Improved treatment in pancreatic cancer, beter verpleegkundig management.....betere resultaten

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Disclosure belangen spreker

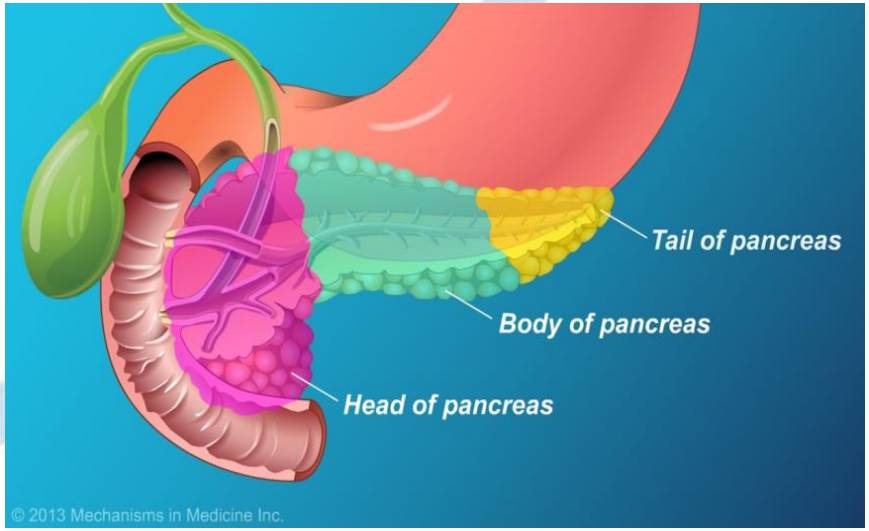
Potentiele belangenverstrengeling	
Voor bijeenkomst mogelijk relevante relatie met bedrijven	Geen
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiele vergoeding) • Aandeelhouder • Andere relatie, namelijk…	Geen

Wat kunnen jullie verwachten

- Een leerzame quiz

- Nieuwe ontwikkelingen t.a.v. behandelingen bij patiënten met een pancreascarcinoom

- Wat willen jullie weten?



Introductie

– Een van de meest agressieve kankersoorten (5jr overleving ±8%).

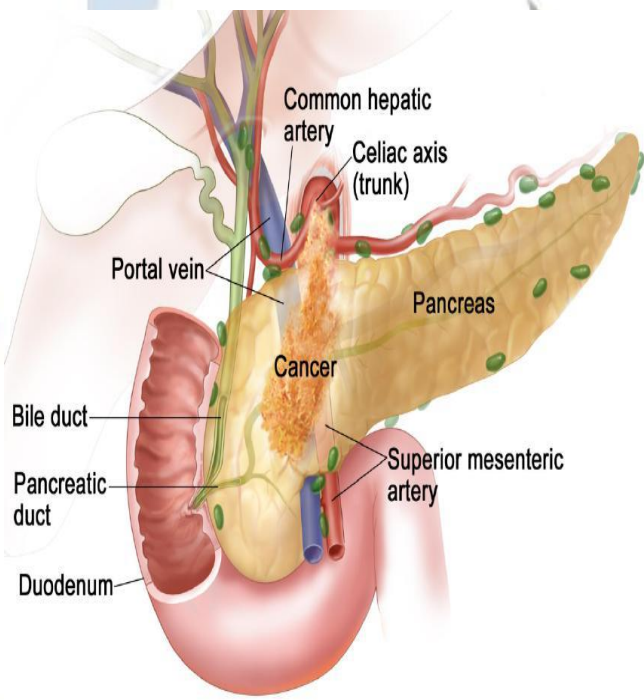
– Wereldwijde incidentie neemt toe (>340.000 pt/jaar)

Bij diagnose:

- 40% metastasen
- 40% lokaal gevorderd, niet-resectabel
- 20% primair resectabel

– 30% locally advanced pancreascarcinoom

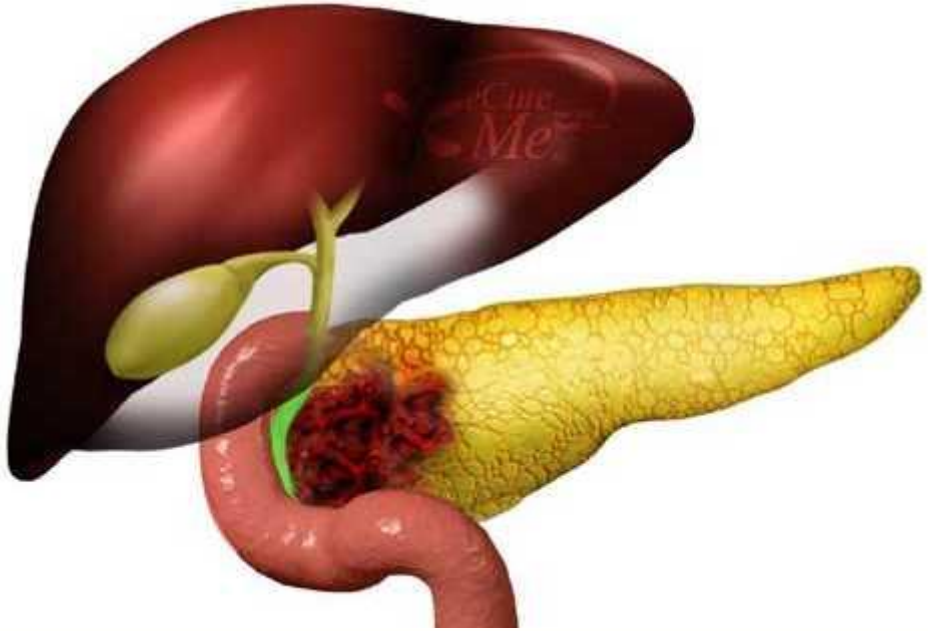
– Mediane overleving van LAPC is ± 12 mnd



Vraag 1

- Eten van vette voeding is een oorzaak voor het krijgen van een pancreascarcinoom.

- Ja
- Nee



Oorzaken pancreascarcinoom

- De precieze oorzaak van alvleesklierkanker is onduidelijk.
- De aandoening komt vaker voor in de westerse landen.
- Een aantal leefstijlfactoren geven mogelijk een verhoogd risico:

- roken,

- te vette voeding en

- overmatig alcoholgebruik.

- erfelijkheid (5 %).
- chronische alvleesklierontsteking

Vraag 2

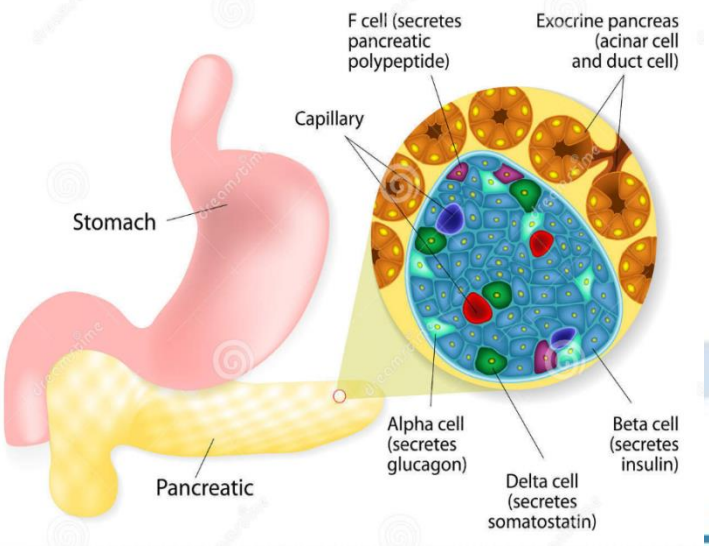
- Vertering van suikers is de specifieke functie van Trypsine in de alvleesklier

- Ja
- Nee

Alvleesklierfunctie

Endocrine fuctie:

Productie hormonen en Regulering bloedsuiker spiegel.



Exociriene functie:

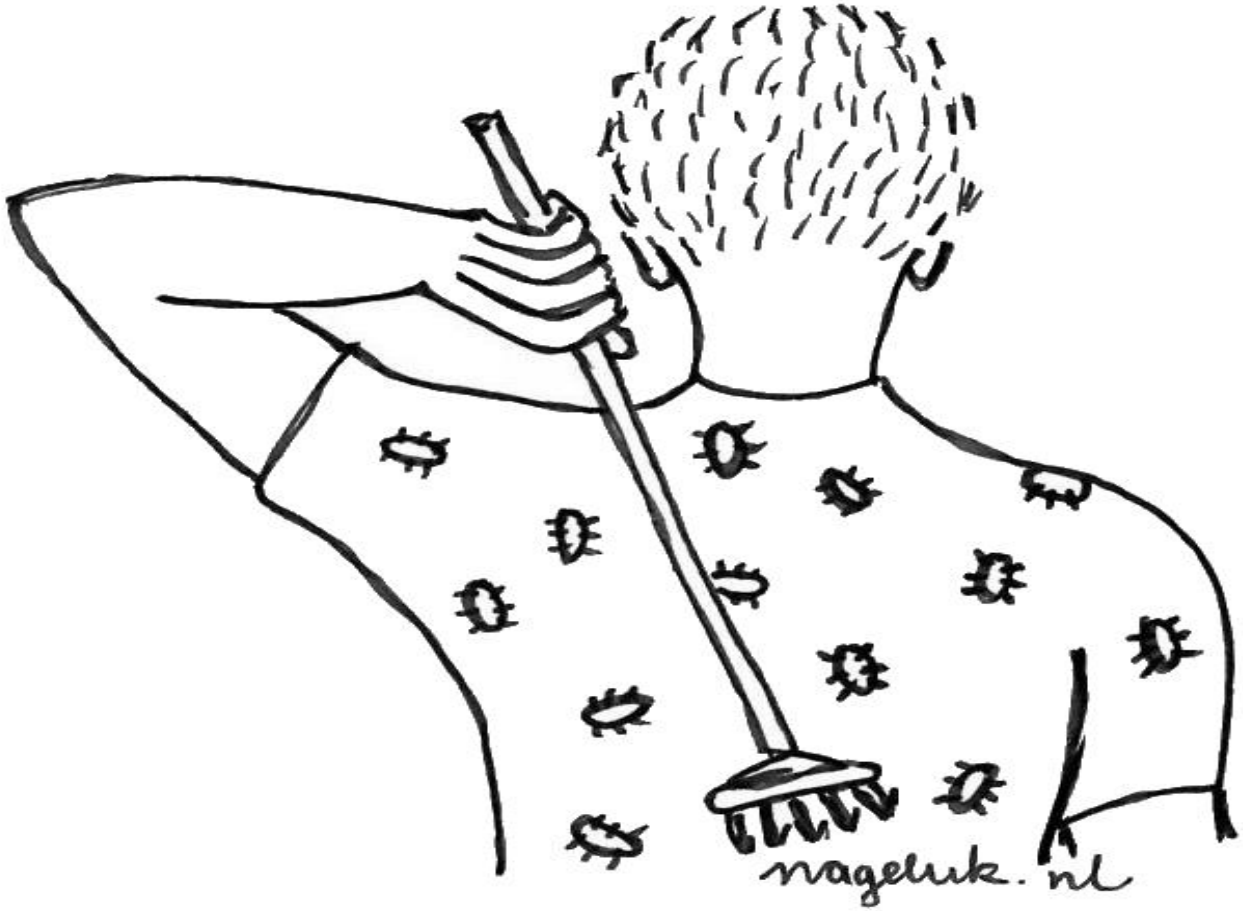
vertering van

Trypsine -> vetten

Amylase -> suikers

Lipase -> vetten

Wat zijn de symptomen van een pancreascarcinoom?



