Head and Neck Cancer Therapy: Impact on Acute Nutritional Status

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Financial Disclosure

- Archimedes – Consultant
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- BMS - Consultant

Nutritional Risk Assessment:

- Baseline:
  - Assessment of nutritional deficiencies that need to be addressed prior to initiating therapy
- During Active Therapy:
  - Frequent assessment do to rapid changes in nutritional status
  - Critical Issue: Adequate energy and protein intake
  - May require a feeding tube
    - When should a tube be placed?
- Recovery Phase:
  - Transition from PEG feedings to oral intake
- Long Term Survivorship:
  - Adequate micro and macronutrients
  - Ensure high fiber diet

Nutrition: Significance

- Incidence
  - 50% of pts with SCHN are malnourished at some point during the trajectory of their disease process
  - Increases with advancing stage of disease
- Baseline malnutriton associated with
  - ***Decreased survival***
  - Decreased QOL

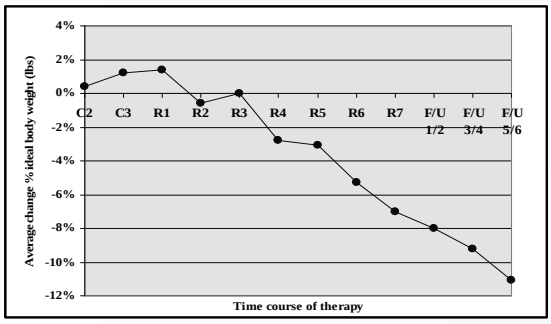
Nutritional Risk Assignment:

Low Risk:
Stable Weight
Serum Albumin ≥ 3.5 g/dl
Moderate Risk:
Recent Weight Loss
(>5% in 1 month, > 10% in 6 months)
Serum Albumin 3.0-3.4 G/dl
Poor intake
High Risk Patients:
Recent Weight Loss
(>5% in 1 month, >10% in 6 months)
Serum Albumin ≤ 3.0 g/dl
Unable to take PO for prolonged periods

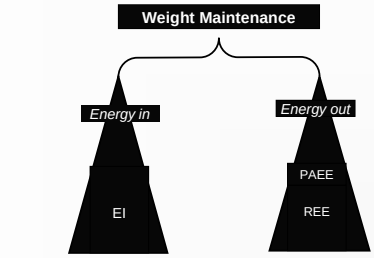
Malnutrition at Baseline

- Decreasing in numbers
  - Now a small percentage of patients
- Potential Explanations:
  - Increasing numbers of young patients with HPV associated tumors
  - Decrease in number of patients with history of heavy smoking and drinking
- Initial Screening Conducted on **All** HNC patients:
  - Weight loss history
  - BMI
  - Current caloric intake
  - Disease status

Chemoradiation Associated Weight Loss:



Concept of Energy Balance



EI = Energy Intake
PAEE = Physical Activity Energy Expenditure
REE = Resting Energy Expenditure

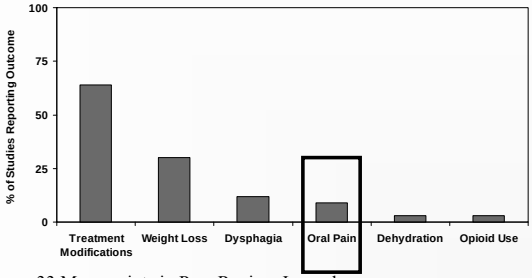
Contributing Factors to Decreased Oral Intake:

- Local Processes
  - Dysphagia
  - **Pain on swallowing due to mucositis**
  - Acute xerostomia
  - Dental loss
  - Taste alterations and alterations in smell
- Systemic Processes
  - Anorexia
  - Gastrointestinal Dysmotility
- Mechanical
  - **Issues with feeding tubes**
- Socioeconomic
  - Lack of insurance coverage for dietary assessment or supplements
  - Caregiver issues: care coordination and management

Acute Mechanisms for Altered Swallowing:

- Cancer related:
  - Anatomic/ physiologic alterations
    - Obstruction by tumor
    - Functional impairment of tissues by tumor
  - **Cancer associated pain**
- Treatment related
  - Tissue loss secondary to surgery
  - **Pain secondary to mucositis**
  - Edema secondary to inflammation
  - Xerostomia
- Loss of dentition
  - Pre-existing or as a consequence of therapy

