A Propensity-Matched Analysis

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Background

- Some preclinical studies suggest that **aspirin may inhibit the growth of vestibular schwannomas (VS)** by downregulating cyclooxygenase-2 (COX-2) mediated inflammatory pathways.[1-3]
- Retrospective studies focusing **exclusively on observed tumors** have demonstrated conflicting results.[4-6]
- Whether aspirin influences **postoperative outcomes** after resection remains unknown.

Objective

- Evaluate the impact of aspirin use on tumor progression following VS resection.

Methods

- Retrospective, single-center study of patients who underwent first-time surgical resection of sporadic VS between 2004 and 2024.
- Chronic regular use of aspirin was confirmed via preoperative and follow-up notes.
- 1:1 propensity-score matching according to age, BMI, prior radiation, preoperative and postoperative tumor volume, EOR, and postoperative adjuvant radiotherapy.

Results: Baseline Characteristics

Variable	Overall (N=290)	Unmatched		
		Aspirin Use (N=105)	No Aspirin Use (N=185)	Sig. (p)
Age, Mean (SD)	52.6 (14.4)	57.8 (13.1)	49.7 (14.3)	<0.001
Female, N (%)	165 (56.9%)	59 (56.2%)	106 (57.3%)	0.855
BMI (kg/m^2), Mean (SD)	27.3 (5.3)	29.4 (5.5)	26.3 (4.8)	<0.001
Insurance, N (%)				0.008
Private/Commercial	132 (50.4%)	35 (38.0%)	97 (57.1%)	*
Medicaid	63 (24.0%)	24 (26.1%)	39 (22.9%)	
Medicare	65 (24.8%)	32 (34.8%)	33 (19.4%)	*
Tricare	2 (0.8%)	1 (1.1%)	1 (0.6%)	
CCI, Median [Range]	1 [0, 7]	2 [0, 7]	1 [0, 6]	<0.001
Prior Radiation Therapy, N (%)	17 (5.9%)	14 (13.3%)	3 (1.6%)	<0.001
Pretreatment Hydrocephalus, N (%)	52 (19.5%)	22 (26.8%)	30 (16.2%)	0.043
Preop Tumor Volume (cm^3), Mean (SD)	9.6 (9.7)	8.1 (8.5)	10.3 (10.2)	0.058
Surgical Approach, N (%)				<0.001
Retrosigmoid	244 (84.1%)	78 (74.3%)	166 (89.7%)	*
Translabyrinthine	42 (14.5%)	26 (24.8%)	16 (8.6%)	*
Middle Fossa	4 (1.4%)	1 (1.0%)	3 (1.6%)	
Op Time (min), Mean (SD)	384 (144)	403 (160)	374 (134)	0.192
Extent of Resection, N (%)				0.003
GTR	59 (21.1%)	31 (30.7%)	28 (15.7%)	
STR	220 (78.9%)	70 (69.3%)	150 (84.3%)	
Postop Tumor Volume (cm^3), Mean (SD)	1.9 (3.0)	1.3 (2.0)	2.2 (3.3)	0.010
30-Day Surgical Complication, N (%)	39 (13.4%)	21 (20.0%)	18 (9.7%)	0.014
30-Day Medical Complication, N (%)	18 (6.2%)	10 (9.5%)	8 (4.3%)	0.078
Adjuvant SRS, N (%)	135 (46.6%)	32 (30.5%)	103 (55.7%)	<0.001
Tumor Progression, N (%)	44 (15.2%)	14 (13.3%)	30 (16.2%)	0.511
Follow Up Duration (y), Median [Range]	3.8 [0.5, 18.2]	4.9 (0.6, 18.2)	3.4 [0.5, 14.6]	0.003

Table 1. Demographic and clinical characteristics are shown before propensity matching. Column percentages are displayed in parentheses for categorical variables. Welch's t-test and Wilcoxon rank-sum test were used to compare differences in continuous variables. Pearson's chi-square test was used to evaluate differences in categorical variables with post-hoc Bonferroni-corrected z-tests for independent proportions.

Results

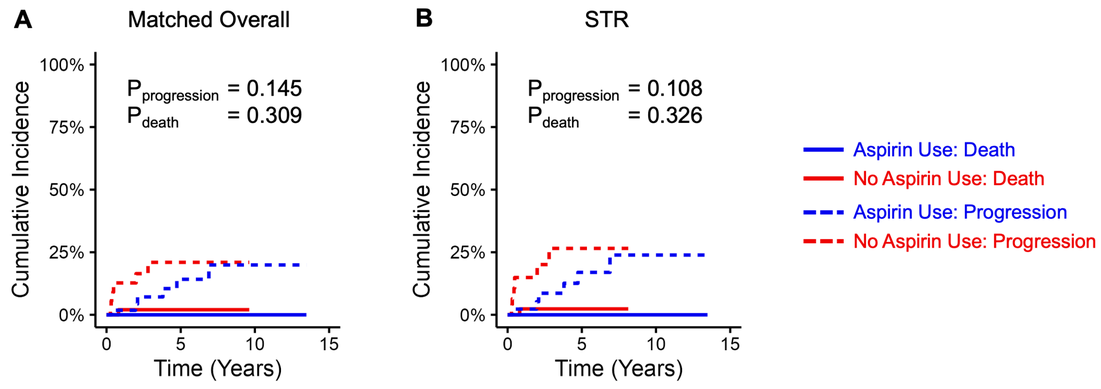

Figure 1. Cumulative incidence of progression and death by aspirin use and extent of resection. Cumulative incidence functions for tumor progression and death are shown for patients with (blue) and without (red) aspirin use following vestibular schwannoma resection. Subfigures show curves for the **(A)** overall matched and **(B)** STR cohorts. The GTR subgroup did not have any progression or death events. Solid lines represent death, and dashed lines represent tumor progression. P-values were obtained from Gray's test comparing cumulative incidence functions between aspirin use and non-use groups within each cohort.