Symptomen

- zeurende pijn boven of midden in de buik of in de rug.
- een verstoord ontlastingspatroon zoals verstopping of vettige ontlasting.
- minder eetlust.
- gewichtsverlies.
- opgeblazen gevoel.
- ongewoon boeren.
- slikproblemen.
- klachten door een afsluiting van de galwegen
- diabetes
- pancreatitis (5%)

Vraag 3

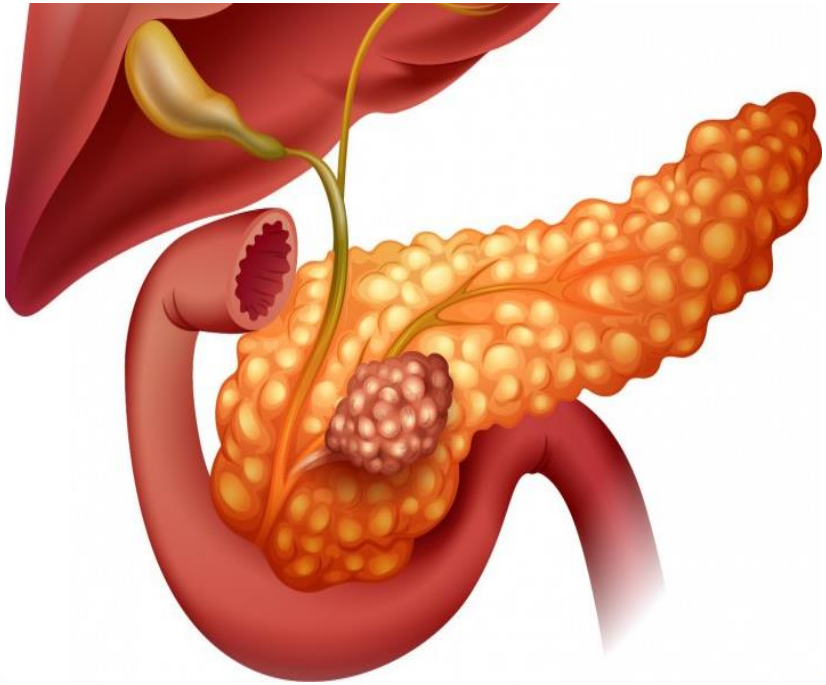
- Een tumor in de alvleesklier komt het meest voor in de kop.

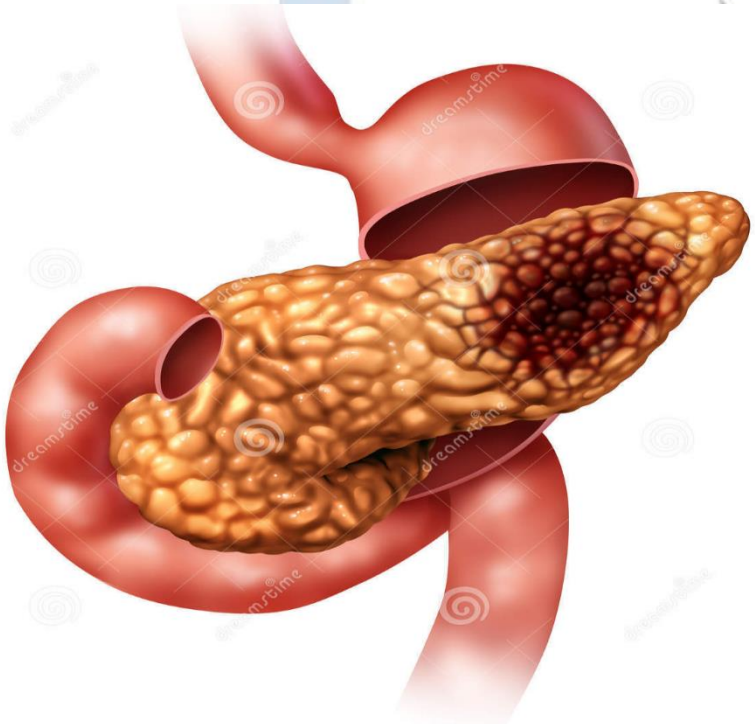
- Ja
- Nee

Locatie Pancreascarcinoom

- 75%

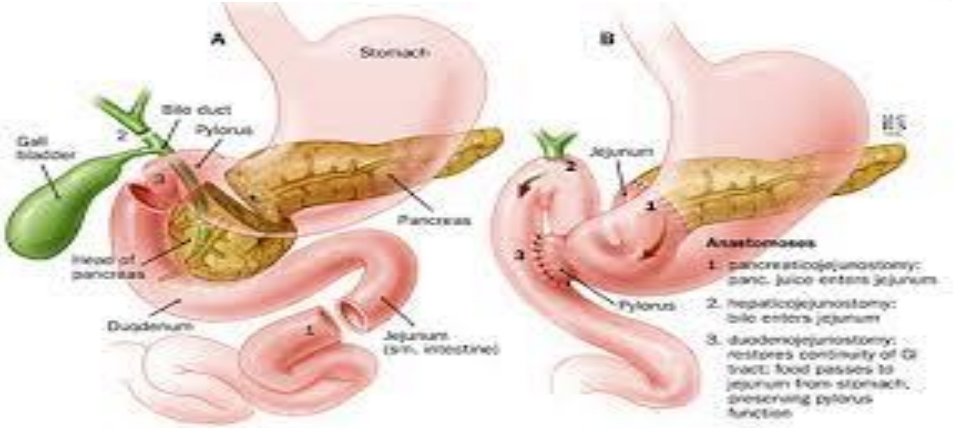
25%



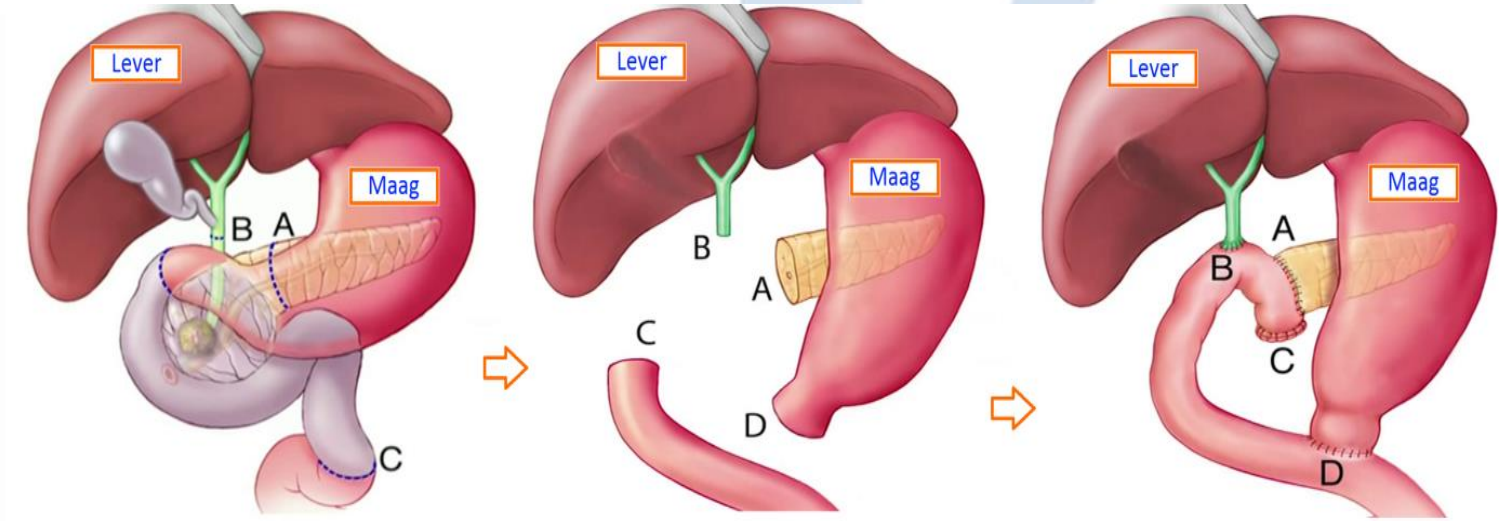


Indien resectabel

- 20% primair resectabel
- 30-40% lokaal gevorderde ziekte (LAPC)



Pylorussparende pancreaticoduodenectomie (PPPD)

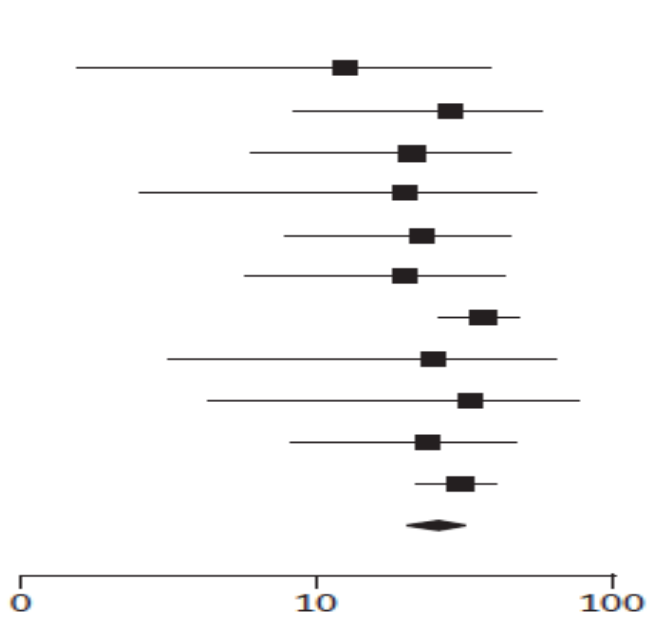


- Risicovolle ingreep
- Hoog risico op complicaties 30-60% (5-10% ernstig)
- Mortaliteit 2-3%

Literatuur kans op resectie

26%, 91 resecties van 325 patiënten

	Events	Patients
Resection		
Conroy, 2005	0	11
Gunturu, 2012	2	16
Hosein, 2012	6	14
Peddi, 2012	4	19
Boone, 2013	2	10
Faris, 2013	5	22
Mahaseth, 2013	4	20
Marthey, 2014	28	77
Moorcraft, 2014	2	8
Hohla, 2014	2	6
Mellon, 2015	5	21
Sadot, 2015	31	101
Total	91	325
25·9% (95% CI 20·2–31·9, I^2 24%)		



[1]Suker et al, Lancet Oncol 2017

Vraag 4

- Chemotherapie na operatie: verlengt het de overleving?
- Ja , het verdubbelt de kans om na 5 en 10 jaar nog te leven”
- Nee, het stelt alleen een recidief uit en verbeterd daarom kwaliteit van leven”

Overleving na resectie

- Zonder adjuvante chemotherapie: Mediaan 12 maanden

5 jaars overleving is 10%

- Met adjuvante chemotherapie: Mediaan 20 maanden

5 jaars overleving: 20%

Vraag 5

- Is het mogelijk om bij een lokaal vergevorderd pancreascarcinoom zonder metastasen een resectie te doen?

