# (MP55-18) Sarcomatoid Urothelial Carcinoma (SARC): Contemporary Analysis of 99 Cases with Emphasis on Patients with pT1 Tumors who underwent Early Cystectomy

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# BACKGROUND

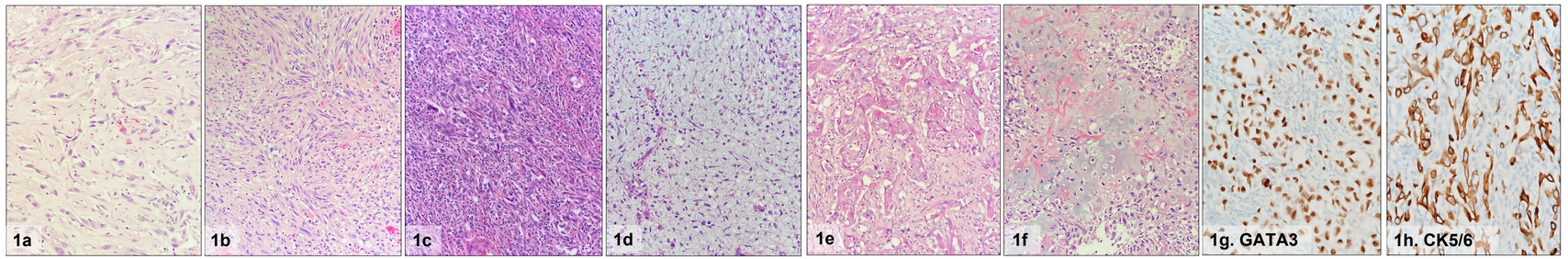
- Sarcomatoid urothelial carcinoma (SARC) is a histologic variant of Urothelial carcinoma (UCa).
- Molecular Classification of Muscle Invasive Bladder Cancer (MIBC):
  - Sarcomatoid urothelial carcinoma falls under Basal -Squamous type (BS) based on RNA expression cluster analysis
  - SARC is characterized by high expression of basal and stem-like markers (CD44, KRT5,KRT6A, KRT14) and squamous differentiation markers (TGM1,DSC3, PI3).
  - Strong expression of flat carcinoma- *insitu* (CIS) signature genes and loss of Sonic Hedgehog (SHH) signaling suggest that SARC developed from basal cells and CIS lesions.
  - SARC has strongest immune expression signature
- Guidelines recommend consideration for early radical cystectomy (RC) in patients with SARC and pT1 tumors.
- We studied clinico-pathologic parameters associated with prognosis including 5 patients with pT1 tumors who underwent early RC.

# METHOD

- A retrospective review identified 99 patients who were diagnosed as SARC between 1993 and 2019.
- H&E were reviewed to annotate tumor size, size of sarcomatous component and percent of sarcoma.
- Univariate Cox regression analyses assessed hazards ratio of clinical and pathological variables for OS.
- The survival curves were generated using Kaplan-Meier method and comparisons are made by log rank test. P values < 0.05 were considered statistically significant.

# RESULTS

- **Demographics**: The median patient age at diagnosis was 70 yrs. Patients were White (83%), Black (14%), Asian (3%). Similar to UCa, SARC was 3-4 times more common in males.
- **Urothelial Bx/TURB**: In 30% of cases, initial biopsy/TURB did not identify SARC component.
- **Surgical procedures**: Twelve patients (Mean±SD =70±13 yrs, Range= 48-82 yrs) did not undergo cystectomy. The remaining 81 underwent the following resection procedures: RC (13), partial cystectomy (4), cystoprostatectomy (59), and pelvic exenteration (5).
- **Non-invasive carcinoma**: 55% of cases had a urothelial precursor lesion (76% CIS, 35% HGTCC, 4% LGTCC).
- **Epithelial components:** 27% are pure SARC with spindle cell morphology **(Fig. 1a-1d)** and 73% were mixed with UCa or with other variants of urothelial carcinoma (**Fig.1)**. Among which 30% of SARC cases were associated with other variants [64%, squamous cell carcinoma (Fig.1e); 32%, glandular/signet cell features; 14%, micropapillary; 10%, small cell carcinoma; 7%, anaplastic; and 7% large cell carcinoma] (**Fig.2.)**. The presence of necrosis in SARC was not associayed with OS (*P*=0.99) (**Fig.2.5)**.
- **Sarcomatous components**: 88% have non-specific malignant spindle cell phenotype and 12% of cases showed specific subtypes of sarcomatous heterologous components (HE); chondroid (Fig. 1f), osteoid, myxoid and rhabdoid differentiation. Heterologous elements (HE) had significant worse overall survival (p=0.045) (**Fig.3)**.
- **Tumor characteristics:** Average size of total tumor and SARC component was 6cm and 4.5cm respectively. Total tumor size, SARC size and maximum depth of invasion had no significant association with OS (p>0.05) (**Fig.4)**
- The mean SARC tumor size at RC among patients receiving no chemotherapy (Chemo) vs Chemo was 4.6 and 2.8 cm respectively. Posterior wall SARC was associated with poor survival (p=0.06)