Symptom Reporting in Head and Neck Cancer Clinical Trials



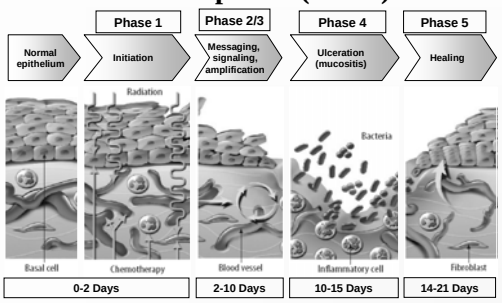
33 Manuscripts in Peer Review Journals

Trotti A. *Int J Radiat Oncol Biol Phys.* 2000;47:1-12.

Mucositis:

- Pan-tissue process affecting the mucosa and underlying tissues
- Results from damage secondary to radiation, chemotherapy or a combination
- Time Course in HNC
  - No symptoms for 1-2 weeks
  - Irritation and mild pain starting week 3
  - Requiring pain medication and altered diet starting weeks 3 through 5
  - Edema and dysphagia starting week 5

Proposed Phases of Mucositis Development (Acute)



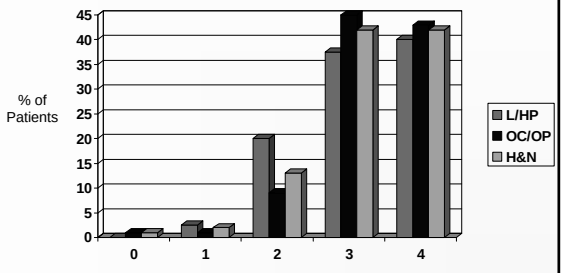
Sonis ST. *J Support Oncol*. 2004;2:21-32.

What is the incidence of severe pain in patients undergoing radiation based therapy for head and neck cancer?

Burden of Illness: Preliminary Analysis in HNC Pts

- Sponsored by MASCC
- Descriptive study
- Design: Prospective, Longitudinal using repeated measures
- Measure: Mucositis Daily Questionnaire
  - Vanderbilt completed trial in 2005 that helped validate this measure
  - Reported in Cancer 2006
- Patient population:
  - Patients undergoing primary therapy with treatments that induce mucositis (both chemotherapy and radiation therapy)
  - Completed the head and neck cohort

Maximum mouth and throat soreness

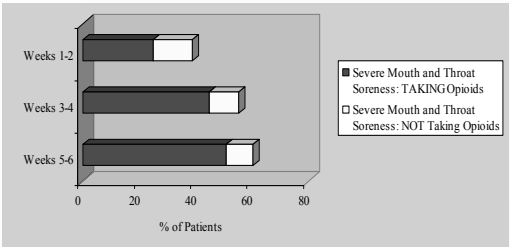


Mucositis PRO: Validation

- 75 HNC patients undergoing radiation-based therapy
- Followed for the first 6 weeks of therapy
- Completed brief questionnaire at baseline, 2, 4 and 6 weeks
- Assessed pain intensity and interference

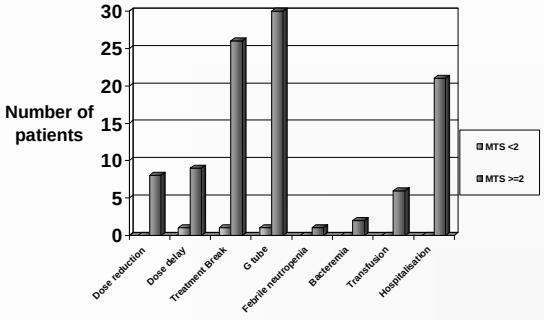
Murphy BA et al Oral mucositis (OM) related morbidity and resource utilization in a prospective study of head and neck cancer (HNC) patients. Supportive Care Cancer

Pain Levels During Chemoradiation

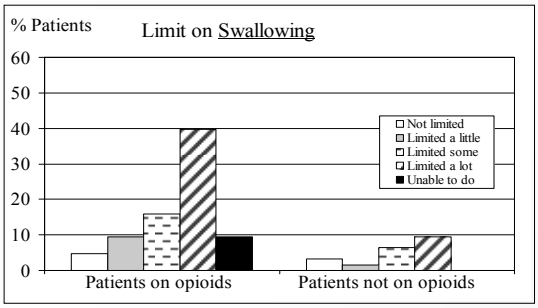


Does pain interfere with critical functioning?