- Ja
- Nee

Impala studie AMC

Ann Surg Oncol
DOI 10.1245/s10434-017-5900-9

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – PANCREATIC TUMORS

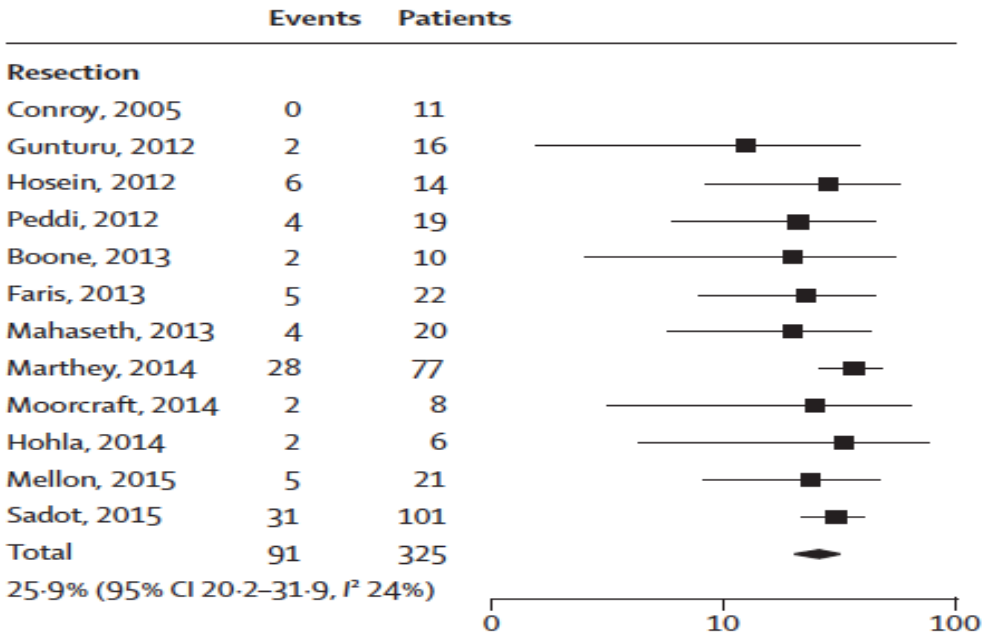
Induction Chemotherapy Followed by Resection or Irreversible Electroporation in Locally Advanced Pancreatic Cancer (IMPALA): A Prospective Cohort Study

Jantien A. Vogel, MD, MSc[1], Steffi J. Rombouts, MD[1], Thijs de Rooij, MSc[1], Otto M. van Delden, MD, PhD, Prof[2], Marcel G. Dijkgraaf, MSc, PhD[3], Thomas M. van Gulik, MD, PhD, Prof[1], Jeanin E. van Hooft, MD, PhD, MBA[4], Hanneke W. van Laarhoven, MD, PhD, Prof[5], Robert C. Martin, MD, PhD, Prof[6], Annuska Schoorlemmer, MSc[1], Johanna W. Wilmink, MD, PhD[5], Krijn P. van Lienden, MD, PhD[2], Olivier R. Busch, MD, PhD, Prof[1], and Marc G. Besselink, MD, MSc, PhD[1]

- 132 ptn met LAPC (sept 2013 - mrt 2015)
- Chemo 70% - hiervan 64% stabiele ziekte na 3 mnd
- 14 ptn resectie – overleving 34 mnd
- Alle ptn: overleving 11 mnd, stabiel na 3 mnd: 20mnd

Overleving resectie na folfirinox

Mediane overleving 34 vs. 15 maanden [2, 3]



Suker, Lancet Oncol 2017; [2] Ferrone, Ann Surg 2015; [3] Vogel, Ann Surg Oncol 2017

Studie uit Boston

FEATURE

Radiological and Surgical Implications of Neoadjuvant Treatment With FOLFIRINOX for Locally Advanced and Borderline Resectable Pancreatic Cancer

Cristina R. Ferrone, MD, Giovanni Marchegiani, MD,* Theodore S. Hong, MD,† David P. Ryan, MD,‡ Vikram Deshpande, MD,‡ Erin I. McDonnell,‡ Francesco Sabbatino, PhD,* Daniela Dias Santos, MD,* Jill N. Allen, MD,‡ Lawrence S. Blaszkowsky, MD,‡ Jeffrey W. Clark, MD,‡ Jason E. Faris, MD,‡ Lipika Goyal, MD,‡ Eunice L. Kwak, PhD,‡ Janet E. Murphy, MD,‡ David T. Ting, MD,‡ Jennifer Y. Wo, MD,† Andrew X. Zhu, PhD,‡ Andrew L. Warshaw, MD,* Keith D. Lillemoe, MD,* and Carlos Fernández-del Castillo, MD**

- 47 patiënten chirurgie na FOLFIRINOX: 40 resecties
- CA19.9 daalde gemiddeld van 169 naar 16
- Onafhankelijk chirurg vooraf: 26/40 niet resectabel
- Overleving mediaan 34 maanden

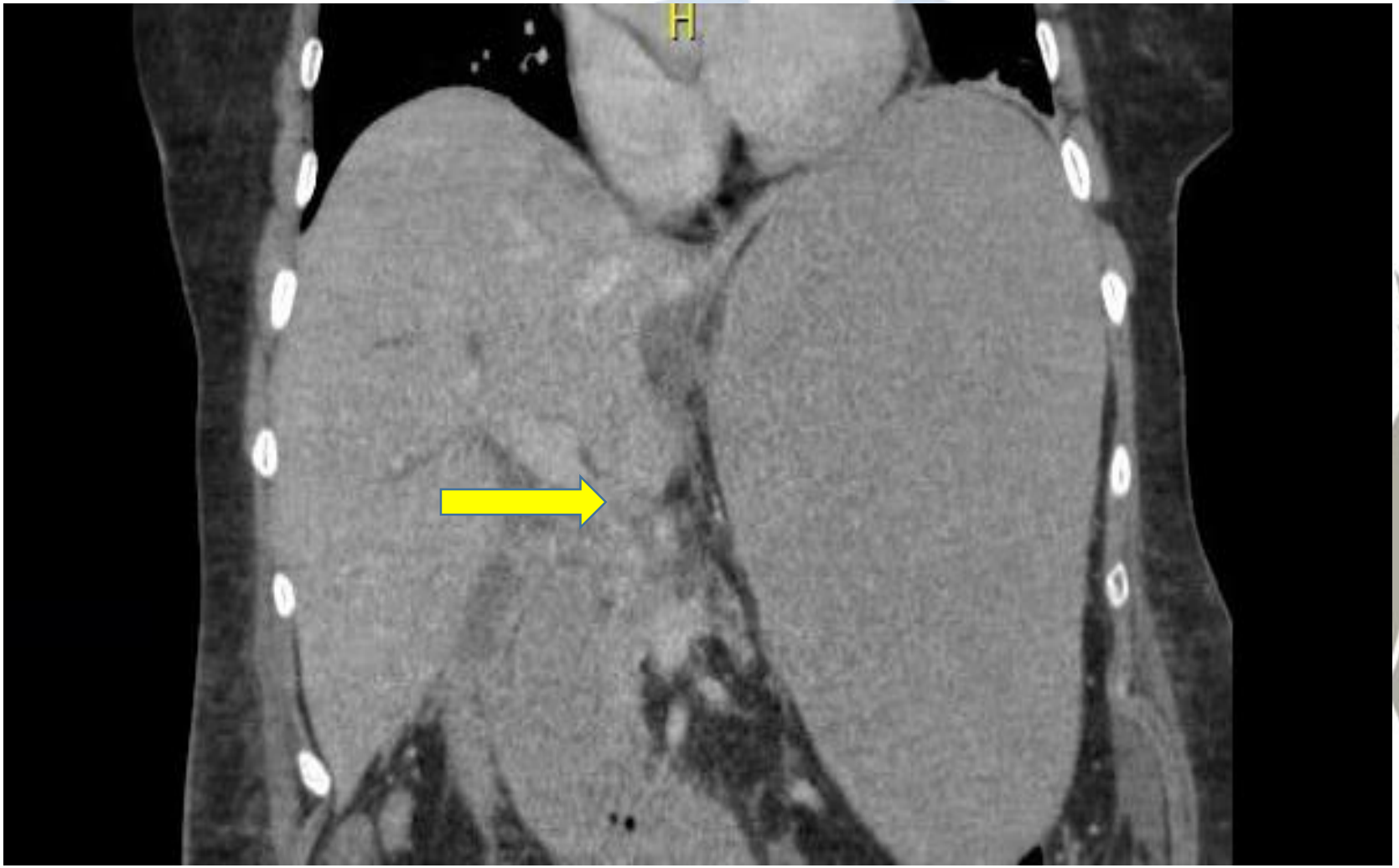
- 1Ferrone et al, Ann Surg 2014

Vraag 6

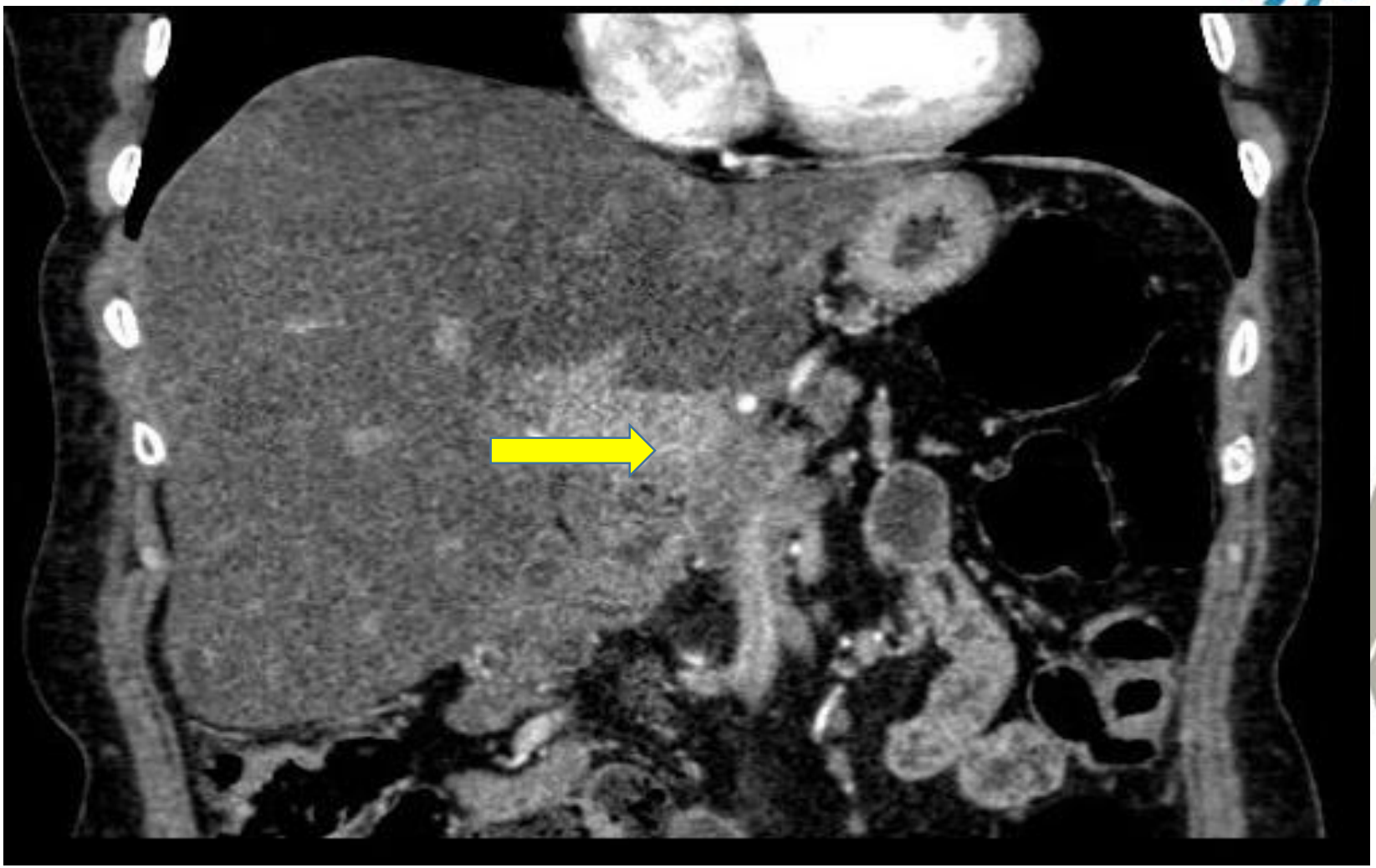
- Kun je met een CT scan het effect van FOLFIRINOX chemotherapie op pancreascarcinoom meestal goed inschatten?