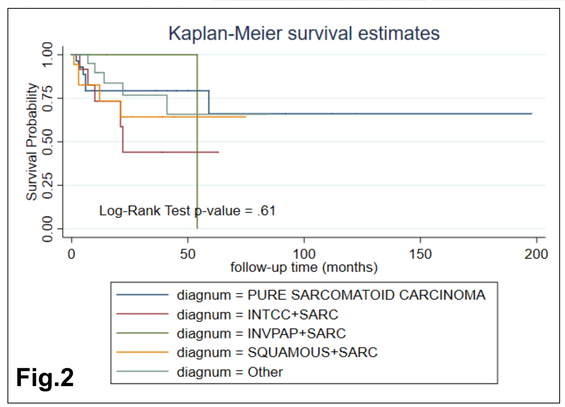



Fig.2

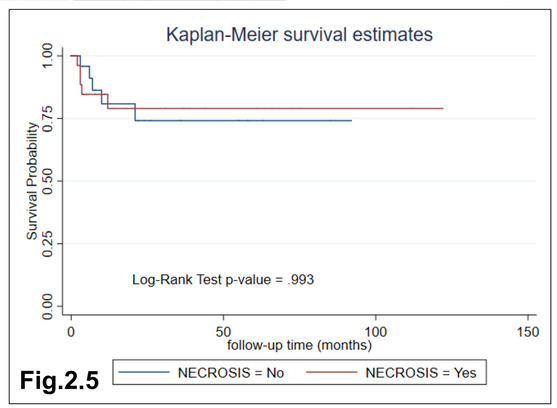


Fig.2.5

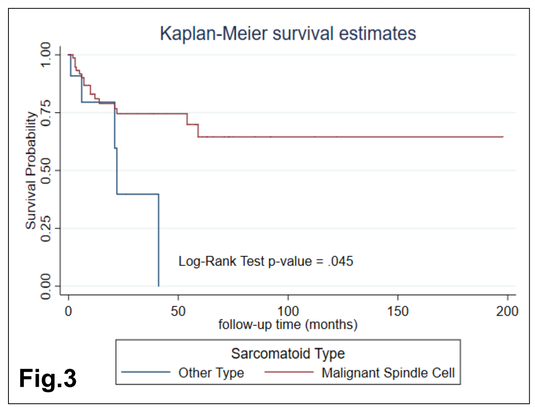


Fig.3

# RESULTS

- **Immunophenotypic classification:** GATA3 **(Fig. 1g)** (luminal) and CK5/6 **(Fig. 1h)** (basal) showed luminal (13), basal (21), mixed (21) and double negative (10) staining. Among SARC cases, there was no association of immunophenotypic classification and survival (p>0.05) (**Fig.5)**
- **TNM Staging:** The distribution by pT stage (pretreatment) was 6%, 31%, 41% and 17% (T1, T2, T3 and T4). T-stage had significant association with OS (p=0.02) (**Fig.6)**. T1T2N0M0 had significant high OS (p=0.007) compared to T1-T4 ≥N1 M1 (**Fig.7)**. Primary tumor LVI and ≥N1 stage are significantly associated with worse survival (p<0.05) **(Fig.7.5)**, Pearson correlation=strong (p<0.05). M0 and M1 had similar OS.
- **Survival outcomes:** Clinical long-term follow up data was available in 51 patients. The survival probability at 1, 2 and 5 year time points is 81%, 71% and 59% respectively. Among all the death events, 86% occurred before 2 year time point. 10% survived beyond 5yrs. (**Fig.8)**. The median OS among patients receiving chemotherapy (both NAC+ADJ) vs no chemotherapy was not significantly different from each other (p= 0.43) [n=83].

**pT1 Subset:**
-All five male patients (mean age 68 years) had RC (N0/M0).
-One patient had LGTCC, 1 had CIS and 3 with no noninvasive component.
-None received chemotherapy.
-One progressed to N0M1; 2 had no recurrent disease; 1 was lost to follow-up. 4/5 patients were alive (mean OS= 49 months)
-1 with >2 urothelial variants and SARC, 1 with heterologous elements (osteosarcoma)