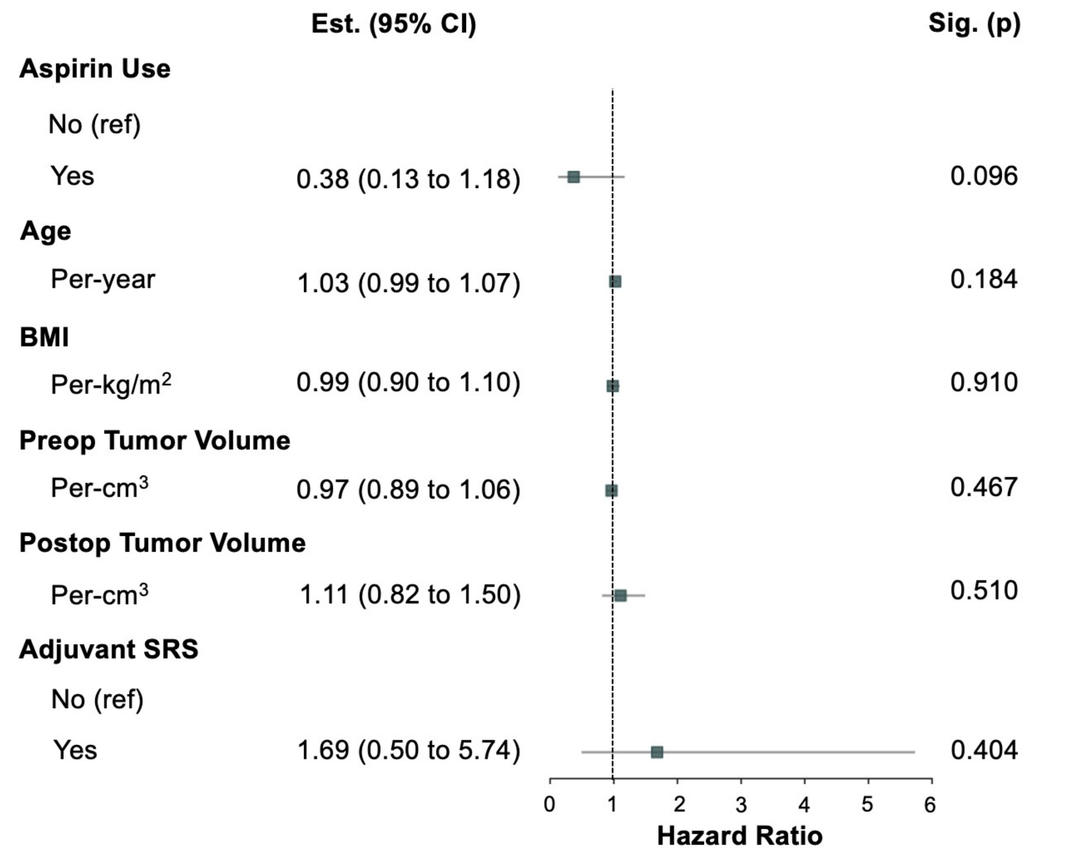

Figure 2. Cox proportional hazards for time to progression following subtotal vestibular schwannoma resection. Forest plot shows Cox proportional hazard ratios and 95% confidence intervals for all candidate predictors entered onto a regression model predicting time to progression following subtotal vestibular schwannoma resection.

Conclusions

- Unlike some preclinical studies, our surgical cohort **did not show an association between aspirin and time to progression following VS resection,** even in the STR subgroup.
- Discrepancy between in vitro and in vivo results may be explained by insufficient oral dosing, the presence of multiple redundant tumor growth pathways beyond COX-2, or an undefined therapeutic time course.
- Future work should investigate other pharmacological therapies such as metformin, mifepristone, or losartan.

References: 1) Hong B, Krusche CA, Schwabe K, et al. Cyclooxygenase-2 Supports Tumor Proliferation in Vestibular Schwannomas. *Neurosurgery*. 2011;68(4):1112-1117. doi:10.1227/NEU.0b013e318208f5c7 **2)** Dilwali S, Kao SY, Fujita T, Landegger LD, Stankovic KM. Nonsteroidal anti-inflammatory medications are cytostatic against human vestibular schwannomas. *Transl Res*. 2015;166(1):1-11. doi:10.1016/j.trsl.2014.12.007 **3)** Kandathil CK, Cunnane ME, McKenna MJ, Curtin HD, Stankovic KM. Correlation Between Aspirin Intake and Reduced Growth of Human Vestibular Schwannoma: Volumetric Analysis. *Otol Neurotol*. 2016;37(9):1428-1434. doi:10.1097/MAO.0000000000001180 **4)** MacKeith S, Wasson J, Baker C, et al. Aspirin does not prevent growth of vestibular schwannomas: A case-control study. *The Laryngoscope*. 2018;128(9):2139-2144. doi:10.1002/lary.27114 **5)** Hunter JB, O'Connell BP, Wanna GB, et al. Vestibular Schwannoma Growth With Aspirin and Other Nonsteroidal Anti-inflammatory Drugs. *Otol Neurotol*. 2017;38(8):1158-1164. doi:10.1097/MAO.0000000000001506 **6)** Marinelli JP, Lees KA, Tombers NM, Lohse CM, Carlson ML. Impact of Aspirin and Other NSAID Use on Volumetric and Linear Growth in Vestibular Schwannoma. *Otolaryngol Neck Surg*. 2019;160(6):1081-1086. doi:10.1177/0194599819827812