

# **INCIDENCE AND CLINICAL SIGNIFICANCE OF THE REFEEDING SYNDROME AMONG HEAD AND NECK CANCER PATIENTS**

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Nutrition

# The people behind the study

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- Irene Wessel, MD, PhD
- Jens Rikardt Andersen, MD, MPA



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# Background

- Head and neck cancer patients
  - Cancers in oral cavity, tongue, pharynx, larynx, salivary gland, nasal cavity, paranasal sinuses, thyroid and cervical metastasis from unknown origin
- Refeeding syndrome in head and neck cancer
  - High nutritional risk (Dysphagia, stenosis etc.)
  - Relatively small tumour mass
    - High risk of adapted weight loss and development of RFS

# Objectives

- ❑ To determine the incidence rates of refeeding phenomena and refeeding syndrome in head and neck cancer patients
  - ❑ Refeeding phenomena (RFF): A decline in p-phosphate
  - ❑ Refeeding syndrome (RFS): Development of clinical symptoms in addition

Symptoms: oedema, dyspnea, hypotension, arrhythmia, confusion and/or seizures

# Objectives

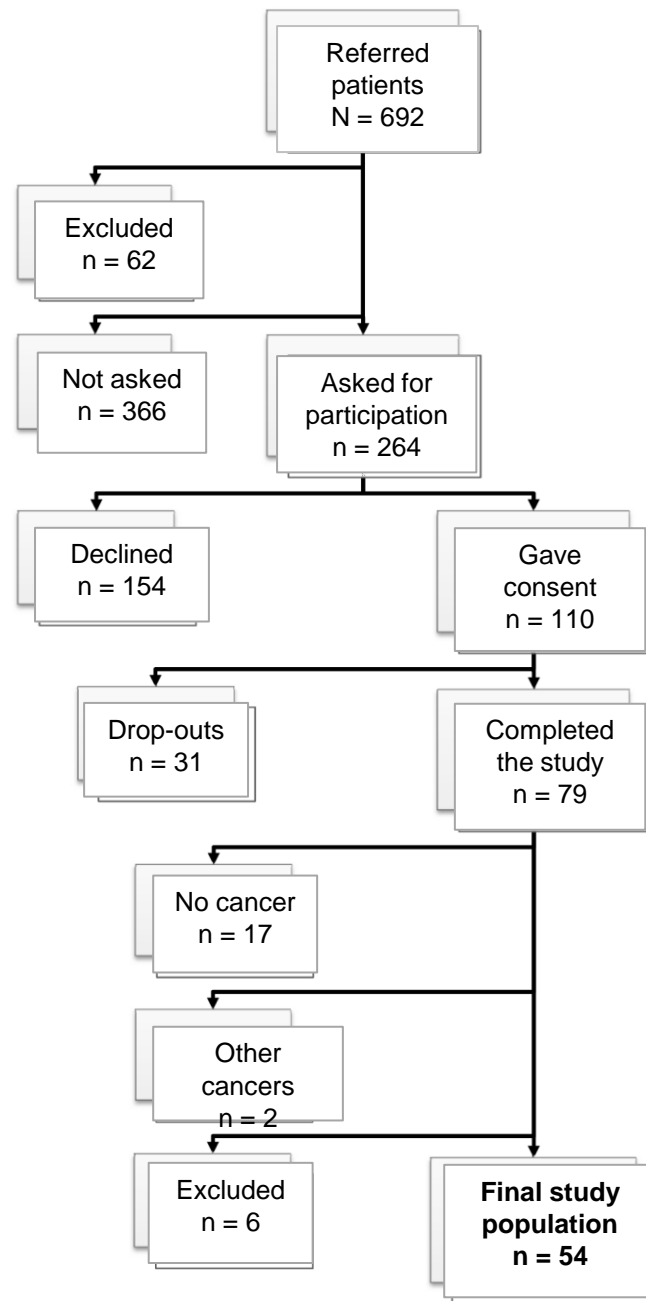
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- ❑ To determine whether factors at baseline could identify patients at high risk of developing refeeding phenomena or refeeding syndrome

# Methods

- ❑ Inclusion criteria
  - ❑  $\geq 18$  years
  - ❑ Referred on suspicion or diagnosis with head and neck cancer
  - ❑ First time referral
  
- ❑ Exclusion criteria
  - ❑ Unable to speak and understand Danish
  - ❑ Severe dementia
  - ❑ Renal impairment

