

Outcomes of Pulmonary carcinoids over a decade: an NCDB analysis

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Rohit Gosain, MD; Sarbajit Mukherjee, MD; Adrienne Groman, PhD; Saikrishna Yendamuri, MD; Renuka Iyer, MD

Roswell Park Comprehensive Cancer Center



ABSTRACT

- Pulmonary carcinoids [typical carcinoid (TC) and atypical carcinoids (AC)] are rare diseases and paucity of randomized studies and disagreements in various guidelines makes the treatment challenging
- Using the National Cancer Database (NCDB), we evaluated the incidence and management of stage I, stage II, stage III pulmonary carcinoids between 2004–2014
- We looked at common surgical approaches used for for stage I, stage II and stage III patients
- We examined the impact of adjuvant therapy in TC compared to AC by stage and node status. TC patients with stage III disease have increased overall survival (OS) with observation post surgery, in comparison to administering adjuvant chemotherapy following surgery, while in stage I and stage II adjuvant therapy vs not were not statistically different.
- On the other hand AC patients with stage I disease have increased OS with observation post surgery, in comparison to adjuvant chemotherapy following surgery, while stage II data was not statistically significant
- AC patients with stage III disease were found to have better OS with adjuvant chemotherapy, but not statistically significant
- Future prospective trials are needed to confirm these findings

METHODS

- Utilized NCDB Participant User File to perform retrospective analysis on pulmonary neuroendocrine tumors (NETs) from 2004 to 2014
- All patients with a diagnosis of TC (8240) and AC (8249) who underwent surgery were included, based on the ICD-0-3/WHO 2008 criteria between years 2004 - 2014
- Patients were assessed based on their analytical stage, use of adjuvant (single or multi-agent) chemotherapy, management site (academic or community hospital)
- Long-term survival among the groups was evaluated using the Kaplan-Meier method with comparisons based on the log-rank test
- To evaluate the role of adjuvant chemotherapy on overall survival, patients with TC and AC, stage I, II, III were compared to surgery followed by observation

INCIDENCE

- Total number of TC cases (8240) – 19,560 (1.5% of total NET)
- Total number of AC cases (8249) – 2,260 (0.2% of total NET)

Table 1: Incidence of TC and AC with respect to total NET

Incidence	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
TC (%)	1.3	1.4	1.4	1.5	1.5	1.5	1.6	1.5	1.6	1.6	1.8
AC (%)	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3

Table 2: Incidence of TC over a decade

Typical Carcinoid												
Stage	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
I	141	190	169	227	229	319	888	939	972	1025	1162	6261
II	24	24	21	15	20	30	162	144	171	163	195	969
III	12	20	19	20	22	18	90	92	96	85	105	579
IV	16	8	12	22	19	26	79	74	80	103	103	542

Table 3: Incidence of AC over a decade

Atypical Carcinoid												
Stage	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
I	18	19	21	35	40	45	65	81	72	98	113	607
II	2	8	10	12	13	10	21	37	28	38	35	214
III	6	9	14	19	15	19	23	35	32	32	48	252
IV	11	5	7	13	18	17	27	26	33	40	65	262

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SURGICAL MANAGEMENT

- For early stage disease surgery is the mainstay treatment
- Common surgeries performed in early stage disease are: lobectomy, sublobar resection, pneumonectomy

Table 4: Common surgical approaches utilized in TC and AC patients

Typical Carcinoid			
Surgery Type	Stage I	Stage II	Stage III
Lobectomy	3144	565	191
Sublobar	1377	110	74
Pneumonectomy	119	42	29
Other	167	37	25
Sub Total	4807	754	319

Atypical Carcinoid			
Surgery Type	Stage I	Stage II	Stage III
Lobectomy	350	125	88
Sublobar	117	13	23
Pneumonectomy	9	14	27
Other	12	6	9
Sub Total	488	158	147

