Prospective study to validate the clinical utility of the existing tool in predicting mucositis in patients receiving either high dose chemotherapy or on chemoradiotherapy

Dr D Vidyasagar *, Dr AVS Suresh*, Dr PS Dattatreya*, Dr SS Nirni*, Dr Vindhya Vasini*, Dr Mohan vamsi Ch**, Dr Mallik S***

*Dept of Medical Oncology, ** Dept of surgical Oncology, *** Dept of Radiation Oncology

Omega Hospitals, Hyderabad

Background

- Mucositis is the leading morbidity that disrupts the QOL significantly in subjects relieving high dose chemotherapy or concurrent chemo-radiotherapy.
- The lesions restrict oral intake, thereby adversely affecting nutritional status and immune status, and they act as entry sites for oral flora and sites of secondary infection.
- It often results in treatment interruption and dose reduction, and may compromise survival in the adjuvant/neoadjuvant settings and quality of life in the palliative setting.
- The incidence of mucositis during cancer chemotherapy ranges from 15% to greater than 70%
- Various studies have identified potential risk factors, including primary diagnosis, age, oral hygiene status, nutritional status, history of oral tobacco use, and nature of treatment (dose, frequency, number of drugs)
- However, risk of mucositis appears to be variable even among patients with similar characteristics receiving identical treatments
- Initial attempts to look for the tools for predicting the probability yielded encouraging results. [1,2]

1. Journal of cancer research and therapeutics :2010 6(4):448-51
2. Gastrointest Cancer Res. 2009 Jan-Feb; 3(1): 4–6.

Rationale

- The striking difference in incidence and severity of mucositis among different patients receiving same protocol often makes the decision difficult to adopt preventive strategies
- Earlier studies found a positive correlation between
  - the markers of local immunity (total WBC counts, comorbid conditions, tobacco use, nutritional status as reflected by the albumin levels)
  - markers of inflammation (ESR which indicate ongoing damage) and
  - markers of healing capacity (performance and nutritional status and comorbid conditions)

  with the severity and incidence of mucositis
- There is no prospective validation of the two scoring system done for predicting development of mucositis in patients getting concurrent chemo-radiation or high dose chemotherapy.
- This study was conducted to validate the risk-scoring system developed by Attili e al to predict probable incidence and severity of mucositis

Tools validated- tool 1

Tool 1				
Group	Score	Incidence of mucositis	Sensitivity to predict mucositis > grade 3	Specificity to predict mucositis > grade 3
High	6–8	Grade 3, 50%, Grade IV- 30%	80%	75%
Intermediate	3–5	Grade 3, 35%, Grade IV 15%	55%	40%
Low	<3	Grade 3, 20% Grade 4, 05%	35%	15%

For developing a risk score, a score of 1 was assigned to each of the following:

✓age greater than 50 years,
✓ESR greater than 3 times upper limit of normal,
✓albumin less than 3.3 g/dL,
✓WBC count less than 2.5 × 10^9/L,
✓WHO performance status greater than 2,
✓disease stage greater than III,
✓use of tobacco,
✓ and presence of any comorbid condition.
✓All other values, absence of tobacco use, and absence of any comorbid condition were assigned a score of 0

Gastrointest Cancer Res. 2009 Jan-Feb; 3(1): 4–6.

Tool 2 - assumptions

Risk group	Score	Incidence of mucositis	Sensitivity to predict mucositis of > grade 3	Specificity to predict mucositis of > grade 3
High	6-8	Grade 3, 40% (87 patients) Grade 4, 45% (98 patients)	90 %	78%
Intermediate	3-5	Grade 3, 35% (76 patients) Grade 4, 15% (33 patients)	62%	46%
Low	<3	Grade 3, 15% (33 patients) Grade 4, 05% (11 patients)	31%	17%

- The cutoff values for high vs. low risk indicated by ROC curve analysis were
- ✓ age > 40 years,
- ✓ ESR > 3 times upper limit,
- ✓ Albumin < 3.0 g/dL,
- ✓ WBC less than 3000/ ¨L
- ✓ PS of more than 2
- ✓ stage III or above disease
- ✓ Use of tobacco and
- ✓ presence of any comorbid conditions

The absence of any of these parameters was assigned a score of 0. For developing a risk score a score of 1 was assigned for each of the parameters having a value above the cutoff values as indicated by ROC curves.

Journal of cancer research and therapeutics :2010 6(4):448-51

Methods

- This is a prospective analysis conducted at a tertiary care cancer center with approximately 6,000 new cases of annually.
- The considered risk factors as per the literature after doing secondary statistical analysis after churning the raw data were the following cutoff values were selected:
  - age > 40 years
  - ECOG PS > 2
  - WBC < 3000/µl
  - elevated ESR,
  - Albumin < 3 gm/dL and
  - more than or equal to stage III disease
  - presence of more than one comorbid conditions.

A score of 1 was assigned for the above risk factors.