# Population



# The final study population

Patient characteristics (n=54)	
Age (years)	59,7 ± 11,8 61 [35;90]
Sex (M/F)	37 M / 17 F (69 % / 31 %)
Body mass index (kg/m <sup>2</sup> )	25,4 ± 5,0 25,7 [15,6;36,8]
Nutritional status at baseline (BMI)	
Below normal	6 % (4/54)
Normal	35 % (19/54)
Above normal	57 % (31/54)
Body weight loss prior to baseline	
Yes	50 % (27/54)
No	50 % (27/54)
Cancer location	
-Nasal cavity	6 % (3/54)
-Paranasal sinuses	2 % (1/54)
-Pharynx	13 % (7/54)
-Larynx	17 % (9/54)
-Oral cavity	35 % (19/54)
-Thyroid	22 % (12/54)
-Salivary glands	6 % (3/54)

**Patient characteristics. Age and body mass index are indicated by mean ± standard deviation and median [range]. All other characteristics are indicated in percentage and number of patients.**



# Methods

Participants were monitored for 8 days

- Day 0

- Interview

- Dietary intake, alcohol, tobacco, medications, eating difficulties, head and neck pain (VAS)
    - Nutritional screening (NRS-2002)

- Blood samples

- Physical tests

- Step test
    - Hand grip strength

# Methods

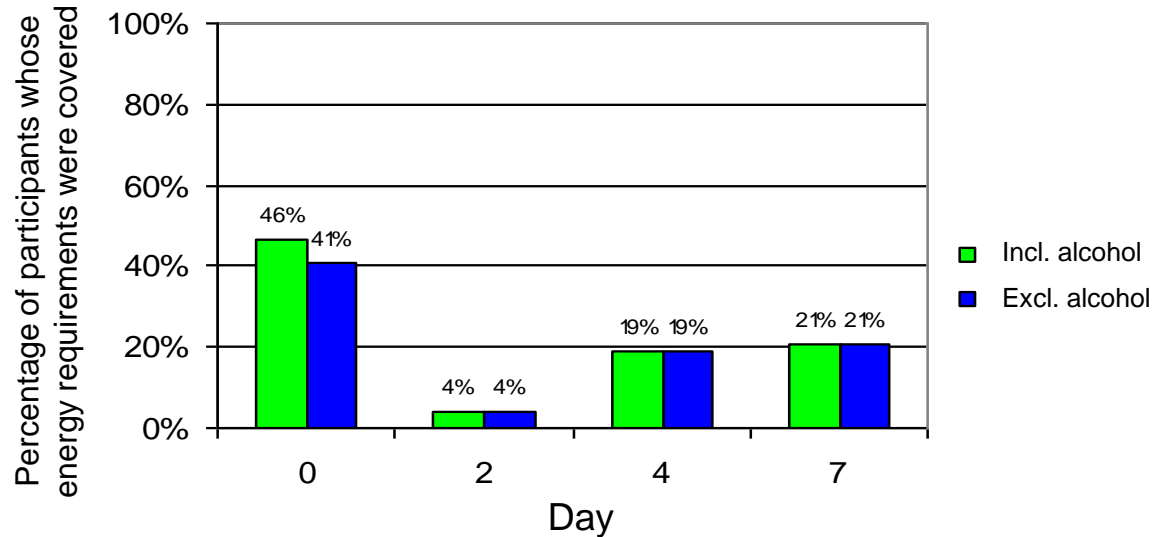
- Day 2, 4, 7
  - Interview
    - 24 hour recall of dietary intake, head and neck pain (VAS)
  - Symptoms
  - Blood samples

# Results

## Incidence and incidence rates

	<b>INCIDENCE %</b>	<b>INCIDENCE RATE Cases per 1000 patients per year</b>
n=54		
RFF & RFS	72 % (39/54)	723
RFF	52 % (28/54)	519
RFS	20 % (11/54)	204

# Results



<b>Changes in p-phosphate vs. changes in percentual coverage of enery requirements (In participants with an increase in percentual coverage of enery requirements)</b>	<b>r<sub>s</sub></b>	<b>p</b>
Baseline to the day of the lowest p-phosphate measurement (n=12)	0,070	NS
Preceeding day to the day of the lowest p-phosphate measurement (n=27)	-0,484	0,011
Baseline to the day of the first observed decline in p-phosphate (n=9)	-0,283	NS
Preceeding day to the day of the first observed decline in p-phosphate (n=19)	-0,703	<0,001

# Results

## Participants who developed clinical symptoms

Participant no.	Decline in p-phosphate	Oedema	Confusion	Dyspnea	Hypotension	Arrhythmia	Seizures
1	Yes				+		
4	Yes	+					
29	Yes	+					
32	Yes		+		+		
35	Yes	+					
47	Yes		+	+			
60	Yes	+	+	+	+	+	
78	No				+		
80	Yes	+			+		
81	Yes				+		
83	Yes				+		
93	Yes			+			

Hypotension: 58 % (7/12)

Oedema: 42% (5/12)