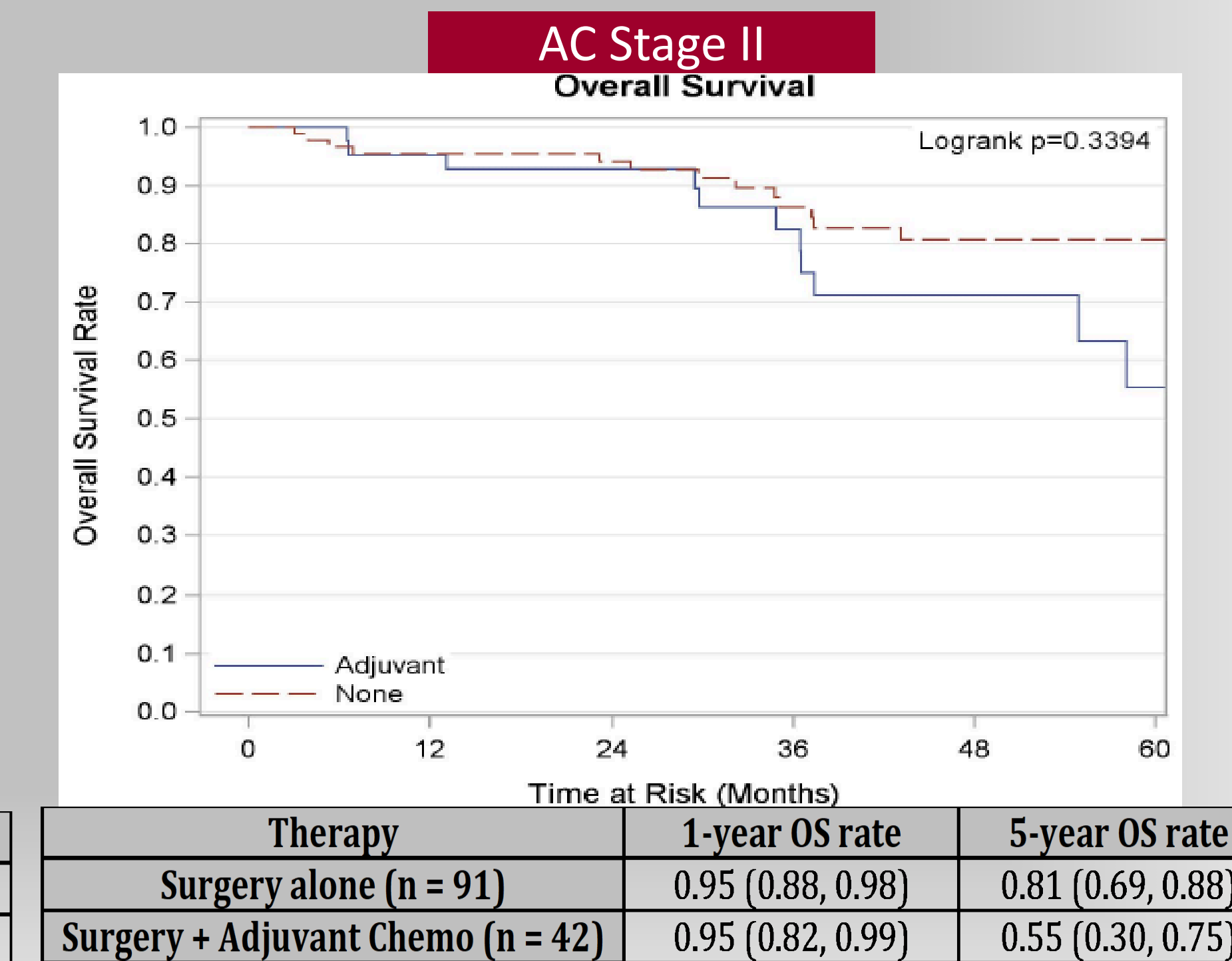