Clinical Outcomes



Interference By Mucositis Pain



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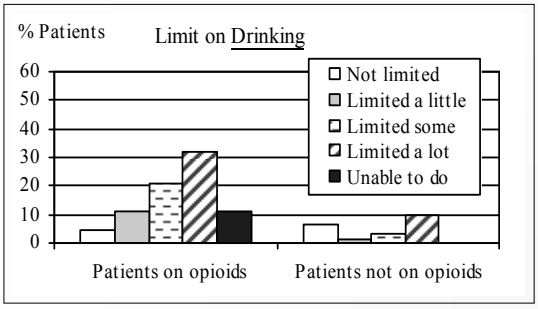

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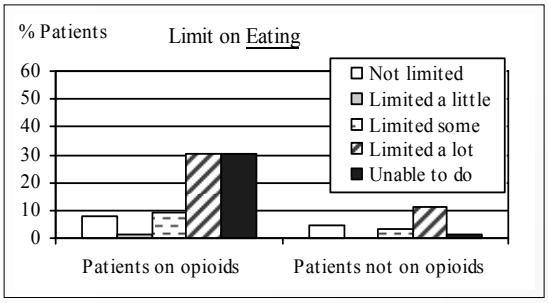
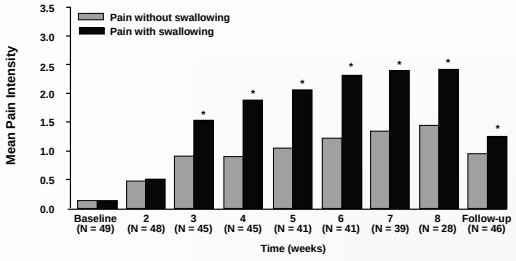


Pain from Mucositis Worsens With Swallowing

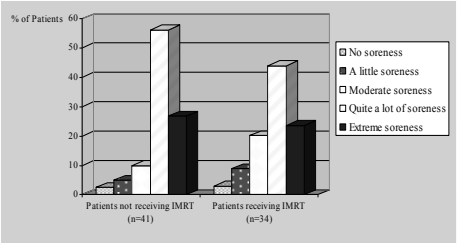


- 96% of patients in this study reported pain when not swallowing

*P = 0.001
Pain scores: 0 = not painful, 3 = extremely painful.
Wong PC, et al. *J Pain Symptom Manage.* 2006;32:27-37.

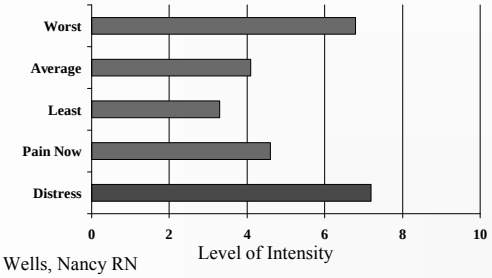
Is IMRT associated with decrease in oral pain?

Pain Levels Associated with Differing Radiation Delivery Systems



Is pain associated with significant distress?

Pain and Distress: Head & Neck Cancer



Wells, Nancy RN

What is the effect of pain on quality of life and quality of life domains?

Vanderbilt Head and Neck Cancer Symptom Survey: Tool Development

- Identification of potential symptoms through literature review and staff interview
- Review by PSMP-RT for face validity
- Two step Patient Card Sort (n=49)
  - Step A: sort symptoms in to yes/no piles
  - Step B: rank order most to least frequent

VHNC Symptom Survey: Card Sort Assessment

- Analysis of frequency distribution
- Identification of symptoms endorsed by 50% of patients
- Identification of overlapping questions
- Identification of high priority, low frequency symptoms
- Final 28 question survey which included the 10 most troubling symptoms

VHNCSS:

- Purpose:
  - Quick tool for symptom screening in clinic
  - Identification of patients with problems that require referral, education or intervention
- 28 questions
- Time required for completion: < 5 minutes