- **Ja**, dat is prima in te schatten”
- **Nee**, meestal wordt effect onderschat”

Casus mw. M. 64 jaar



mw. M. na 2 maanden FOLFIRINOX



Wel of niet resectabel?

Beeldvorming na FOLFIRINOX

- CT niet langer betrouwbaar:
  - Onderscheid vitale tumor en fibrose niet mogelijk
  - Minderheid patiënten heeft radiologische regressie
- Exploratie in patiënten met stabiele ziekte
  - Echter 40-60% blijft niet-resectabel
  - Eventueel lokale behandeling mogelijk

Intra-operatieve echo

- Tijdens chirurgische exploratie nu standaard intraoperatieve
- Echo
- Geeft veel waardevolle informatie
- Soms alsnog resectie o.b.v. echo uitslag mogelijk

– Vaak kleiner deel vitale tumor dan gedacht

– Minder vaatbetrokkenheid

Vraag 7

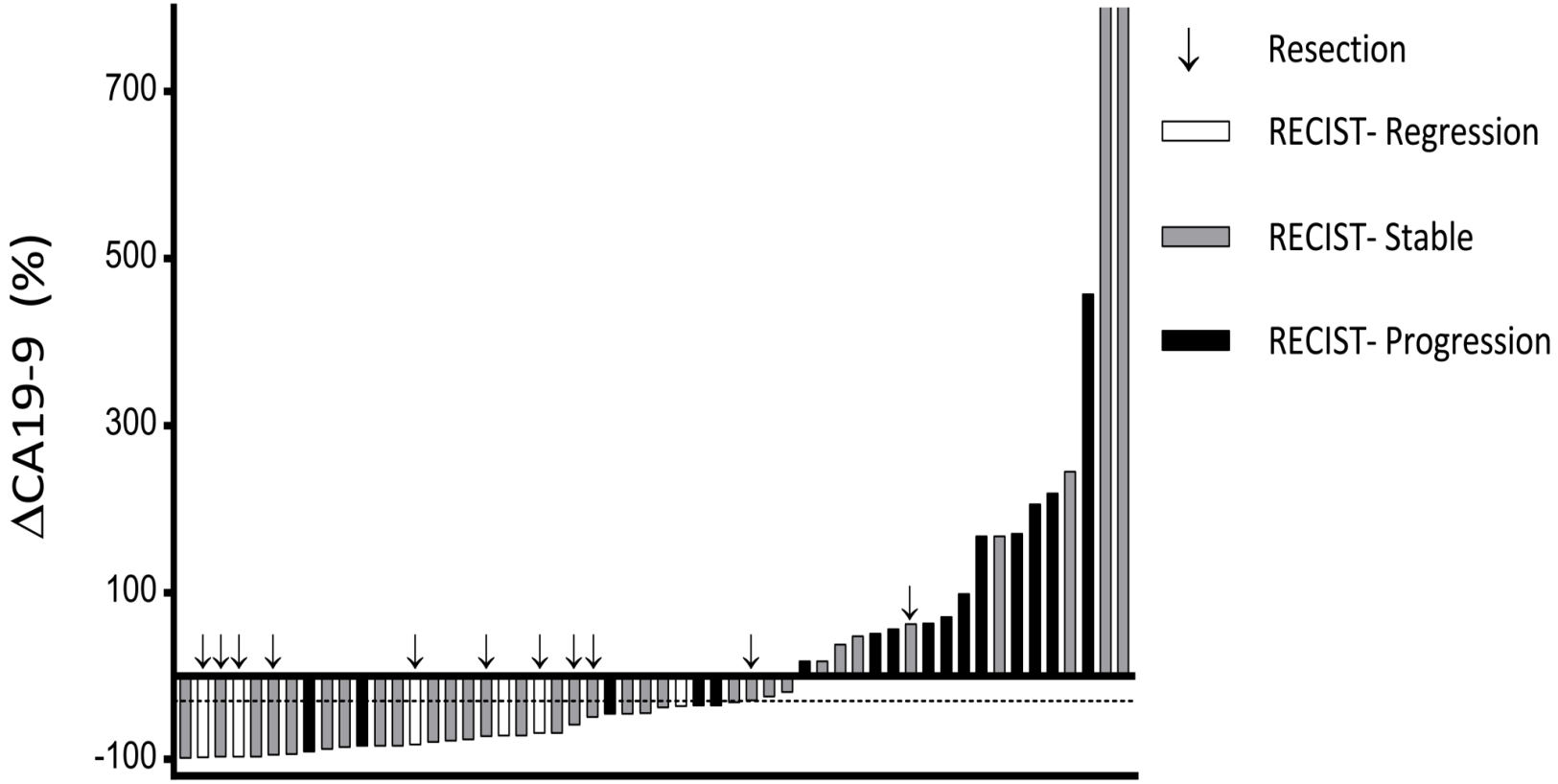
Na neo-adjuvant chemotherapie is het meten van CA 19.9 sensitief om in te schatten of een patient resectabel is?

Ja

Nee

CA19-9 tumormarker (Impala studie).

30% daling in CA19.9: 91% sensitief voor resectie



Van Veldhuisen, HPB 2018

Concluderend

- 25% lokaal gevorderd pancreascarcinoom toch resectie na FOLFIRINOX mogelijk

Ca 50% van de patiënten met stabiele ziekte na FOLFIRINOX

- Overleving na resectie veelbelovend
- CT niet betrouwbaar voor resectabiliteit na chemo

– Intraoperatieve Echo

– CA19.9 = sensitief

Casus mevr W

- Patiënt 60 jaar
- Resectie gehad bij pancreascarcinoom
- Officiële diagnose
- Als gevolg van operatie klachten van

- Diarree en
- DM 2
- Gewichtsverlies
- Dumping syndroom
- psychische belasting

- Maart 2018 metastasen

Vergelijking omgaan met diabetes bij pancreatectomie versus pancreaduodenotectomie

The Comparison of Diabetes Associated Distress and Self-care Activities in Pancreatic Cancer Patients after Total Pancreatectomy and Pancreaticoduodenectomy: A Propensity Score-matched Analysis

Hsuan-Ju Kuo[1]; Yu-Wen Tien[2]; Shiow-Ching Shun[1]

[1]School of Nursing, College of Medicine, National Taiwan University, Taipei, Taiwan; [2]Department of Surgery, College of Medicine, National Taiwan University and Hospital, Taipei, Taiwan.

Purpose

Total pancreatectomy (TP) was introduced to avoid the complications of pancreaticoduodenectomy (PD). The performance of TP was increasing due to better diagnostic techniques, and more patients with diffused pancreatic disease were identified. However, diabetes resulted from TP was a major concern for patients and healthcare providers. The impact of diabetes for patients after TP was seldom explored. Therefore, the purpose of this study was to (1) compare diabetes associated distress and self-care activities between patients after TP and PD, and (2) explore the associated factors for self-care activities in the overall population.

Methods

The conceptual framework of the study is shown in **Figure 1**. A cross-sectional approach was used. The data was collected via purposive sampling of 50 subjects in an outpatient pancreatic surgical department. The Summary of Diabetes Self-care Activities (SDSCA) questionnaire was used to measure self-care activities. Diabetes associated distress was measured based on patients' perceived diabetes treatment interference and diabetes symptom distress on a scale of 0 to 10 (0 meaning no interference/ distress; 10 meaning worst interference/ distress). The data went through propensity score 1:2 matching. The balance of the matched set was examined by standard mean difference **(Table 1)** and the propensity score distribution dot plot (**Figure** 2). Mann-Whitney U Test, Chi-squared Test, and Generalized Estimating Equation (GEE) were used.

Results

- There were no statistical significant difference in diabetes treatment interference, diabetes symptom distress, and overall self-care activities between the groups (**Table** 2).
- TP group reported less days in a week of consuming at least 5 servings of fruits and vegetables than PD group ($p<.001$; **Table** 2).
- The significant associated factor with self-care activities was marital status. Patients who were married ($\beta=1.326$, $p=.008$) reported more frequent self-care activities per week than patients who were not (**Table 3**).

Discussion and implications

The present study suggested that nurses should evaluate the frequency and servings of vegetables and fruits consumed in patients after TP. We observed that patients after TP would avoid fruits due to their fear of hyperglycemia. In addition, nurses should pay extra attention to those who were not married, since they may have less family support to complete daily self-care activities. Further research with larger sample size should be done to examine self-care activities among both groups and intervention should also be developed accordingly.

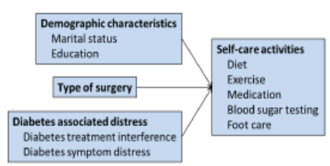


Figure 1. Conceptual framework of the study

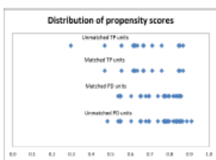


Figure 2. Distribution of propensity scores after matching

Table 1. Demographic and clinical disease characteristics of all patients and the propensity score-matched subset of patients[a]

Variables	All patients (n=50)			Matched set (n=39)		
	TP[b] (n=14)	PD[c] (n=36)	SMD[d]	TP[b] (n=13)	PD[c] (n=26)	SMD[d]
Age, years	62.1±10.2	67.5±12.2	**0.49**	63.8±8.3	66.4±12.1	0.25
Education, years	11.3±4.3	9.5±4.3	**0.43**	10.9±4.2	9.5±4.7	0.16
Gender			0.22			0.08
Male	8 (57.1)	17 (47.2)		7 (53.8)	13 (50.0)	
Female	6 (42.9)	19 (52.8)		6 (46.2)	13 (50.0)	
Marital status			**0.32**			0.16
Married	10 (71.4)	21 (58.3)		9 (69.2)	16 (61.5)	
Single/divorce/widow	4 (28.6)	15 (41.7)		4 (30.8)	10 (38.5)	
Postoperative time, months	3.9±3.3	19.2±18.1	**1.18**	3.4±4.0	20.3±19.4	**1.21**
BMI[e]	21.1±2.1	22.5±3.5	**0.49**	21.1±2.2	22.7±3.6	0.25
Number of comorbidities	2.1±1.2	2.5±1.0	**0.29**	2.2±1.2	2.5±0.9	0.11
DM[h] duration, months	43.6±15.5	61.3±55.0	**0.44**	46.9±24.6	44.4±28.9	0.09
HbA1C	7.9±1.9	7.1±1.2	**0.50**	8.0±1.9	7.1±1.1	**0.30**
KPS[i]	76.4±6.3	76.9±9.2	0.06	76.9±6.3	76.9±8.4	<0.01
Diagnosis			0.14			0.24
PDAC[j]	10 (71.4)	23 (63.9)		10 (76.9)	17 (65.4)	
NET[k]	0 (0.0)	2 (5.6)		0 (0.0)	2 (7.7)	
IPMN[l]	3 (21.4)	6 (16.7)		2 (15.4)	3 (11.5)	
Chronic pancreatitis	1 (7.1)	5 (13.9)		1 (7.7)	4 (15.4)	
Cancer stage			0.19			0.18
Benign	3 (21.4)	9 (25.0)		3 (23.1)	6 (23.1)	
I	1 (7.1)	7 (19.4)		1 (7.7)	6 (23.1)	
II	9 (64.3)	17 (47.2)		8 (61.5)	12 (46.2)	
III	0 (0.0)	2 (5.6)		0 (0.0)	1 (3.8)	
IV	1 (7.1)	1 (2.8)		1 (7.7)	1 (3.8)	
DM[h] treatment			**0.98**			**1.70**
OHA[m]	0 (0.0)	27 (75.0)		0 (0.0)	22 (84.6)	
Insulin	13 (92.9)	3 (8.3)		12 (92.3)	2 (7.7)	
OHA[m]+insulin	1 (7.1)	6 (16.7)		1 (7.7)	2 (7.7)	

[a]The data are presented as mean ± standard deviation or number (%). [b]TP: Total Pancreatectomy. [c]PD: Pancreaticoduodenectomy. [d]SMD: standard mean difference > 0.25 was the indicator for imbalance of the two groups. [g]BMI: body mass index. [h]DM: diabetes mellitus. [i]KPS: Karnofsky Performance Scale. [j]PDAC: pancreatic ductal adenocarcinoma. [k]NET: neuroendocrine tumor. [l]IPMN: intraductal papillary mucinous neoplasm. [m]OHA: oral hypoglycemic agents.

