

High Grade Neuroendocrine Carcinoma of the Uterine Cervix: Outcomes and the Role of Radiation and Chemotherapy – The University of Iowa Experience

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Background

- High-grade neuroendocrine carcinoma of the uterine cervix (cNEC) is a rare and aggressive cancer
- The prognosis of cNEC is poor with most patients succumbing to metastatic disease
- Due to the rarity of this malignancy, the optimal treatment is uncertain
- The aim of this study was to further characterize the natural history of cNEC and treatment outcomes

Methods

- All cases diagnosed at the University of Iowa Hospitals and Clinics were identified by searching our institutional databases
- Only patients with confirmed histological diagnosis of cNEC were included in our analysis
- Tumors of other histologies including non-small cell neuroendocrine tumors were excluded
- Survival was ascertained by using both institutional databases and public death registries
- Survival was estimated using the Kaplan-Meier method

Conclusion

- The age at diagnosis is similar to the age at diagnosis of the much more common squamous cell cancer of the uterine cervix (according to data from SEER)
- Thirty-nine percent of the patients had disease considered resectable (stages less than IB2)
- The overall survival was poor, especially for patients with unresectable disease
- Complete resection in conjunction with chemotherapy can result in prolonged survival (median survival 50 months)
- Relapses are common and usually fatal within a year
- The role of radiation therapy is not clear
- Chemotherapy was associated with better survival in patients with unresectable disease
- The effect of the second line chemotherapy remains undefined

Summary

- High grade neuroendocrine carcinoma of the cervix is a rare and very lethal malignancy
- Unresectable disease is nearly uniformly fatal despite aggressive chemotherapy or chemo-radiotherapy
- The optimal therapy of localized disease remains uncertain
- Chemotherapy is commonly used for advanced disease with the intent of prolonging survival
- Better understanding of the biology and clinical behavior of this malignancy is needed
- The treatment outcomes remain unsatisfactory; better treatment options are needed

Patient Characteristics

- 36 patients were identified
- The patients were diagnosed between 1977 and 2010
- The median age of the patients was 49 years (range 26-77)
- 15 women (42%) were smokers

Table 1: FIGO Staging

FIGO Stage	%
IB - NOS	19.4
IB1	19.4
IB2	8.3
IIA	5.6
IIB	13.9
IIIB	11.1
IV	5.6
IVA	2.8
IVB	13.9

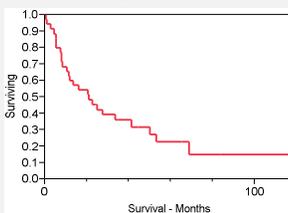
FIGO: International Federation of Gynecology and Obstetrics

Table 3: Overall survival for all patients

Median OS	20.7 months
5-year OS	23%

OS: Overall Survival

Figure 1: Overall survival for all patients



Staging

- Table 1 shows the FIGO staging of the patients
- Seven patients (19%) had regional nodal involvement, 12 patients (33%) were node-negative, and information on nodal status could not be found in 17 patients (47%)
- Eight patients (22%) had distant metastases at the time of diagnosis
 - Liver – 6 patients
 - Bone – 2 patients

Initial Treatment

- Seventeen patients (47%) underwent resection
- Twenty patients (56%) received radiotherapy
- Twenty seven patients (75%) had chemotherapy
- The majority of patients received multimodality treatment

Table 2: Resectability

FIGO Stage	%
IB2 or higher	61
IB1 or less	39
Surgery	47

FIGO: International Federation of Gynecology and Obstetrics

Table 4: Survival of the entire cohort according to therapy

Treatment type	Median OS (months)	5-year OS
Surgery	50.0	49.7%
No Surgery	9.3	0%
Radiation*	14.8	10.3%
No Radiation*	22.6	38.5%
Chemo†	10.8	0%
No chemo †	2.7	0%

* Patients undergoing radiation had a disease of higher stage compared with those who did not have radiation.
† Only 6 patients did not have chemotherapy.

Results

Survival

- The median overall survival for the entire group was 20.7 months (Table 3)
- The 5-year overall survival for the entire group was 23%
- Advanced stage at diagnosis was a strong predictor of shorter survival (Figure 2)
- Patients with resectable disease did better than those who were unable to undergo full resection (Figure 3)
- Radiation therapy was not associated with improved survival in the patients who did not undergo resection or in the post-operative setting (Figures 4 and 5)
- Seven of the 17 patients who underwent resection relapsed with a median time to relapse of 19.4 months
- Six of the 7 relapsed patients died from progressive cancer with a median time from the relapse to death of 11.4 months
- All but one of the 18 patients who did not undergo surgery and had follow-up information available, died with a median survival of 14.2 months

Survival

- Chemotherapy was associated with better survival in patients with unresectable disease (MS 10.8 ms vs. 2.7 ms [p=0.006]). None of these patients survived > 5 years.
- Platinum with etoposide were used in 73%
- Partial response or stable disease were seen in 50% of patients with mean duration of response of 9.1 months.
- Second line chemotherapy at progression was used in 44.4% of patients.
- Pre- and post-operative chemotherapy in resectable disease did not impact survival (MS 45 ms with chemotherapy vs. 156.5 ms without [p=0.37]).

Figure 2: Stage at diagnosis and survival

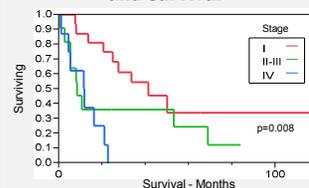


Figure 3: Surgery and survival

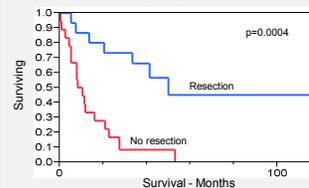


Figure 4: Radiation therapy and survival in unresected patients

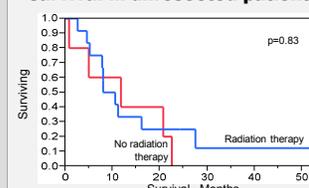


Figure 5: Post-operative RT

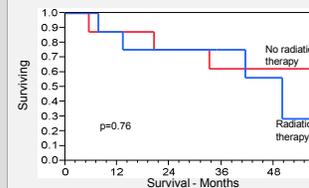


Figure 6: Chemotherapy and Survival