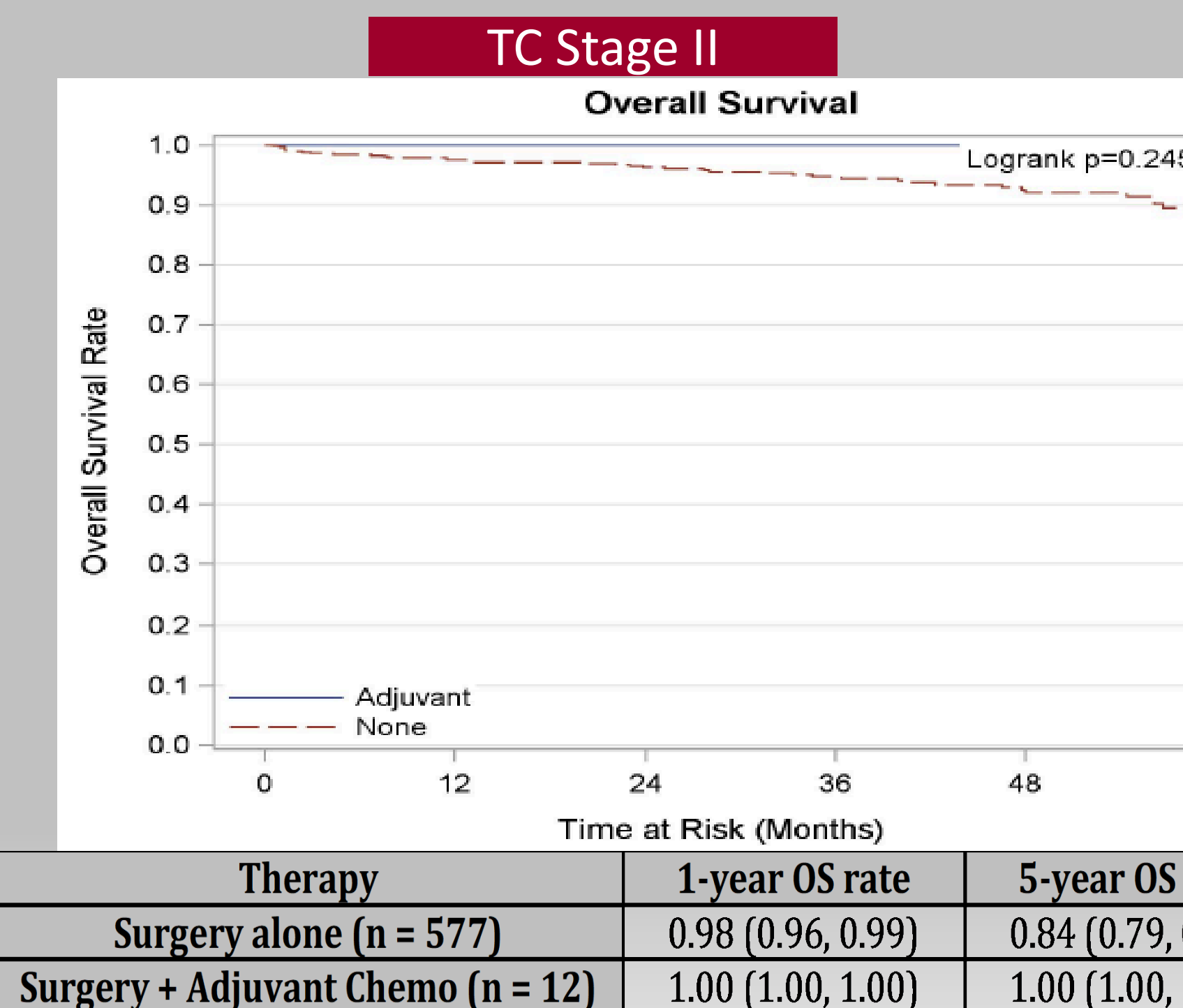
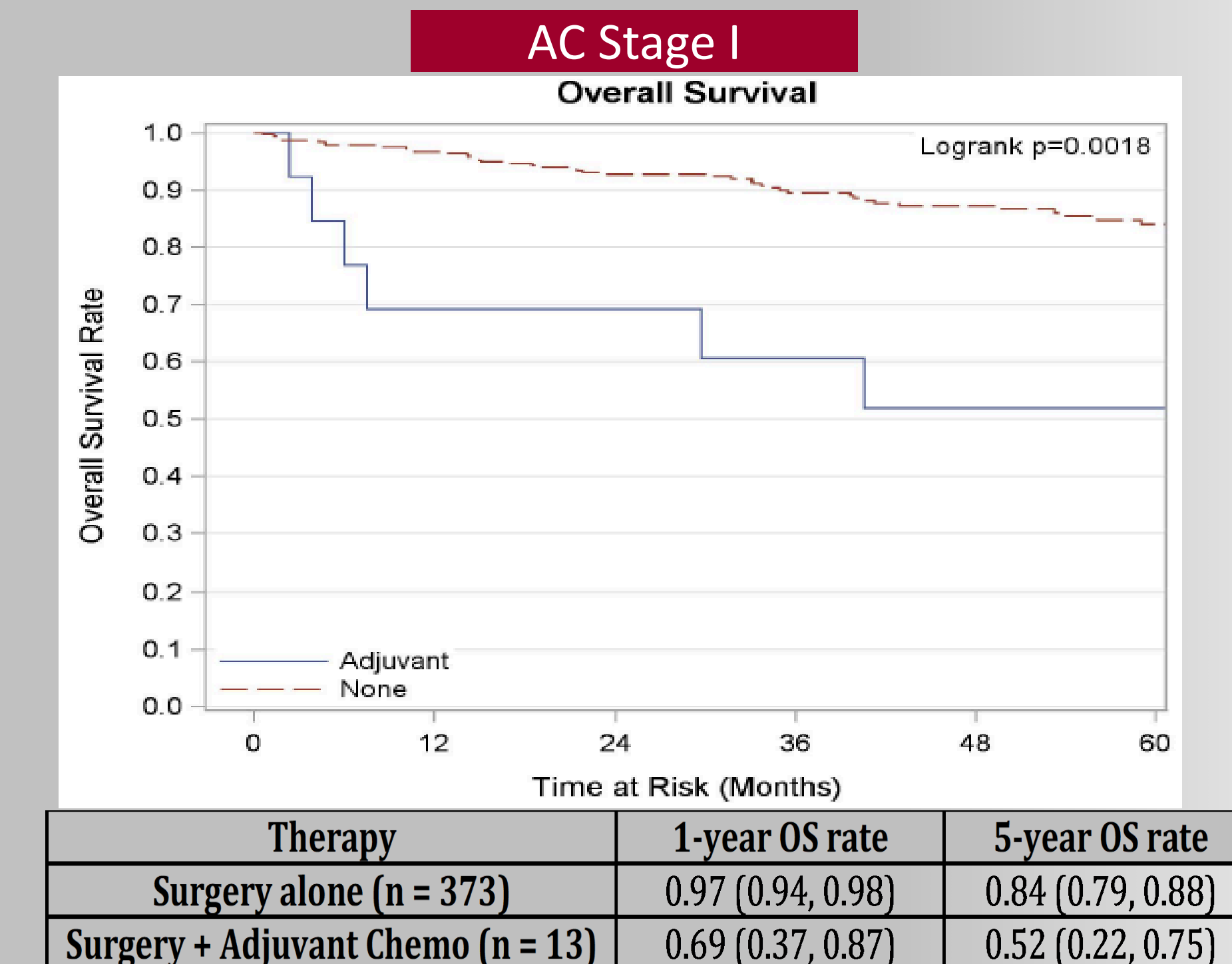
