**Introduction:**

Neo-adjuvant chemotheraphy and radiotherapy (NACRT) has been shown to bring favourable outcomes in patients undergoing surgery for rectal cancer. Serum carcinoembryonic antigen (CEA) is used as a prognostic marker for rectal cancer. Recent studies have tried to link the pre and post NACRT serum CEA values with clinical outcomes in various ways. Studies conducted were mostly retrospective (data from 3-9 years). These studies have grouped the patients mostly into three groups, namely those with low CEA values both pre and post NACRT, those with high CEA prior to NACRT but significant reduction in post NACRT, and those with persistently high CEA levels throughout their course of treatment.

Huang et al showed that survival was poor in patients with CEA levels >5 ng/mL with a pre to post NACRT reduction of less than 50%. Another study concluded CEA ratio to be an independent predictor for pathological complete response. A pre NACRT of > 6 ng/mL with a reduction ratio of < 70% was shown to be a risk factor for recurrence and bad prognosis. These clinical studies did not explore the use of biological variation, reference change values (RCV), marker kinetics or prediction equation used to determine optimal kinetic application in clinical use. We attempt to describe elements of a comprehensive CEA report using CEA kinetics, RCVs and prediction of significance of change. These ‘unconventional’ uses of CEA in can be developed from patient data but the real challenge lies in pressing them into clinical service using appropriate trials.

**Methodology:**

Curation of databases from 2011 – 2014.

Classification of imaging features from CT or MRI into four post-surgical categories (no remnant tumor-1, stable disease-2, progressive disease-3, and metastasis-4).

The biological variation calculated from patients who had values below 3 ng/mL (as per the current reference interval). The CV\textsubscript{within-individual} (CV\textsubscript{w}) and CV\textsubscript{between-individual} (CV\textsubscript{b}) were calculated based on literature\textsuperscript{6}. CV\textsubscript{w} was calculated as 100(\sqrt{\text{variance}})/M and CV\textsubscript{b} as 100(\sqrt{\text{variance}})/M. The coverage interval was calculated as per the method suggested by IUPAC.

The (RCV) was calculated based on \(\sqrt{\text{X}^2 \times 1.65 \times \sqrt{\text{CV}^2 + \text{CV}^2}}\).

The significance of change (1-p) was calculated from the collated values of CEA and a prediction model was constructed.

Kinetics of CEA was calculated from individuals who had a raised baseline followed by declining post-NACRT and two post surgical follow-up values. Non-compartmental analysis was used to calculate half-lives.

**Results:**

The basic demographic data is as follows:

<table>
<thead>
<tr>
<th>Age (Median) (Years)</th>
<th>Age interval (Years)</th>
<th>Total patients (analyzable)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>24-89</td>
<td>37</td>
<td>28</td>
<td>11</td>
</tr>
<tr>
<td>High serum CEA values</td>
<td></td>
<td>18</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>

Calculation of Coverage interval:

- 52 patients or follow up

Calculation of Biological variation:

- 33 patients on follow up

Biological variation:

<table>
<thead>
<tr>
<th>CV\textsubscript{w}</th>
<th>CV\textsubscript{b}</th>
<th>Index of individuality</th>
<th>RCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>29%</td>
<td>65.97%</td>
<td>0.25</td>
<td>69%</td>
</tr>
</tbody>
</table>

Coverage interval:

\(0 - 2.94 \text{ ng/mL with uncertainty of the } 0.95 \pm 0.08\)

Regression equation to calculate significance (1-p) of percent change of serum CEA

\[\text{Probability of significance of change in serum CEA} = 0.5 \times \left(\frac{1}{1 + \text{exp}(-1.2)}\right)\]

\[\text{Number of patients} = \text{N=60}

Comparison of half life according to radiological groupings

\(\text{N=18}\)

**Discussion:**

- There is sparse data on the utility of serial serum CEA data from patients receiving NACRT in rectal cancer.
- The demographics reveal that 49% of our patients have raised CEA with a preponderance of males (78%) in the hospital catchment area. This cancer is seen mostly in the middle aged to the elderly.
- The coverage interval in patients derived from the first post surgical follow-up is 0 – 2.94 ± 0.08 ng/mL.
- The biological variation derived from the post-surgical follow up values in patients with over three years in follow up is higher than the published data.
- The reference change value is to the tune of 69% which is also higher as compared to published studies.
- The study reveals that the half-life of CEA in category 1 patients is lower as compared to the other 3 radiologic categories.
- We developed a bi-exponential model to explain CEA kinetics. An increased number of data points from a larger data set are required for increasing the robustness of the model.
- The complement of probability construct model (1-p) versus change in CEA values provides an intuitive way to calculate the significance of change. It reveals the construct to be polynomial.
- We are in the process of collecting additional data from a larger subset of the population to increase the robustness of the study.
- In future we would look into the kinetics using compartment models and population models (both parametric and non-parametric) to establish their clinical use.

**References:**


**Acknowledgements:**

1. Mr S. Sugumar, Mr Sandip Rath and Mr. Ranjan Bhattacharya, Department of Biochemistry, Tata Medical Center, Kolkata.
2. Dr Mammen Chandy, Director, Tata Medical Center, Kolkata.