Determinants of Survival Outcomes in Parathyroid Carcinoma: Analysis Using NCDB Data

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Abstract

Background: Malignant parathyroid tumors are rare; treatment patterns and outcomes are poorly described.
Methods: Using the NCDB 2022 PUF, we identified C750 cases with malignant behavior and histology 8010 (Carcinoma) or 8140 (Adenocarcinoma). Separate multivariable Cox models and KM curves by surgery type were fit for Carcinoma and Adenocarcinoma.
Results:
Carcinoma (n=1104; 306 events): vs **No Surgery** (reference), adjusted HRs for death were **0.35** (95% CI 0.20–0.60) for **Partial/Total**, **0.37** (0.18–0.76) for **Biopsy/Local**, and **0.52** (0.28–0.99) for **Radical/En bloc/Other**; all p≤0.047. Higher comorbidity (CDCC 1–3) increased hazard (HRs 1.75–2.10). Medicare (HR **3.98**) and Medicaid (HR **2.59**) carried higher risk vs Private insurance. KM curves by surgery type showed strong separation (**p < 0.0001**). PH assumptions were acceptable (global p=0.083).
Adenocarcinoma (n=120; 27 events): estimates were imprecise with warning for separation. Signals included higher hazard with **Not insured** (HR **27.29**, wide CI) and **Medicare** (HR **17.16**), **Black** race (HR **5.32**), and **CDCC=2** (HR **22.8**); KM separation modest (**p = 0.038**). PH global p=0.045 (borderline).
Conclusions: In parathyroid **carcinoma**, receipt of surgery—especially partial/total resection—is associated with markedly better overall survival after adjustment. Non-clinical factors (comorbidity, insurance) are strong correlates. **Adenocarcinoma** findings are hypothesis-generating only due to small sample size.

Introduction

Parathyroid carcinoma and adenocarcinoma are a rare but aggressive malignancy of the parathyroid glands. It accounts for under 1% of primary hyperparathyroidism cases yet is clinically significant due to the severe hypercalcemia it causes and its potential for invasive growth[1,2]. Patients often present with signs of end-organ damage from elevated calcium (kidney stones, osteoporosis, neurocognitive symptoms) and may have a palpable neck mass or hoarseness if the tumor invades locally[1,2]. The cornerstone of treatment is en bloc surgical resection of the tumor, which offers the only chance of cure[1,3]. Complete removal at the first operation is critical, as it dramatically improves survival and reduces recurrence[1,3]. Adjuvant therapies are used selectively, and there is no proven effective chemotherapy, so recurrent disease is managed with additional surgery and rigorous control of hypercalcemia (using agents such as cinacalcet and bisphosphonates)[4]. Despite frequent relapses, many patients can achieve long-term survival with repeated interventions - 5-year survival is around 80% - but ongoing surveillance is required, and death often results from the complications of hypercalcemia rather than the tumor itself[1,2,4].

Methods and Materials

Data source & cohort: NCDB 2004-2022 PUF; primary site: Parathyroid; malignant behavior; histology **8010** (Carcinoma) or **8140** (Adenocarcinoma).
Outcome: Overall survival (months from diagnosis to last contact/death)
Key exposures/covariates: Insurance, income quartile, race/Hispanic override, tumor size (mm grouped: 1–10, 11–20, 21–30, 31–40, >40, no mass, unknown), surgery type: No Surgery; Biopsy/Local; Partial/Total; Radical/En bloc/Other, surgical margins, sex, CDCC (0–3).
Analysis: Separate KM curves (log-rank p) and multivariable Cox models for Carcinoma and Adenocarcinoma. Factors were set with clinically sensible references (e.g., No Surgery, Private insurance, Negative margins, CDCC=0).

Results

A total of 1,309 malignant parathyroid tumors were identified, including 1,138 carcinomas (86.9%), 146 adenocarcinomas (11.2%), 23 other or non-descript malignancies (1.8%), and 2 in-situ lesions (0.2%). Patients with carcinoma had a median age of 58 years (IQR 48–68), compared to 57.5 years (IQR 47.2–66.0) in adenocarcinoma and 65 years (IQR 56–72) in other histologies. Most patients were White (65% of carcinoma, 53% of adenocarcinoma), though Black patients represented nearly one-third of adenocarcinoma cases. Over half of carcinoma patients (81%) and most adenocarcinoma patients (71%) underwent partial or total resection

Kaplan–Meier Survival:
In carcinoma, surgical management was associated with significantly higher overall survival ($p < 0.0001$) (Figure 1). Five-year survival exceeded 70% with surgery, compared with ~45% without surgery. Survival benefit was evident across biopsy/local, partial/total, and radical operations.
In adenocarcinoma, surgery was also associated with improved survival ($p = 0.038$) (Figure 2), though interpretation was limited by small numbers and wide confidence intervals.