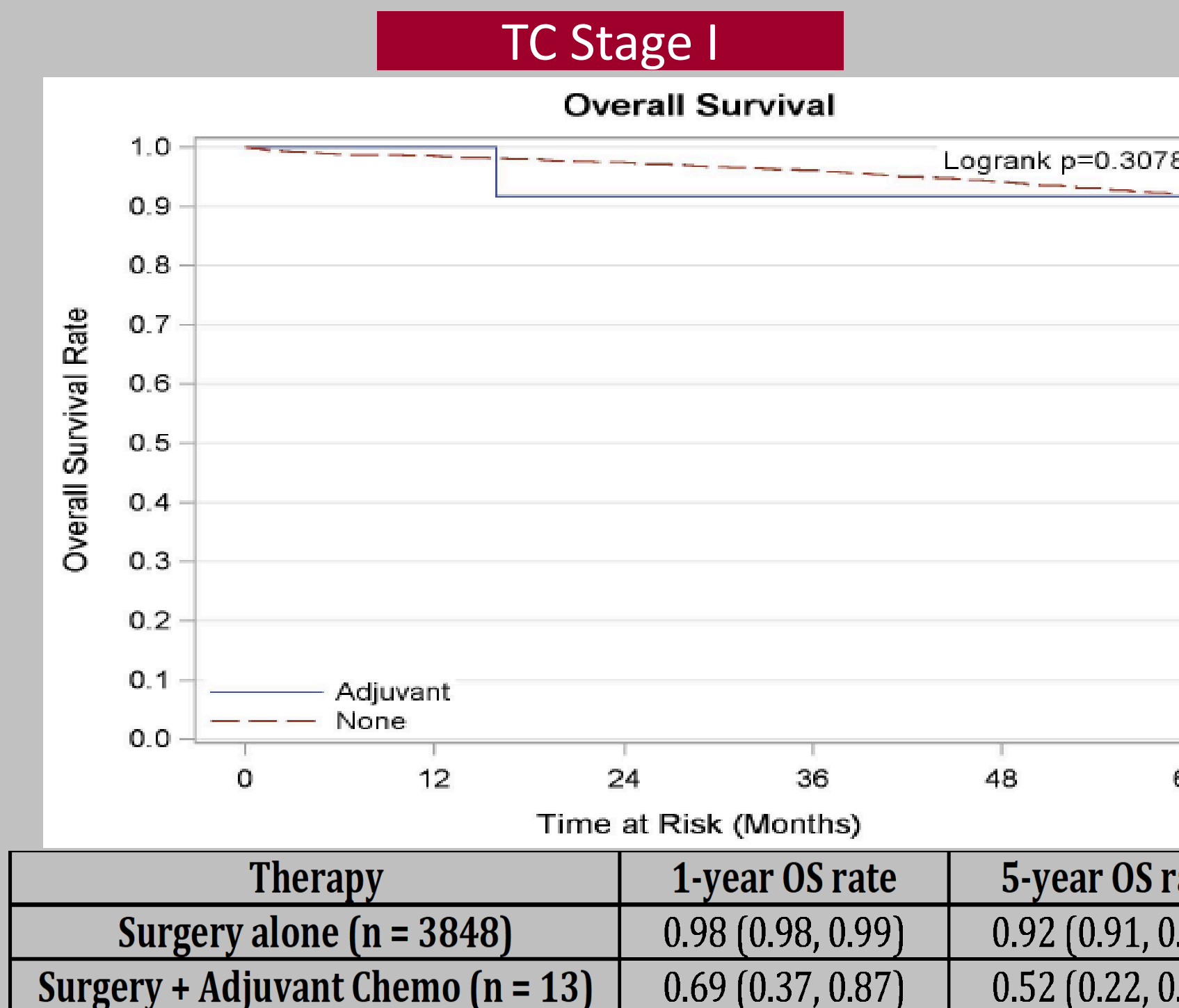
ADJUVANT THERAPY