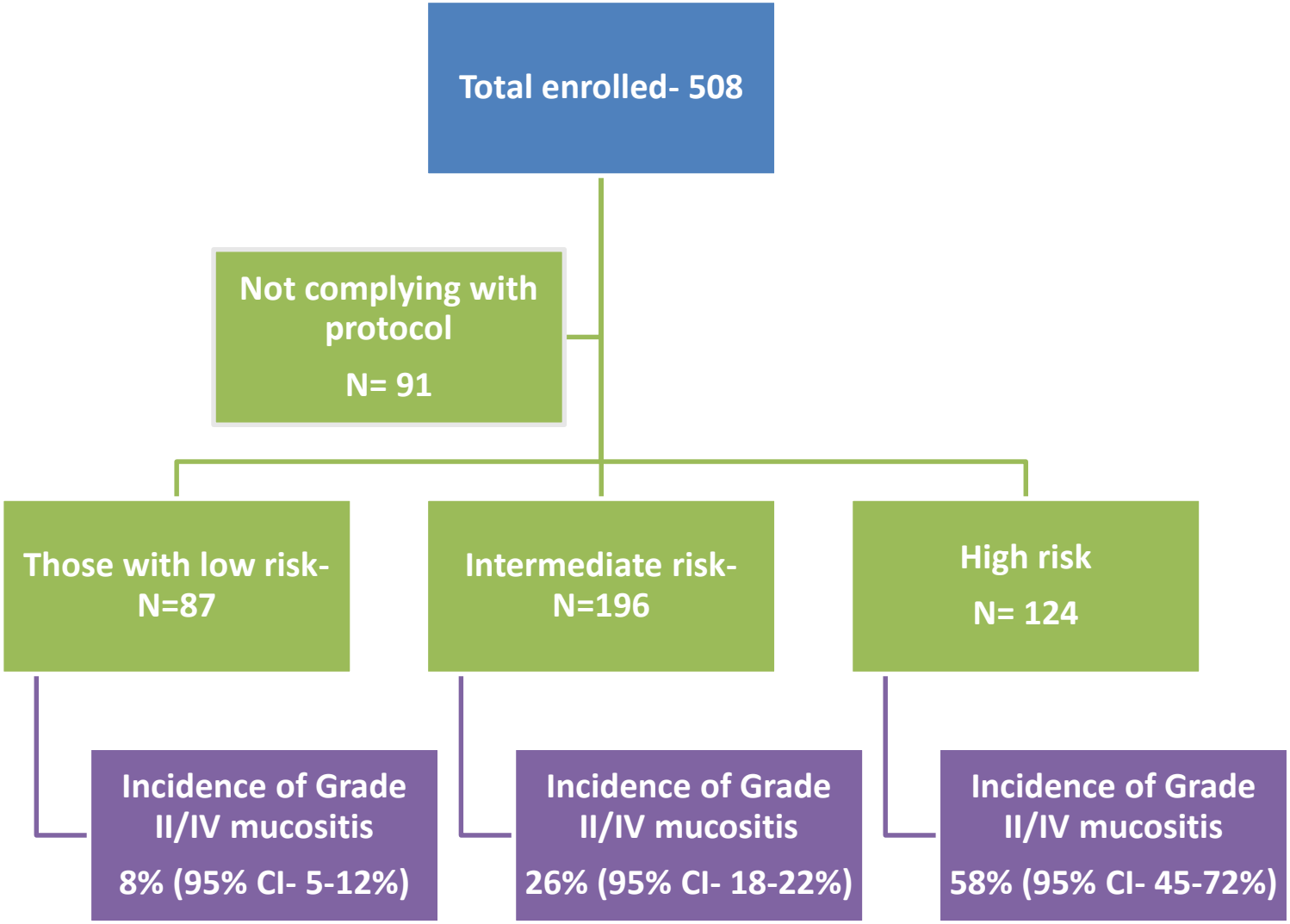
Results

- Number of subjects-A total of 508 patients were enrolled for initial screening
- Study period of 18 months from 2017 Jan till June 2018
- Follow up period- from June 2018- Dec 2018
- Eligibility criteria
  - Age 18-65
  - Patients with proven malignancy, where it is clinically indicated to received either chemoradiation (cisplatin 40 mg/m2 /week along with local radiation of 60-70 Gy depending on primary site) or high dose chemotherapy.
  - Able to consent voluntarily to use their clinical data and agree for follow ups as advised by physician
  - Adequate renal hepatic and bone marrow reserves

Results

- Subjects were prospectively classified into
  - Low risk (score less than 3%),
  - Intermediate risk (score of 4-6) and
  - high risk (score of more than 6).
- All the patients received either chemoradiation (cisplatin 40 mg/m2 /week along with local radiation of 60-70 Gy depending on primary site) or high dose chemotherapy.
- For patients, the
  - low risk subjects there is 8% (95% CI- 5-12%) probability of developing grade 3 or 4 mucositis,
  - while patients having intermediate risk have 26% (95% CI- 18-22%) and
  - high risk [patients have 58% (95% CI- 45-72%) of sever mucositis
- The positive (86%) and negative (89%) predictive values were also favoring the use of the same in clinical practice

Pictorial representation of analysis



Patient characters

Characteristic	Value/No. patients
Age (mean ± SD)	45 ± 14 years
Ratio men: women	4:1
Stage of disease, n (%)	
I	10.5%
II	36%
III	44%
IV	19.5%
ESR (mean ± SD)	25 ± 16 in 1st hour
WHO performance status, n (%)	
1	16%
2	32%
3	48%
4	4%
Serum albumin (mean ± SD)	2.8 ± 2.2 g/dL
Tobacco use, (%)	48%
Comorbid conditions, n (%)	32%

conclusions

- we could successfully validate the clinical utility of the existing tool in predicting mucositis in patients receiving either high dose chemotherapy or on chemoradiotherapy.
- This will further help clinicians to adopt preventive strategies as well as better counseling.