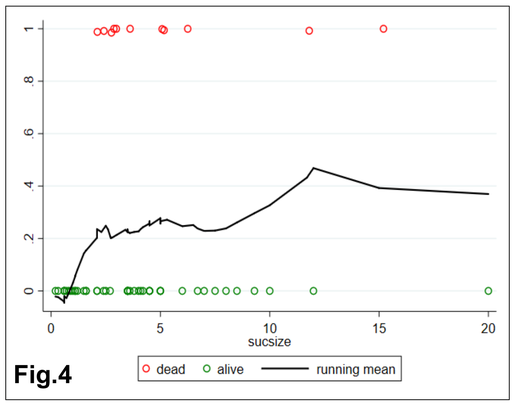


Fig.4

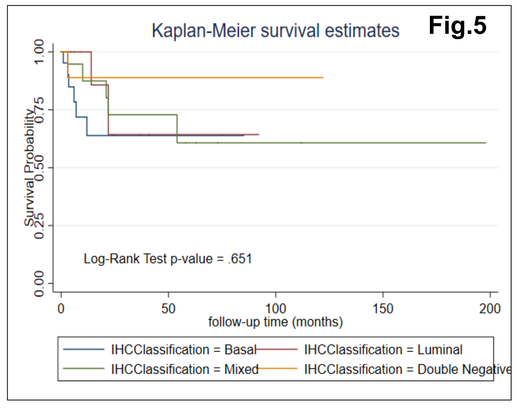


Fig.5

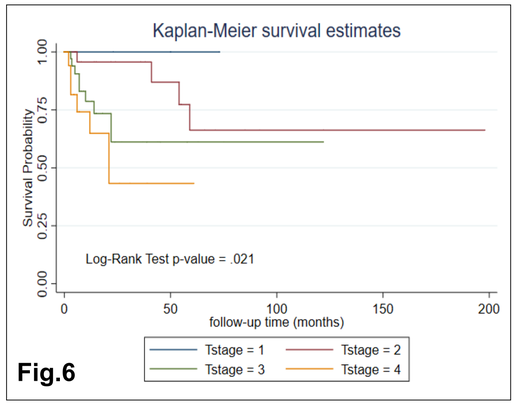


Fig.6

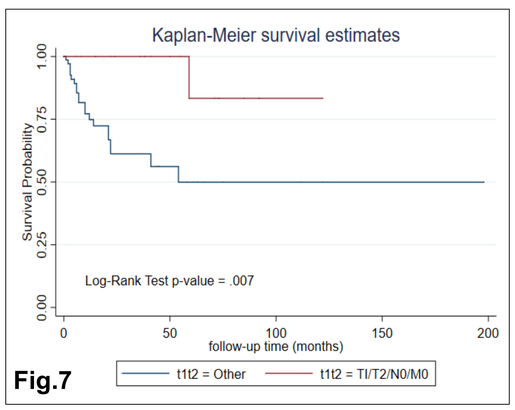


Fig.7

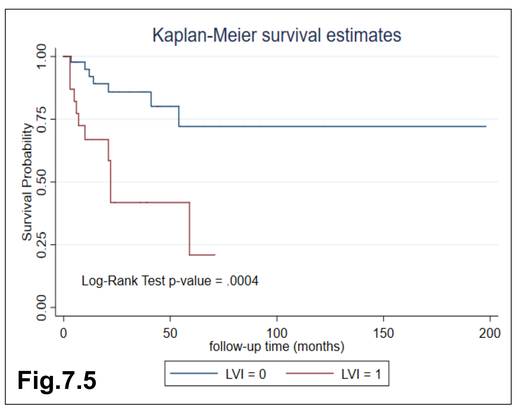


Fig.7.5

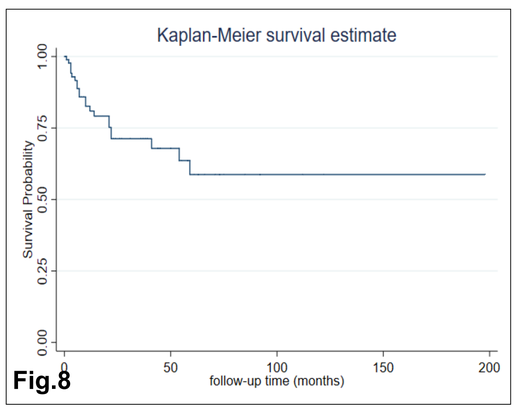


Fig.8

# SUMMARY

- Depth of invasion, size of total tumor and the proportion of the SARC component did not correlate with poor survival.
- Pure SARC (sarcomatoid carcinoma) and mixed SARC with other epithelial invasive carcinoma (carcinosarcoma) had similar survival.
- Posterior bladder wall SARC are associated with poor OS
- SARC patients with heterologous elements had significantly poor overall survival.
- IHC classification did not show any association to OS
- >T1T2N0M0 had significant high OS compared to rest of the stages.
- The presence of LVI and nodal disease (≥N1) was significantly associated with poor survival.
- Among all the death events, 86% occurred before 2 year time point. 10% survived beyond 5yrs.
- Despite the small number of patients with pT1 tumors, they seem to have better survival after RC suggesting that early radical cystectomy in this patient group could be beneficial.