- We evaluated overall survival (OS) trends in stage I, stage II, stage III patients who underwent surgery alone versus surgery followed by adjuvant treatment
- In stage III TC, patients who received chemo did worse than those who did not receive chemo on multivariate analysis, with 5 year OS rate of 41% vs. 88% respectively ($p < 0.001$)
- In stage III AC had slight survival benefit with chemo in comparison to patients who did not get chemo, with 5 year OS rate of 46% vs. 54% respectively but not statistically significant ($p = 0.2412$)

Table 5: Adjuvant therapy recommendations based on different guidelines

	NCCN	NANETS	ENETS	ESMO
Adjuvant Regimen	Stage IIIa ACs chemotherapy +/- radiation	No recommendations	Consider adjuvant therapy in ACs with positive lymph nodes	No recommendations

SURGERY ALONE vs. SURGERY FOLLOWED BY ADJUVANT THERAPY



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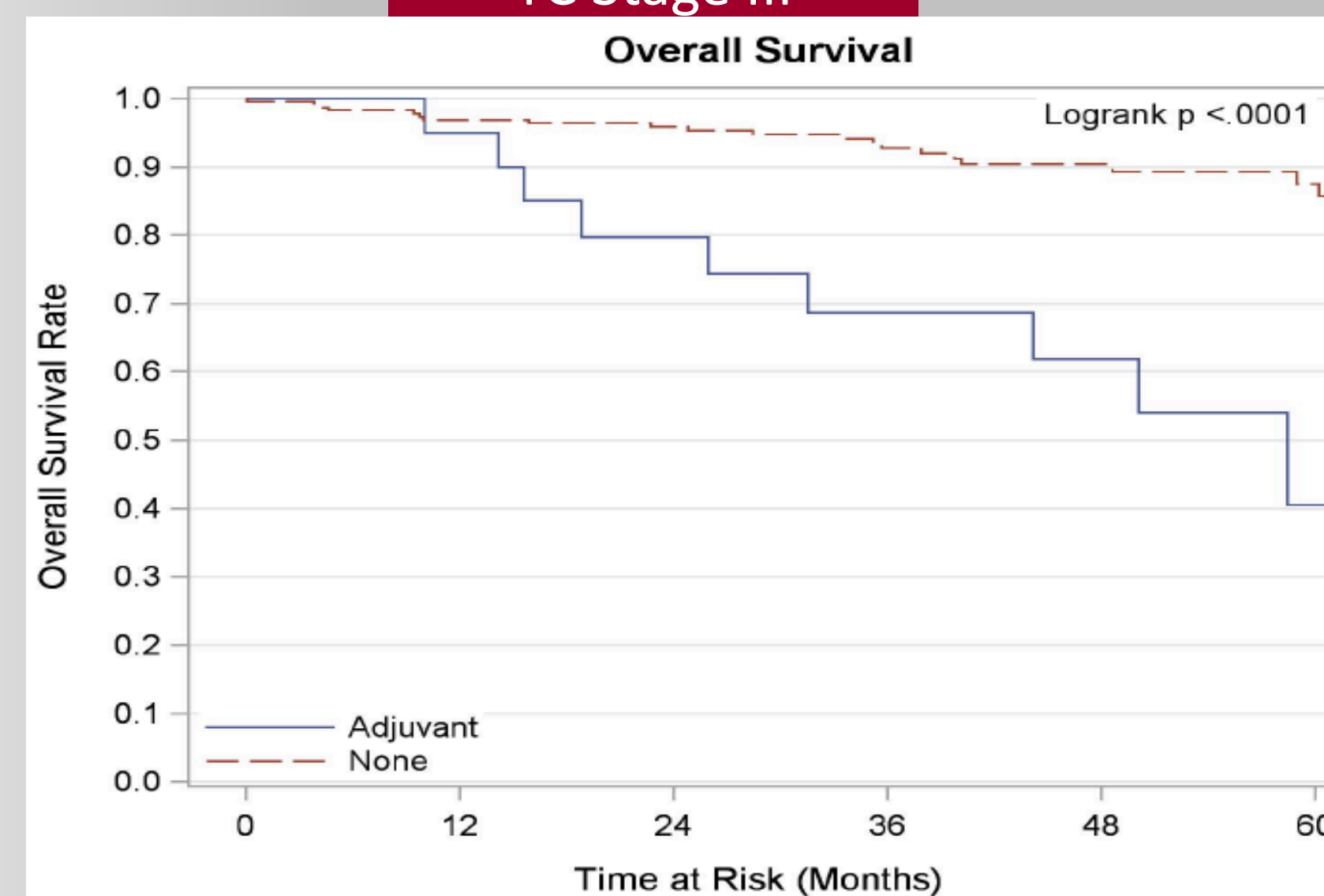
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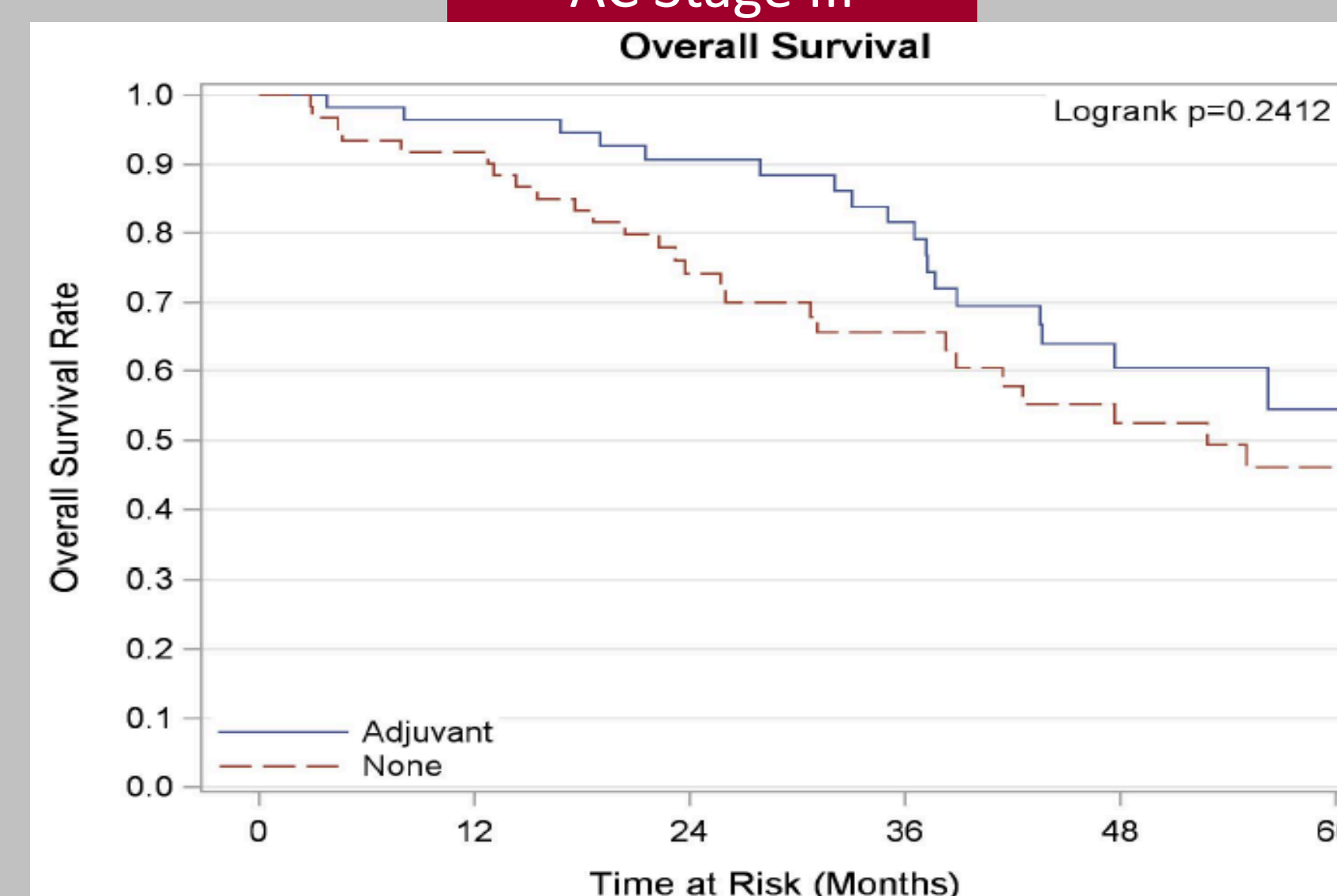
SURGERY ALONE vs. SURGERY FOLLOWED BY ADJUVANT THERAPY