Table 2. Matched-pairs analysis of self-care activities, diabetes treatment interference, and diabetes symptom distress after propensity score matching

Items	TP[a] (n=13) Mean	TP[a] SD	PD[b] (n=26) Mean	PD[b] SD	p-value[c]
The summary of diabetes self-care activities (SDSCA)	4.61	1.57	4.25	1.63	.790
Diet	5.81	1.35	6.21	1.12	.201
1. On how many of the last seven days did you eat five or more servings of fruits and vegetables	5.00	2.61	6.38	1.63	**<.001**
2. On how many of the last seven days did you not eat high fat foods	6.62	0.96	6.04	1.46	.241
Exercise	3.19	3.03	4.31	2.81	.695
3. On how many of the last seven days did you participate in at least 30 minutes of physical activity	3.08	3.35	4.58	2.85	.426
4. On how many of the last seven days did you participate in a specific exercise session other than what you do around the house or as part of your work	3.31	3.25	4.04	3.00	.944
Medications					
5. On how many of the last seven days did you take your recommended diabetes medication	6.77	0.83	6.77	0.82	.291
Blood sugar testing					
6. On how many of the last seven days did you test your blood sugar	7.00	0.00	2.88	3.06	.311
Foot care	3.23	3.63	2.53	3.23	.962
7. On how many of the last seven days did you check your feet	3.23	3.63	2.46	3.37	.905
8. On how many of the last seven days did you inspect the inside of your shoes	3.23	3.63	2.42	3.40	.722
9. On how many of the last seven days did you dry your feet after bathing	3.23	3.63	2.69	3.47	.894
Diabetes treatment interference	4.54	3.26	1.67	2.74	.421
Diabetes symptom distress	3.62	3.12	1.73	2.66	.398

[a]TP: Total Pancreatectomy. [b]PD: Pancreaticoduodenectomy. [c]p value was examined by generalized estimating equation based on exchangeable working correlation with adjustment of post operation in months, HbA1C and current treatment of diabetes to compare the two groups; the reference group was PD.

Table 3. Exploring the associated factors among demographic and clinical characteristics, diabetes treatment interference, and diabetes symptom distress for self-care activities in the generalized estimating equations analysis[a] (N=39)

Variables	*Coefficient*	*Std. Err.*	*Wald chi-square*	*p-value*
Total Pancreatectomy/ PD[b]	-.327	.946	.119	.730
Insulin/ OHA[c]	-.561	1.241	.204	.651
OHA[c] & insulin/ OHA[c]	1.383	.724	3.654	.056
Married/ Single or divorced or widowed	1.326	.499	7.068	**.008**
Education in years	.074	.050	2.201	.138
Diabetes treatment interference	-.023	.087	.069	.792
Diabetes symptom distress	.009	.079	.013	.911
HbA1C%	-.035	.167	.044	.834
Postoperative time in months	-.022	.016	2.063	.151
Intercept	4.847	1.882	6.635	.010

[a]Generalized estimating equation was based on exchangeable working correlation matrix with adjustment of HbA1C, postoperative time in months, and current treatment of diabetes. [b]PD: Pancreaticoduodenectomy. [c]OHA: oral hypoglycemic agents.

References

Adamina, M., Guller, U., Weber, W. P., & Oertli, D. (2006). Propensity scores and the surgeon. *British Journal Surgery, 93*(4), 389-394. doi:10.1002/bjs.5265
Barbier, L., Jamal, W., Dokmak, S., Aussilhou, B., Corcos, O., Ruszniewski, P., . . . Sauvanet, A. (2013). Impact of total pancreatectomy: short- and long-term assessment. *The Journal of the International Hepato Pancreato Biliary Association (Oxford), 15*(11), 882-892. doi:10.1111/hpb.12054
Casadei, R., Ricci, C., Taffurelli, G., Guariniello, A., Di Gioia, A., Di Marco, M., . . . Minni, F. (2016). Is total pancreatectomy as feasible, safe, efficacious, and cost-effective as pancreaticoduodenectomy? A single center, prospective, observational study. *Journal of Gastrointestinal Surgery, 20*(9), 1595-1607. doi:10.1007/s11605-016-3201-4
Cui, Y., & Andersen, D. K. (2011). Pancreatogenic diabetes: special considerations for management. *Pancreatology, 11*(3), 279-294. doi:10.1159/000329188
Maeda, H., & Hanazaki, K. (2011). Pancreatogenic diabetes after pancreatic resection. *Pancreatology,* 11(2), 268-276. doi:10.1159/000328785
Toobert, D. J., Hampson, H.E., & Glasgow, R.E. (2000). The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. *Diabetes Care, 23*, 943-950.

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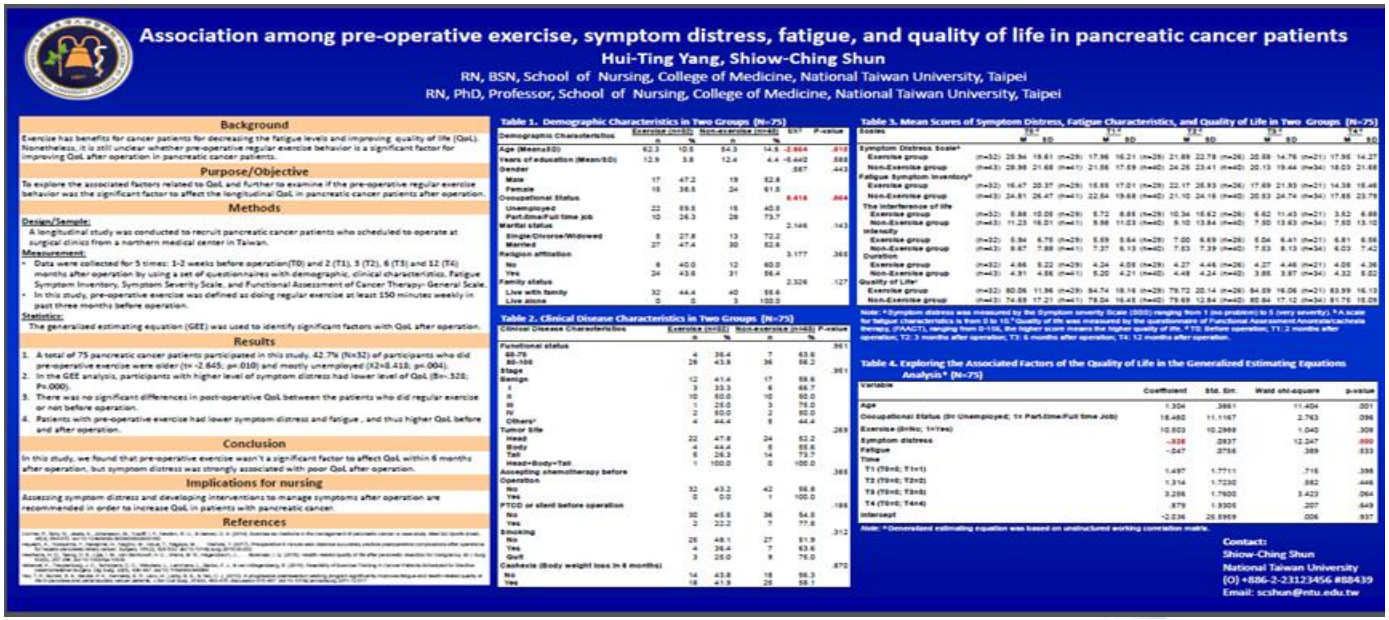
Fysieke training preoperatief



Association among pre-operative exercise, symptom distress, fatigue, and quality of life in pancreatic cancer patients

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RN, PhD, Professor, School of Nursing, College of Medicine, National Taiwan University, Taipei

Background

Exercise has benefits for cancer patients for decreasing the fatigue levels and improving quality of life (QoL). Nonetheless, it is still unclear whether pre-operative regular exercise behavior is a significant factor for improving QoL after operation in pancreatic cancer patients.

Purpose/Objective

To explore the associated factors related to QoL and further to examine if the pre-operative regular exercise behavior was the significant factor to affect the long-tudinal QoL in pancreatic cancer patients after operation.

Methods

Design/Sample:
A longitudinal study was conducted to recruit pancreatic cancer patients who scheduled to operate at surgical clinics from a northern medical center in Taiwan.

Measurement:
- Data were collected for 5 times: 1-2 weeks before operation(T0) and 2 (T1), 3 (T2), 6 (T3) and 12 (T4) months after operation by using a set of questionnaires with demographic, clinical characteristics, Fatigue Symptom Inventory, Symptom Severity Scale, and Functional Assessment of Cancer Therapy- General Scale.
- In this study, pre-operative exercise was defined as doing regular exercise at least 150 minutes weekly in past three months before operation.

Statistics:
The generalized estimating equation (GEE) was used to identify significant factors with QoL after operation.

Results

1. A total of 75 pancreatic cancer patients participated in this study. 42.7% (N=32) of participants who did pre-operative exercise were older (t= -2.645; p=.010) and mostly unemployed (X2=8.418; p=.004).
2. In the GEE analysis, participants with higher level of symptom distress had lower level of QoL (B=-.328; P=.000).
3. There was no significant differences in post-operative QoL between the patients who did regular exercise or not before operation.
4. Patients with pre-operative exercise had lower symptom distress and fatigue , and thus higher QoL before and after operation.

Conclusion

In this study, we found that pre-operative exercise wasn't a significant factor to affect QoL within 6 months after operation, but symptom distress was strongly associated with poor QoL after operation.

Implications for nursing

Assessing symptom distress and developing interventions to manage symptoms after operation are recommended in order to increase QoL in patients with pancreatic cancer.