Validation Cohort:

- 332 patients on five studies
  - Diet Adaptation Trial
  - Resource Utilization Assessment
  - Coping Styles in Head and Neck Cancer Patients and Significant Others
  - Correlation with Modified Barium Swallow
  - Energy Balance Study

Cluster Analysis:

Label	# Items	Cronbach's alpha
Swallow	7	.931
Nutrition	5	.812
Mucous/Dry Mouth	6	.886
Pain	**4**	**.773**
Voice	2	.855
Dentition	1	NA
Hearing	1	NA

	FACT-G Subscale				HN Mod.
VHNSS	**Physical**	**Social**	**Emotional**	**Functional**	
Global	.764	.288	.275	.699	.775
Cluster					
Swallow	.775	.008	.511	.614	.568
Nutrition	.607	.170	.279	.609	.687
M/DM	.579	.500	.114	.545	.662
Pain	**.705**	**.214**	**.277**	**.643**	**.725**
Voice	.719	.098	.332	.512	.564
Dentition	.333	.069	.079	.241	.336
Hearing	.337	.079	.165	.306	.210

	EORTC Subscale			
VHNSS	**Swallow**	**Eating**	**Pain**	**Speech**
Global	.836	.757	.527	.575
Cluster				
Swallow	.853	.715	.416	.546
Nutrition	.647	.658	.371	.352
M/DM	.722	.640	.406	.419
Pain	**.523**	**.550**	**.777**	**.502**
Voice	.563	.355	.423	.644
Dentition	.209	.254	.250	.291
Hearing	.277	.350	.106	.207

Conclusions:

- Pain is prevalent and severe in patients undergoing chemoradiation
- Pain interferes with critical functions such as swallowing
- Pain is associated with distress
- Pain is associated with decrease in global QOL.

How well do we do controlling pain?

Use of Supportive Care Measures

	ALL %	Inter-Group Comparisons: Academic %	Community %	*p* Value
Feeding tube placed	55	59	48	0.001
Tracheotomy tube placed	13	16	9	0.002
Opioid analgesics prescribed	79	89	59	<0.0001
Anti-emetics prescribed	78	83	68	<0.0001
Amifostine prescribed	15	17	11	0.02

Contributing Factors to Decreased Oral Intake:

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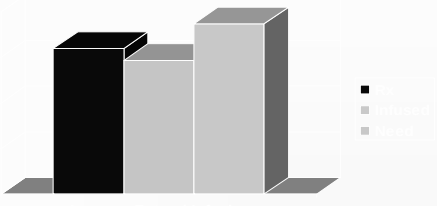
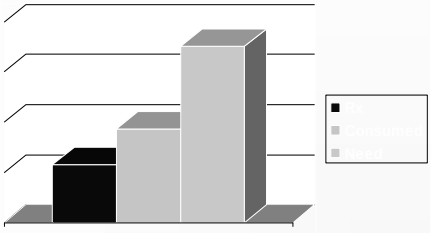
Enteral Feeding: Less Effective Than We Think?

N = 30



Silver et al. Older Adults Receiving Home Enteral Nutrition: Enteral Regimen, Provider Involvement, and Health Care Outcomes. *J Parenter Enter Nutr 2004;*28:92-98.

Water Intake:



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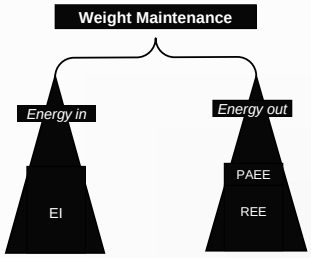

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REE = Resting Energy Expenditure

Metabolic Changes in HNC

- Glucose:
  - Decreased first phase insulin response in underweight and nl weight HNC patients
  - Improved post-op glucose utilization
  - No evidence of increased hepatic glucose production in HNC
- Protein:
  - Cytokine (Il-1, Il-6, TNF) induced changes in protein synthesis
- Elevation of Resting Energy Expenditure:
  - Weight loss may continue despite adequate caloric intake (Herber,1986)

Endotoxin Production: Predictor of Survival?