TC Stage III



Therapy	1-year OS rate	5-year OS rate
Surgery alone (n = 236)	0.97 (0.94, 0.99)	0.88 (0.80, 0.92)
Surgery + Adjuvant Chemo (n = 20)	0.95 (0.69, 0.99)	0.41 (0.13, 0.67)

AC Stage III



Therapy	1-year OS rate	5-year OS rate
Surgery alone (n = 61)	0.92 (0.81, 0.96)	0.46 (0.31, 0.60)
Surgery + Adjuvant Chemo (n = 57)	0.96 (0.86, 0.99)	0.54 (0.35, 0.70)

- Regardless of the stage we evaluated patients based on node status, and found 5 year OS rate of 91% in node negative group, while 78% in node positive group (p < 0.0001)
- When evaluating for OS data based on academic vs. community practice, patients were found to have increased OS at academic institution in comparison to community institution

DISCUSSION

- Incidence of pulmonary NETs has been increasing over the years; mainly from recent advancements in imaging modalities what % increase was seen, that tabel has numbers but not as a % of all lung
- We observed decline in OS in patients who received adjuvant chemotherapy in comparison to surgery alone (except stage III AC)
- We further looked into use of adjuvant chemotherapy, but were restricted to single and multiagent chemotherapy use, but the duration and specifics were not available
- More prospective trials warranted especially in the AC early stage disease to assess the need of adjuvant chemotherapy

CONCLUSION

- There has been increase in incidence of pulmonary NETs over the years
- Surgical resection is the mainstay treatment for locoregional TC and AC
- Common surgeries performed in early stage disease are lobectomy, sublobar resection and pneumonectomy
- We observed adjuvant therapy is harmful in patients with TC stage III and AC stage I patients (p < 0.05), and not beneficial in other patient population (except stage III AC)
- Stage III AC patients had OS benefit with adjuvant chemotherapy, but not statistically significant

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