# Results

## Participants with RFS vs. other participants

	Participants with RFS (n=11)	Other participants (n=43)	
<b>Decline in p-phosphate* (mmol/L)</b>	0,41 [0,22;0,78] 0,43 ± 0,17	0,10 [-1,04;0,65] 0,02 ± 0,28	<b>p &lt;0,001</b>
<b>Lowest p-phosphate (mmol/L)</b>	0,63 [0,49;0,76] 0,62 ± 0,08	0,90 [0,53;1,97] 0,96 ± 0,26	<b>p &lt;0,001</b>

\*From baseline to the day of the lowest p-phosphate measurement

# Results

Associations between changes in p-phosphate\* and number of symptoms

	$r_s$	p
<b>All participants (n=54)</b>	-0,5411	p<0,001
<b>Participants with RFS (n=11)</b>	0,0640	NS

\*From baseline to the day of the lowest p-phosphate measurement

Associations between changes in p-phosphate\* and number of symptoms

	$r_s$	p
<b>All participants (n=54)</b>	-0,5212	p<0,001
<b>Participants with RFS (n=11)</b>	0,2428	NS

# Results

- ❑ No correlations were found between changes in energy intake and changes in p-phosphate in participants with RFS

	<b>Participants with RFS (n=11)</b>	<b>All participants (n=54)</b>	
<b>Participants with NG-tube</b>	91 % (10/11)	18,6 % (8/43)	<b>p&lt;0,001</b>



# Results

Length of stay – Participants with RFS vs. other participants

	Participants with RFS (n=11)	Other participants (n=43)	
LOS (days)	16 [10;28] 17,1 ± 5,1	4 [2;26] 5,3 ± 4,0	p <0,001

# Results

## When did it become clinically relevant?

<b>Lowest p-phosphate (mmol/L)</b>	<b>Number of participants below cut off (total)</b>	<b>Number of participants with RFS below cut off</b>	<b>Percentage of RFS-patients identified by cut off (%)</b>	<b>Percentage of participants below cut off with RFS (%)</b>
< 0,80	23	11	100	48
< 0,75	17	10	91	59
< 0,70	15	10	91	67
< 0,65	9	7	64	78
< 0,60	6	4	36	67
< 0,55	3	2	18	67

# Results

## When did it become clinically relevant?

Changes in p-phosphate* (mmol/L)	Number of participants below cut off (total)	Number of participants with RFS below cut off	Percentage of RFS-patients identified by cut off (%)	Percentage of participants below cut off who developed RFS (%)
≤ -0,10	34	11	100	32
≤ -0,15	28	11	100	39
≤ -0,20	21	11	100	52
≤ -0,22	16	11	100	69
≤ -0,25	12	9	82	75
≤ -0,30	11	8	73	73
≤ -0,35	11	8	73	73
≤ -0,40	8	6	55	75
≤ -0,45	7	5	45	71
≤ -0,50	5	4	36	80

\*From baseline to the day of the lowest p-phosphate measurement

# Results – Risk factors

## Correlations with changes in p-phosphate\*

Potential risk factor	n	r <sub>s</sub>	p
Head and neck pain at baseline (VAS)	54	-0,322	0,018
Alcohol intake (units per day)	53	-0,275	0,046

\*From baseline to the day of the lowest p-phosphate measurement

## Odds ratio in relation to development of a decline in p-phosphate $\geq 0,22$ mmol/L

Potential risk factor	Odds Ratio
Low hand grip strength at baseline	8,8 (CI:1,1-394,1)
Presence of eating difficulties	8,3 (CI: 1,8-51,5)
Previous radiation therapy	4,4 (CI: 1,1-19,1)

# Results – Screening tools

Screening tools in relation to development of a decline in p-phosphate  $\geq 0,22$  mmol/L

<b>NRS 2002 A-score =1</b>		<b>NRS 2002 Total score <math>\geq 3</math></b>		<b>NICE guidelines</b>	
PV <sub>pos</sub>	62,5 %	PV <sub>pos</sub>	30,0 %	PV <sub>pos</sub>	40,0 %
PV <sub>neg</sub>	76,1 %	PV <sub>neg</sub>	70,5 %	PV <sub>neg</sub>	74,4 %
Sensitivity	31,3 %	Sensitivity	18,8 %	Sensitivity	37,5 %
Specificity	92,1 %	Specificity	81,6 %	Specificity	76,3 %

# Conclusions

- ❑ **Incidence rates (cases per 1000 patients per year)**
  - ❑ Refeeding syndrome: 204
  - ❑ Refeeding phenomena: 519
  - ❑ Total: 723
  
- ❑ **A decline in p-phosphate was clinically relevant when  $\geq 0,22$  mmol/L**
  
- ❑ **Risk factors**
  - ❑ Head and neck pain
  - ❑ Presence of eating difficulties
  - ❑ Previous radiation therapy
  - ❑ High alcohol intake
  - ❑ Low hand grip strength
  
- ❑ **Not only patients with low BMI developed refeeding syndrome**

THANK YOU FOR  
YOUR  
ATTENTION