References

Table 1. Demographic Characteristics in Two Groups (N=75)

Demographic Characteristics	Exercise (n=32)		Non-exercise (n=43)		t/χ²	P-value
	n	%	n	%		
Age (Mean±SD)	62.3	10.6	64.3	14.8	-2.664	.010
Years of education (Mean/SD)	12.9	3.8	12.4	4.4	-0.440	.588
Gender					.567	.443
Male	17	47.2	19	52.8		
Female	15	38.5	24	61.5		
Occupational Status					8.418	.004
Unemployed	22	59.5	15	40.5		
Part-time/Full time job	10	26.3	28	73.7		
Marital status					2.146	.143
Single/Divorce/Widowed	8	27.6	13	72.2		
Married	27	47.4	30	52.6		
Religion affiliation					3.177	.365
No	8	40.0	12	60.0		
Yes	24	43.6	31	56.4		
Family status					2.326	.127
Live with family	32	44.4	40	55.6		
Live alone	0	0	3	100.0		

Table 2. Clinical Disease Characteristics in Two Groups (N=75)

Clinical Disease Characteristics	Exercise (n=32)		Non-exercise (n=43)		P-value
	n	%	n	%	
Functional status					.961
60-70	4	36.4	7	63.6	
80-100	28	43.8	36	56.2	
Stage					.991
Benign	12	41.4	17	58.6	
I	3	33.3	6	66.7	
II	10	50.0	10	50.0	
III	1	25.0	3	75.0	
IV	2	50.0	2	50.0	
Others*	4	44.4	5	44.4	
Tumor Site					.269
Head	22	47.8	24	52.2	
Body	4	44.4	5	55.6	
Tail	5	26.3	14	73.7	
Head+Body+Tail	1	100.0	0	100.0	
Accepting chemotherapy before					.365
Operation					
No	32	43.2	42	56.8	
Yes	0	0.0	1	100.0	
PTCD or stent before operation					.185
No	30	45.5	36	54.5	
Yes	2	22.2	7	77.8	
Smoking					.312
No	28	48.1	27	51.9	
Yes	4	36.4	7	63.6	
Quit	3	25.0	9	75.0	
Cachexia (Body weight loss in 6 months)					.870
No	14	43.8	18	56.3	
Yes	18	41.9	25	58.1	

Table 3. Mean Scores of Symptom Distress, Fatigue Characteristics, and Quality of Life in Two Groups (N=75)

Scales	T0		T1		T2		T3		T4	
	M	SD	M	SD	M	SD	M	SD	M	SD
Symptom Distress Scale*										
Exercise group	(n=32) 20.94	19.61	(n=29) 17.96	16.21	(n=28) 21.89	22.78	(n=26) 20.88	14.76	(n=21) 17.95	14.27
Non-Exercise group	(n=43) 28.98	21.68	(n=41) 21.86	17.69	(n=40) 24.26	23.41	(n=40) 20.13	19.44	(n=34) 18.03	21.68
Fatigue Symptom Inventory*										
Exercise group	(n=32) 16.47	20.37	(n=29) 15.55	17.01	(n=29) 22.17	26.93	(n=26) 17.69	21.93	(n=21) 14.38	16.46
Non-Exercise group	(n=43) 24.81	26.47	(n=41) 22.64	19.68	(n=40) 21.10	24.16	(n=40) 20.63	24.74	(n=34) 17.65	23.79
The interference of life										
Exercise group	(n=32) 8.88	10.06	(n=29) 8.72	8.66	(n=29) 10.34	16.62	(n=26) 6.62	11.43	(n=21) 3.62	6.66
Non-Exercise group	(n=43) 11.23	16.01	(n=41) 9.66	11.03	(n=40) 9.10	13.64	(n=40) 7.50	13.63	(n=34) 7.50	13.10
Intensity										
Exercise group	(n=32) 5.94	6.76	(n=29) 5.69	5.64	(n=29) 7.00	6.69	(n=26) 5.04	6.41	(n=21) 6.81	6.06
Non-Exercise group	(n=43) 8.67	7.66	(n=41) 7.37	6.13	(n=40) 7.63	7.39	(n=40) 7.63	8.13	(n=34) 6.03	7.42
Duration										
Exercise group	(n=32) 4.66	5.22	(n=29) 4.24	4.08	(n=29) 4.27	4.46	(n=26) 4.27	4.46	(n=21) 4.05	4.36
Non-Exercise group	(n=43) 4.91	4.56	(n=41) 5.20	4.21	(n=40) 4.48	4.24	(n=40) 3.88	3.87	(n=34) 4.32	5.02
Quality of Life*										
Exercise group	(n=32) 80.06	11.96	(n=29) 84.74	10.14	(n=29) 79.72	20.14	(n=26) 84.59	16.06	(n=21) 83.99	16.13
Non-Exercise group	(n=43) 74.69	17.21	(n=41) 78.04	16.45	(n=40) 79.69	12.84	(n=40) 80.84	17.12	(n=34) 81.75	16.09

Note: *Symptom distress was measured by the Symptom severity Scale (SSS) ranging from 1 (no problem) to 5 (very severity). *A scale for fatigue characteristics is from 0 to 10.* Quality of life was measured by the questionnaire of Functional Assessment/Anorexia/cachexia therapy, (FAACT), ranging from 0-156, the higher score means the higher quality of life. *T0: Before operation; T1: 2 months after operation; T2: 3 months after operation; T3: 6 months after operation; T4: 12 months after operation.

Table 4. Exploring the Associated Factors of the Quality of Life in the Generalized Estimating Equations Analysis* (N=75)

Variable	Coefficient	Std. Err.	Wald chi-square	p-value
Age	1.304	.3961	11.404	.001
Occupational Status (0= Unemployed; 1= Part-time/Full time Job)	18.480	11.1167	2.763	.096
Exercise (0=No; 1=Yes)	10.503	10.2969	1.040	.308
Symptom distress	-.328	.2837	12.247	.000
Fatigue	-.047	.2756	.389	.533
Time				
T1 (T0=0; T1=1)	1.497	1.7711	.716	.398
T2 (T0=0; T2=2)	1.314	1.7230	.582	.446
T3 (T0=0; T3=3)	3.256	1.7600	3.423	.064
T4 (T0=0; T4=4)	.879	1.9305	.207	.649
Intercept	-2.036	26.5959	.006	.937

Note: *Generalized estimating equation was based on unstructured working correlation matrix.

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- Conclusie = hogere score op distress is lagere kwaliteit van leven
- Geen verschil in kwaliteit van leven tussen patiënten die niet of normaal bewogen
- Een hogere kwaliteit van leven bij patienten die een bewegingsprogramma volgde zowel pre als postoperatief vn op vermoeidheid en distress.

Vraag 8

- Aanvullende voeding postoperatief verminderd de kans op ontsteking.

- Ja
- Nee

Rol van voeding na pancreatectomie

- Het gebruik van immunomodulerende voeding wordt geadviseerd omdat het de immuun status van de postoperatieve patiënt zou verbeteren en de ontstekingsreactie als gevolg van de ingreep zou verminderen. Zodoende zou het postoperatieve beloop positief beïnvloed worden.

- De meest bestudeerde immunonutriënten zijn arginine, glutamine, omega-3-meervoudig onverzadigde vetzuren en nucleotiden

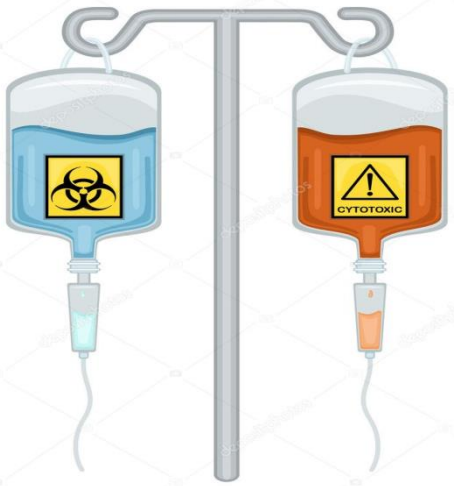
Casus dhr B

- Man 67 jaar
- Sinds ongeveer 3 maanden erge buikpijn. Rondom de navel, straalt met name naar de rug uit. Neemt af bij het bewegen. Bij pittig eten wordt de pijn erger.
- De eetlust is afgenomen. Hij eet licht verteerbaar eten maar wel erg minimaal.
- Het ontlastingspatroon is niet veranderd, wel was de ontlasting iets lichter. Mictie donker.
- CA 19.9 230 kU/l
- Patiënt wil niet starten met chemotherapie.


THUIS STERVEN? IK GELOOF DAT JE NU ECHT ZIEK BENT
STEFAN VERVEY

Palliatieve behandelingen chemotherapie

- Folfirinox
- Gemcitabine mono therapie
- Nab-paclitaxel met gemcitabine



Vraag 9

Is het goed om vitamine- en mineralen pillen te slikken of anti-oxidanten als je chemotherapie krijgt?

- Ja
- Nee

Supplementen

- Baadt het niet – schaadt het niet geldt hierbij niet!
- Hoog gedoseerde supplementen kunnen de werking van bestraling en chemotherapie tegengaan
- Supplementen kunnen gewone voeding niet vervangen
- Alleen bij tekorten in de voeding

Vraag 10

- Is kurkuma effectief bij de behandeling van (alvleesklier) kanker?

- Ja
- Nee

Kurkuma

- Kurkuma (curcumine) = werkzame stof
- Onderzoek in tumorcellen en proefdieren curcumine lijkt de groei van kankercellen te kunnen remmen
- Hoge doseringen (6-8 gram per dag)
- Alleen effect als het in zijn geheel in de bloedbaan komt
- Curcumine wordt in menselijk lichaam snel inactief gemaakt in de darm en door de lever afgebroken

(Bron dr Michael Heger, AMC)

Vraag 10

- Help vasten voor een beter effect van de chemotherapie?

- Ja
- Nee

Vasten bij chemotherapie

Theorie; tumorcellen zouden door vasten kwetsbaarder worden

•Onderzoek met muizen

-minder bijwerkingen chemotherapie

-remming tumorgroei

Onderzoek bij mensen is gestart

nog geen resultaten bekend

- Bij ouderen en bij patiënten met een slechte voedingstoestand vasten extra ongunstig voor slechte conditie

(www.voedingen kankerinfo.nl)

Vraag 11

- Pancreassuppletie helpt bij klachten van diarree zowel post operatief als in de palliatieve fase.

- Ja
- Nee

Pancreas enzymen

Pancreasinsufficientie door:

- Minder verteringssappen
- Meer vet in dunne darm -> diarree-> minder tijd voor opname
- Pancreas maakt basis sap om maagzuur te neutraliseren

Behandeling

- Enzymsuppletie (25-75.000 units per maaltijd en 10-20.00/snack).
- Dosering 1-1-2 of 2-2-4 capsules (6-12 capsules per dag)
- Bij de eerste hap en halverwege
- Schriftelijke informatie of enzymen app of site www.enzymgebruik.nl

Vraag 12

- Een pancreascarcinoom geeft vooral noceceptieve pijn.

- Ja
- Nee

Vraag 13

- Methadon is effectiever dan een plexus coeliacus blokkade.