Multivariable Cox regression (Carcinoma):
Independent predictors of overall survival included:
Surgery: Any resection was protective relative to no surgery (biopsy/local HR 0.37, 95% CI 0.18–0.76; partial/total HR 0.35, 0.21–0.60; radical HR 0.52, 0.28–0.99).
Comorbidity: Increasing comorbidity burden was associated with stepwise worse survival (HR 1.75 for one condition; HR 2.09 for two; HR 2.10 for three or more).
Insurance: Compared with private insurance, Medicare (HR 3.98), Medicaid (HR 2.59), and other government insurance (HR 6.08) were each associated with higher mortality risk.

Figure 1: Kaplan-Meier Curve on Overall Survival by Surgery Type in Parathyroid Carcinoma

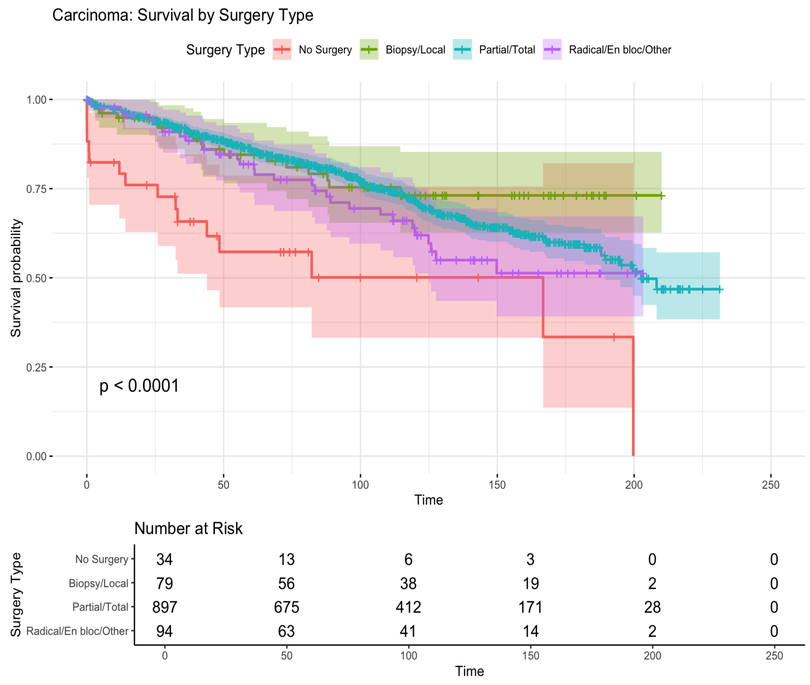

Table 1: Demographic Characteristics of Parathyroid Malignancies

Characteristic	Carcinoma (n = 1,138)	Adenocarcinoma (n = 146)
Age, median [IQR]	58 [48–68]	58 [47–66]
Sex	Male 595, Female 543	Male 74, Female 72
Race	White 739, Black 215, Other 184	White 78, Black 46, Other 22
Insurance	Private 569, Medicare 368, Medicaid 97, Other/Uninsured 104	Private 77, Medicare 49, Medicaid 12, Other/Uninsured 8
Tumor size >40 mm	653	121
Surgery	1,102	140
Partial/Total	925	104
Radical/En bloc	95	17
Biopsy/Local	82	19
Negative margins	617	87
Charlson–Deyo score = 0	924	111

Table 2: Cox-Hazards Predictors of Survival in Parathyroid Carcinoma

Variable	HR	95% CI	p-value
Surgery			
No surgery	Ref	–	–
Biopsy/Local	0.37	0.18–0.76	0.007
Partial/Total	0.35	0.21–0.60	<0.001
Radical/En bloc	0.52	0.28–0.99	0.048
Comorbidity (vs 0)			
1	1.75	1.29–2.38	<0.001
2	2.09	1.31–3.32	0.002
3+	2.1	1.07–4.14	0.031
Insurance (vs Private)			
Medicare	3.98	3.02–5.23	<0.001
Medicaid	2.59	1.63–4.10	<0.001
Other Gov't	6.08	1.82–20.3	0.003
Not Insured	1.74	0.94–3.24	0.078
Unknown	1.88	0.89–3.97	0.1

Discussion

In this large national cohort, **surgical resection was the most important determinant of survival** in parathyroid carcinoma. Any form of surgery conferred a substantial benefit, with similar outcomes for limited and more extensive resections, emphasizing surgery as the cornerstone of management. **Comorbidity burden** independently predicted worse survival, underscoring the influence of patient health status. **Insurance type** was also strongly associated with outcomes, suggesting disparities in access to care and specialized treatment. Other factors, including tumor size, sex, and margin status, were not consistent predictors after adjustment, highlighting that treatment and patient factors may outweigh tumor-specific characteristics in prognosis.
Adenocarcinoma cases were rare but showed a trend toward inferior survival compared with carcinoma, though numbers were insufficient for definitive conclusions.

Conclusions

- Surgical resection is associated with significant survival benefit in parathyroid carcinoma.
- More extensive surgery does not appear to provide added advantage over limited resection.
- Comorbidity and insurance status are strong predictors of outcomes, highlighting both clinical and socioeconomic influences.
- Future collaborative studies are needed to clarify management of adenocarcinoma and other rare parathyroid histologies.

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