- 49 pts with HNC
  - undergoing surgery
  - >10% weight loss
  - measure TNF and IL-6 pre and post treatment
- Results:
  - TNF and IL-6 associated with decrease survival

Van Bokhorst-de van der Scheur, JPEN, 2000

Treatment Associated Wasting Syndrome

- Manifestations:
  - Fatigue
  - Accelerated weight loss
  - Rapid wasting of muscle
  - Rapid depletion of fat stores
  - Rapid decreased physical functioning
- Time course
  - 3-4 weeks
  - Recovery may be prolonged
  - Associated with aggressive therapy and size of port?

Starvation vs Cancer Cachexia

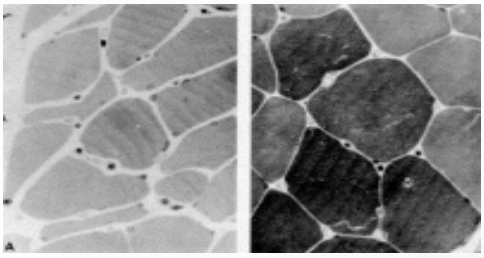
Starvation:

- Decrease in calories
- Decrease in REE to spare calories
- Increased hepatic production of ketones from fatty acids
- Increased peripheral use of fatty acids
- Sparing of muscle

Cancer Cachexia:

- Decrease in calories
- Increased REE
  - Futile cycling
- Increased lipolyisis
- Increase muscle breakdown with loss of lean muscle mass

Cancer Cachexia: Effects on Lean Muscle Mass



Cachexia Normal

Pilot Trial: Metabolic effects of Chemoradiation in HNC

- Patient population: (n-17)
  - Stage 3 and 4 treated with CCR
- Measures:Pre and post treatment
  - DEXA scan to measure LBM
  - metabolic cart to assess REE
  - diet intake using 24 hour diet recalls
  - cytokine production: TNF-A, IL-1B, Il-6, IL-10, IL20p70
  - measures of oxidative stress
  - physical function
    - ADL and IADL
    - Reuben's Physical Performance Test
    - Modified Baecke Physical Activity Questionnaire

PI – Heidi Silver, PhD

Hypotheses

- **CCR results in a decreased food, energy & nutrient intakes. However, this decrease will not be sufficient to explain the degree of body wt lost.**
- **CCR result in the following:**
  - **Increased resting energy expenditure (REE)**
  - **Decreased physical performance/function (PPF)**
  - **Decreased body fat mass**
  - **Decreased fat-free mass (LBM)**
  - **Increased plasma levels of pro-inflammatory cytokines**

Change in Body Composition:

Variable	Baseline	1-month post	P-value
Weight	87.0±15.32	77±10.63	0.000
BMI	28.7±3.61	25.3±2.47	0.000
% Fat	32.7±6.67	34.0±5.75	0.802
Fat mass kg	28.0±5.34	24.5±4.48	0.003
Lean mass kg	52.3±11.3	46.6±96.534	0.005
REE (kcal/d)	1666.7±238.33	1645.9±210.0	0.736
REE/FFM (kcal/kg	30.6±3.22	34.9±6.60	0.019
Energy Intake	2454±938	2108±780	0.200
EI/REE (%)	1.45±0.55	1.22±0.42	0.165
Cal to Nitrogen Ratio	158.0±24.22	154.3±30.4	.630
RQ (VCO2/VO2)	0.74±0.11	0.77±0.12	0.457

Change in Physical Performance and Function

Variable	Baseline	1month post treatment	P-value
Total Physical Activity Score	5.33±4.58	1.64±1.75	0.003
Physical Performance Test	14.6±1.59	12.50±4.16	0.140
ADL Score	0.00±0.00	2.36±3.34	0.020
IADL Score	3.21±2.12	6.07±2.76	0.003

Inflammatory Mediators:

	Pre-treatment	Post-Treatment	P-value
CRP	5.04	10.32	.09
IL-6	5.7	14.1	.08

Nutritional Considerations:

- Good baseline assessment
- Ongoing evaluation by dietician
- Aggressively treat reversible problems such as pain
- Placement of a feeding tube if and when needed
- Follow-up to ensure adequate feeding tube function and proper utilization
- Recognition that patients may require increased caloric intake for weight maintenance
- Recognize that metabolic alterations may impact on ability to maintain a stable weight during and immediately after treatment.