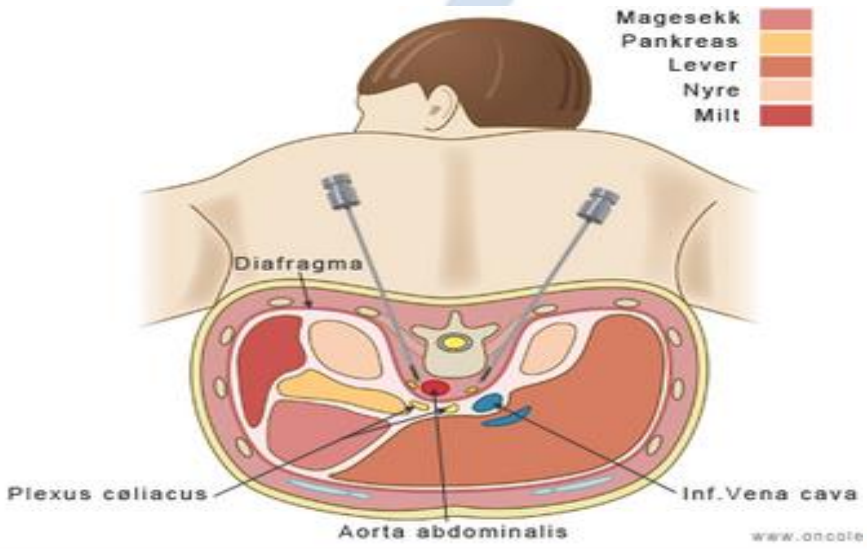
- Ja
- Nee

Pijn bij pancreascarcinoom

- Pancreastumor ->een zenuw of het ruggenmerg drukt, of daarin groeit,
- Spreken we van zenuwpijn of neuropatische pijn.

Behandeling pijn bij pancreascarcinoom

De plexus coeliacus is een netwerk van zenuwen aan de achterzijde in de bovenbuiksholte. Bij een plexus coeliacus blokkade zet de arts via een naald een elektrisch stroompje op de zenuwbanen. Hierdoor kunnen de zenuwen geen pijnsignalen meer doorgeven aan de hersenen.



Methadon

Lange en variabele halfwaarde tijd:

steady state na 5 – 7 dagen

- -Groot verdelingsvolume na 1 gift 1% in plasma **CAVE OVERDOSERING**
- Kans op cumulatie en overdosering
- Start dosering 3 x dgs 5 mg, na 3 a 4 dagen 2 x dgs 5 mg

Studies

Vele kleine studies en case series met + effect

(Manfredi 1997, Lawlor 1998, Mercadante 1999, Mancini 2000, Ripamonti 2002, Moryl 2005, Benitez-Rosario 2009)

- Cochrane review pijn bij kanker (2007):

effectiviteit methadon = morfine (9 RCT's)

- 2 reviews: switching opioid → methadon:

>50% + effect

rotatie voor studie:

- Moryl 2002: 13 ptn methadon → opioid: 12 terug (pijn en bijwerkingen)
- Cubero 2010: 50 ptn morfine → methadon: 71% voorkeur -> methadon

Cave Psychische belasting

Angst, boosheid, frustratie, irritatie, machteloosheid, paniek, radeloosheid, schaamte, somberheid, verbijstering, verdriet, wanhoop, wantrouwen.

Onderzoek naar de relatie tussen sociale, familiaire en persoonlijke karakteristieken in relatie met psychosociale uitkomsten zoals distress.

DANA-FARBER CANCER INSTITUTE

Psychosocial outcomes of individuals with inherited pancreatic cancer risk

Meghan Underhill-Blazey PhD, APRN, AOCNS ®[1]; Janette Lawrence, CGC[2]; Traci Blonquist, MS[1]; Fangxin Hong, PhD[1]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Massachusetts General Hospital, Boston, MA

HARVARD MEDICAL SCHOOL

BACKGROUND

- Pancreatic cancer is now recognized as a component tumor within hereditary cancer predisposition syndromes
- Lifetime risks within these syndromes range from 3.6-40%
- Little is known about the patient experience living with inherited risk for pancreatic cancer
- Through qualitative research we found that family characteristics shaped the personal experience of living with risk

PURPOSE

Explore relationships between participant self-reported personal or familial characteristics (age, gender, highest level of education, marital status, personal and family history of cancer and cancer-related death, experience as a family caregiver, and social support) and psychosocial outcomes (global health, pancreatic cancer risk related distress, cancer risk perception and cancer worry) in participants at high risk for inherited or familial pancreatic cancer.

METHODS AND MEASURES

- Guided by Health Belief Model, Theory of Genetic Vulnerability, and preliminary qualitative data
- Multi-site survey study using a tailored online and paper survey method
- Sample
  - Participants were recruited through two large academic medical centers in the Northeastern United States from January 2016 through January 2017
  - Eligible participants were adults without a diagnosis of pancreatic cancer who had been evaluated by a genetic counselor and determined to have hereditary or familial pancreatic cancer risk and were offered pancreatic surveillance by a physician
- Self-reported measures
  - Cancer history, family caregiver experience, gender, marital status, household income.
  - Outcome variables: Cancer Worry, Pancreatic cancer risk distress (Impact of Event Scale), Risk Perception, Patient Reported Outcome Measures (PROMIS) Social support and overall global health
- Medical Record Data Collection
  - Race, ethnicity, age

ANALYSIS

- Personal and family characteristics and outcome measures were summarized with descriptive statistics
- Univariate associations were assessed with a t-test for continuous variables and with Chi-square test/Fisher's exact test for categorical variables
- Variables with $p<0.1$ were retained for multivariable analysis

RESULTS

- N=132 (response rate 71.5%); 67.4% were female and 91.7% white with some college education or more; 47.6% had a personal history of cancer; 66.7% lost a family member to cancer and of those 33% were pancreatic, 52% lost a family member to cancer <5years ago

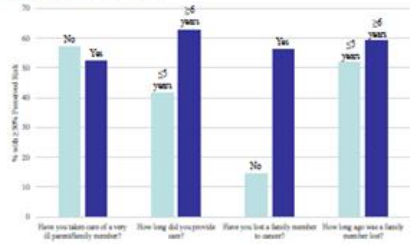


Figure 1. Cases with ≥ 50% Perceived Cancer Risk Based on Caregiver Experience

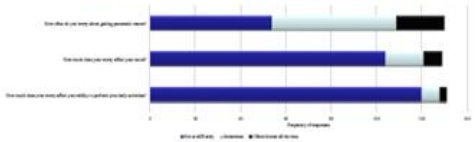


Figure 2. Frequency and impact of Cancer Worry (N=132)

RESULTS, cont.

Table 1. Univariate analysis of associations between personal and familial characteristics and psychosocial outcomes

	IES-R Total M (SD)	Global Health: Mental M (SD)	Global Health: Physical M (SD)
Have you had cancer?			
No	8.29 (12.79)	49.73 (10.12)	54.42 (5.06)
Yes	11.31 (16.16)	49.46 (11.30)	52.06 (5.56)
Gender			
Male	5.96 (7.81)	51.63 (9.75)	53.36 (5.88)
Female	11.37 (16.58)	48.53 (11.03)	53.21 (5.03)
Age			
<50	9.25 (14.25)	47.23 (12.64)	52.34 (5.71)
≥50	9.94 (14.71)	50.52 (9.69)	53.55 (5.24)
Marital Status			
Married/Partnered	8.53 (13.18)	51.75 (10.27)	54.49 (7.76)
All other	12.27 (17.27)	44.11 (9.87)	49.95 (8.96)
Highest Level of Education			
High school degree or lower	17.22 (15.81)	38.66 (10.50)	45.81 (9.72)
Some college or higher	8.59 (14.27)	50.51 (10.21)	53.84 (6.87)
Have you taken care of a very ill parent or close family member?			
No	7.48 (10.44)	49.06 (10.35)	49.50 (8.93)
Yes	10.81 (16.04)	49.88 (10.77)	54.78 (7.68)
How long ago did you provide this care?			
≤5 years	15.0 (19.09)	50.5 (10.02)	55.72 (7.08)
≥6 years	5.51 (9.21)	49.93 (10.87)	54.30 (7.80)
Have you lost a family member to cancer?			
No	6.67 (11.24)	54.23 (7.02)	54.88 (7.75)
Yes	9.90 (14.69)	49.13 (10.79)	53.20 (5.41)
How long ago did you lost a family member to pancreatic cancer?			
≤5 years	10.71 (16.34)	48.21 (10.98)	53.17 (8.02)
≥6 years	9.15 (13.25)	50.25 (10.73)	53.21 (5.87)

Note: test in bold was statistically significant at $p<.05$ in univariate analysis; Household income was not included due to amount of missing data attributed to a response item "prefer not to answer"

DISCUSSION AND IMPLICATIONS

- Individuals with inherited or familial pancreatic cancer risk experience cancer worry, distress, and have increased risk perceptions, specifically in the period following caring for a loved one with cancer
- Routine evaluation of distress in this setting, as well as the development of supportive care resources, will help support patients living with risk for pancreatic cancer
- Findings shed light on the needs of an understudied and vulnerable population. The study implications are focused on person-centered care within the context of personalized medicine

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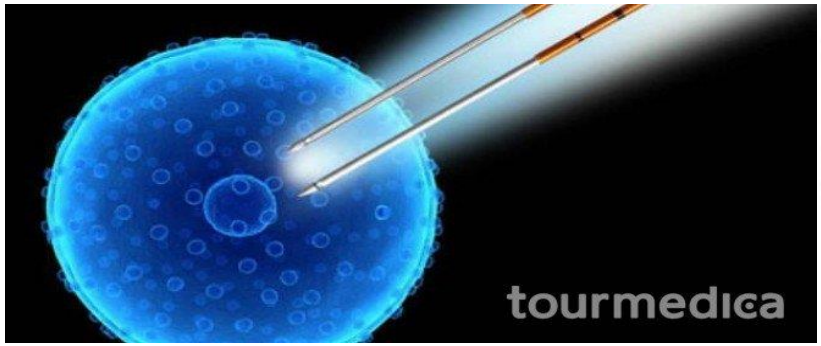
Nieuwe ontwikkelingen palliatief 1

- Nanoknife bij recidief en lokaal gemetastaseerd pancreasca pancreasca.
- Met de beeldgestuurde kankertherapie Irreversibele elektroporatie (IRE), ofwel nanoknife, vernietigen elektrische stroomstootjes de tumorcellen.
- Pancreascarcinoom kan tijdelijk worden afgeremd.



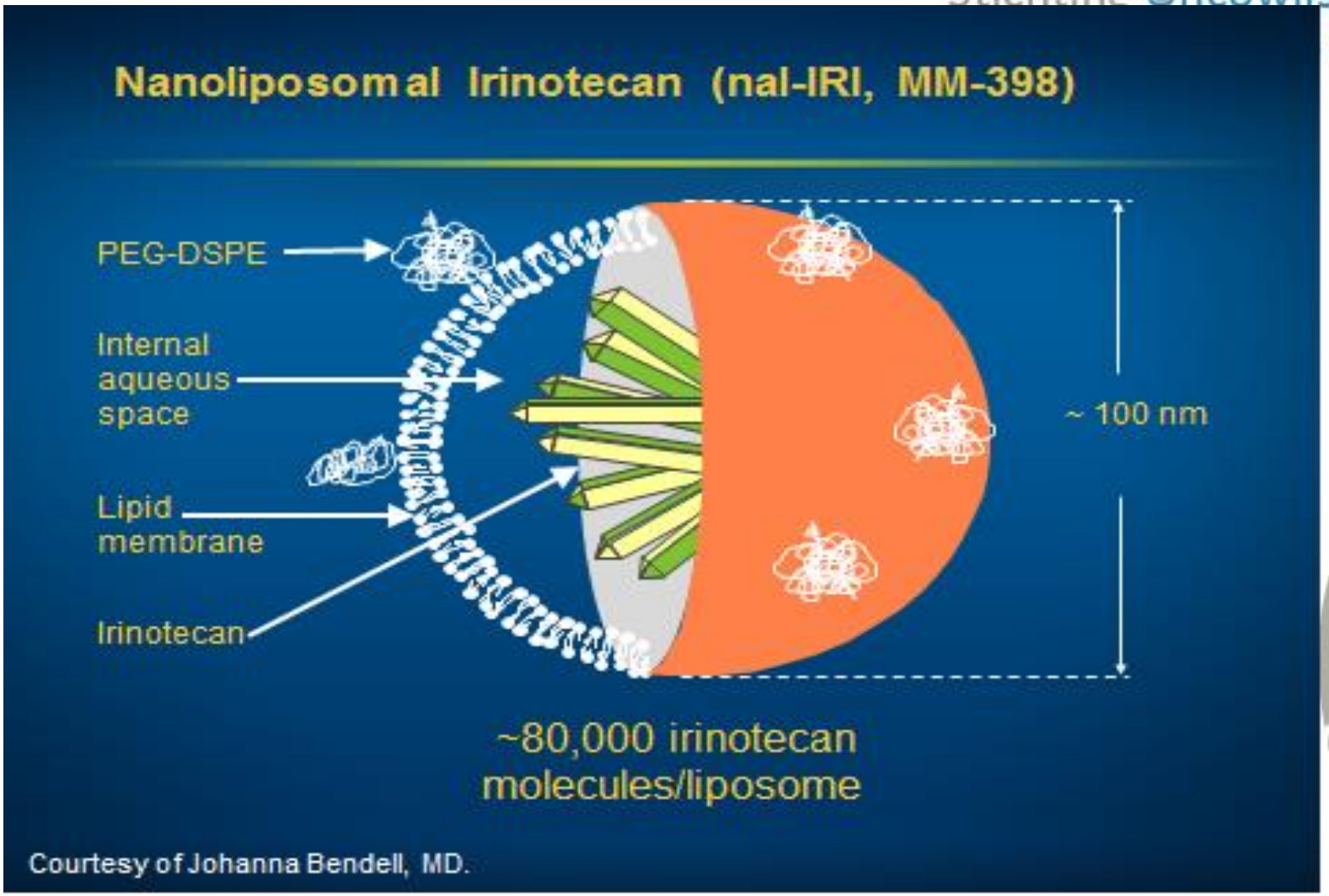
Hester Scheffer*Lightning strikes' – irreversible electroporation in interventional oncology*

Nieuwe ontwikkelingen palliatief

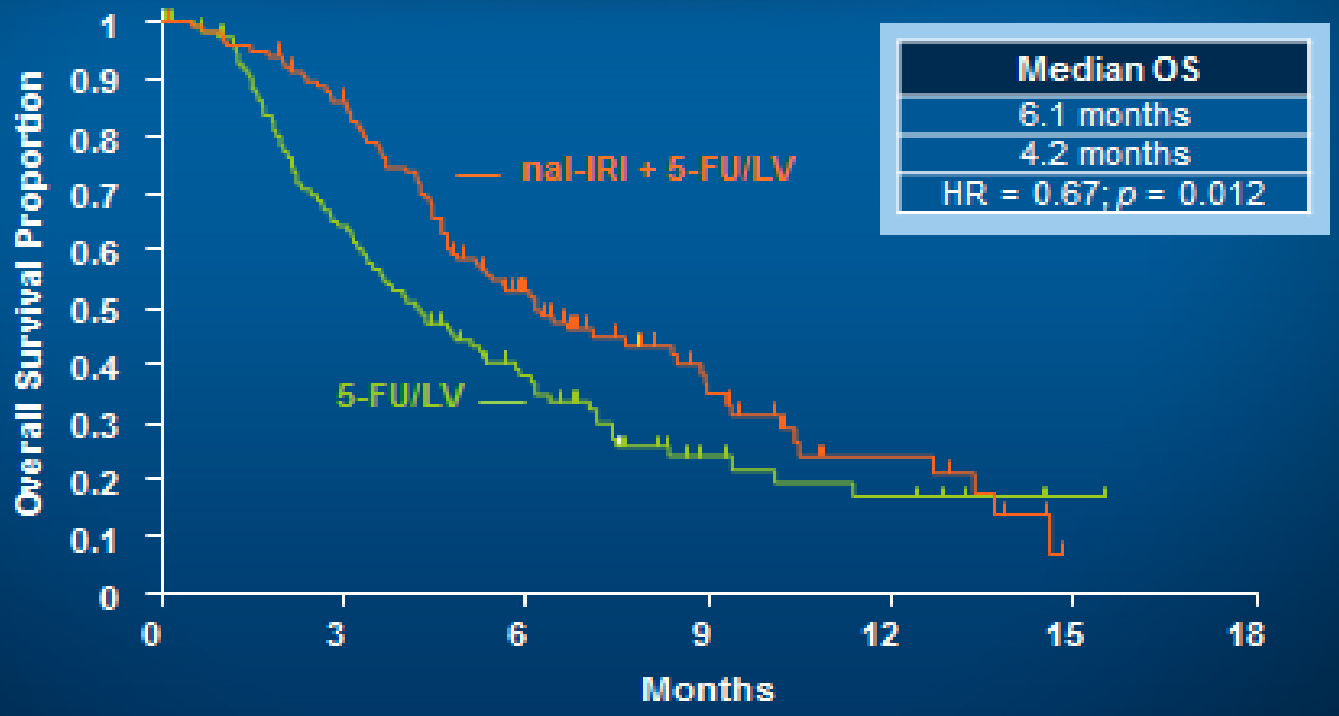
- Onivyde (liposomaal irinotecan), samen met 5fU en leucoverin.

- blokkeert een enzym met de naam topoisomerase

- In Onivyde wordt irinotecan omhuld door zeer kleine vetdeeltjes (de zogenaamde ‘liposomen’). Liposomen hopen zich op in de tumor daardoor wordt de chemotherapie langzaam afgegeven , waardoor de snelheid waarmee irinotecan uit het lichaam wordt verwijderd afneemt en het langer kan werken.


Nanoliposomal Irinotecan (nal-IRI, MM-398)
PEG-DSPE
Internal aqueous space
Lipid membrane
Irinotecan
~ 100 nm
~80,000 irinotecan molecules/liposome
Courtesy of Johanna Bendell, MD.

NAPOLI-1: Overall Survival with nal-IRI with 5-FU/LV in Metastatic Pancreatic Adenocarcinoma



No difference between Nal-IRI monotherapy and 5-FU/LV

Wang-Gillam A et al. *Lancet* 2016;387:545-57.

Nanoliposomal Irinotecan (Nal-IRI)

- **Mechanism of action:**
  - Topoisomerase inhibitor
- **Indication:**
  - In combination with 5-FU and leucovorin to treat patients with metastatic pancreatic cancer who have been previously treated with gemcitabine-based chemotherapy
- **Dosing/schedule:**
  - 70 mg/m^2 intravenous infusion over 90 minutes every 2 weeks
  - Recommended starting dose in patients homozygous for UGT1A1*28 allele is 50 mg/m^2 every 2 weeks

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468654.htm; Package insert for Nal-IRI

NAPOLI-1: Safety

	Nal-IRI + 5-FU/LV (n = 117)	Nal-IRI (n = 147)	5-FU/LV (n = 134)
Neutropenic sepsis	3%	4%	0%
Growth factors received	17%	12%	1%
Grade ≥3 nonhematologic AEs in >5% patients			
Fatigue	14%	6%	4%
Diarrhea	13%	21%	4%
Vomiting	11%	14%	3%
Nausea	8%	5%	3%

Wang-Gillam A et al. *Lancet* 2016;387:545-57.

Toekomst

- FOLFIRINOX ook bij resectabel/borderline resectabel
- Pancreascarcinoom: PREOPANC-2 trial
- Nieuwe imaging technieken om vooraf kans op resectie te vergroten
- Meer resecties bij lokaal gevorderd pancreascarcinoom.
- Verder ontwikkelen nanoknife
- Immunotherapie?
- Nieuwe chemotherapeuticum?

Lopende studies 1

- **PACAP ->**
  - Gegevens voor PancreasAudit, DPCA van patienten die voor operatie in aanmerking komen (ism DICA, MRDM)
  - Gegevens van patiënten die niet voor operatie in aanmerking komen (ism IKNL, NKR+)
  - Patient Reported Outcome measures (PROs), inclusief kwaliteit van leven (ism IKNL, PROFILES)
- PancreasParel (Dutch Pancreatic Biobank, is Parelsnoer)
- Online Expertpanel voor patiënten met pancreaskanker of pancreascysten
- Klinische studies
- **Leopard 1 en 2-**> laparoscopisch versus open resectie
- **Sphinx** -> Reduceert een endoscopische biliaire sfincterotomie voorafgaand aan fully covered metalen stentplaatsing het risico op een post-ERCP pancreatitis?
- **PACYFIC study** -> Het bepalen van de opbrengst van de huidige pancreascyste surveillance.

Lopende studies 2

- **PREOPANC->** Wel of geen preoperatieve radiochemotherapie voor resectabele en borderline resectabele pancreascarcinomen.
- **PELICAN ->** Onderzoeken of RFA gevolgd door chemotherapie een verlenging van leven kan geven t.o.v. chemotherapie alleen (huidige standaardbehandeling).
- **LAPC-1 ->** Bewijzen van de meerwaarde van stereo tactische bestraling aanvullend op de standaard folfirinox als adjuvante therapie.
- **Porsch trial ->** de implementatie van een best practice algoritme gericht op diagnostiek en behandeling van postoperatieve pancreasfistels het risico op ernstige complicaties en mortaliteit verminderd.
- **Panode ->** Doel van het onderzoek is het evalueren van de survival in patiënten met en zonder lymfekliermetastasen buiten het standaard resectiegebied.

Lopende studies 3

- **Picasso ->** Pasireotide ter preventie van pacreas fistel na resectie
- **Panorama: ->** retroprospectieve studie naar de kwaliteit van leven en diabetes management na pancreatectomie.
- **Spacious ->** Identificatie van mRNA, miRNA en lncRNA expressieprofielen en genetische veranderingen die de uitkomst na chirurgie en de respons op chemotherapie voorspellen voor resectabele en irresectabele PDAC (pancreatic ductal adenocarcinomas correlated) patiënten.
- **Pancos ->** In dit project wordt een pancreaschirurgie-specifiek core outcome set ontwikkeld middels de Delphi-methode. Een core outcome set is een lijst van 6-8 belangrijkste outcomes binnen een onderzoeksgebied.
- **Pancreasanastomose->** Het doel van deze studie is het maken van een overzicht van alle beschreven pancreasanastomoses.

Lopende studies 4

- **PANDORA ->** Om beter inzicht te krijgen in het gedrag van kleine pNET en het effect van een conservatieve behandeling (afwachten) te monitoren, zullen alle patiënten met een kleine pNET (<2cm) prospectief worden geregistreerd en vervolgd.
- **PROPAN ->** Het PROPAN project is bedoeld voor mensen met een duidelijk verhoogd risico op alvleesklierkanker die de optie van totale verwijdering van de alvleesklier (met een minimaal invasieve operatie) willen bespreken.

Bronnen

- Presentatie Dr. M.G.H. Besselink, chirurg, AMC, Amsterdam, P Hendricks (VS, JBZ), L Corpelijn (VS, UMCM)
- Methadon in de praktijk M van den Beuken van Everdingen
- www.oncoline.nl
- www.dpcg.nl
- www.iknl.nl
- Hester Scheffer*Lightning strikes' – irreversible electroporation in interventional oncology*
- *Wang- Gillian A et al. Lancet 2016*
- Posters: www.ons.org