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*International Society
for the Study of Pleura
and Peritoneum*



QUALITY OF LIFE & SURGICAL PALLIATION

Frailty, Prehab and HIPEC/PIPAC

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Advancing Innovative Therapies for Cancers That Invade the Peritoneum and the Pleura

Disclosures

- Grant/Research Support from Bristol Myers Squibb, CAPNOMED GmbH, and Pierre Fabre
- Consultant for Gamida, LEO Pharm, and Roche.

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This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Prehabilitation : questions for practice

A “prehabilitation” program should increase functional capacity in anticipation of an upcoming stress. It should occur after the surgical consultation and before surgery, and is based on three components: (1) physical care; (2) nutritional support; and (3) psychological support, **during 6 to 8 weeks**. The aims of prehabilitation are to improve both nutritional status and pre- and postoperative fitness, and to reduce postoperative complications.

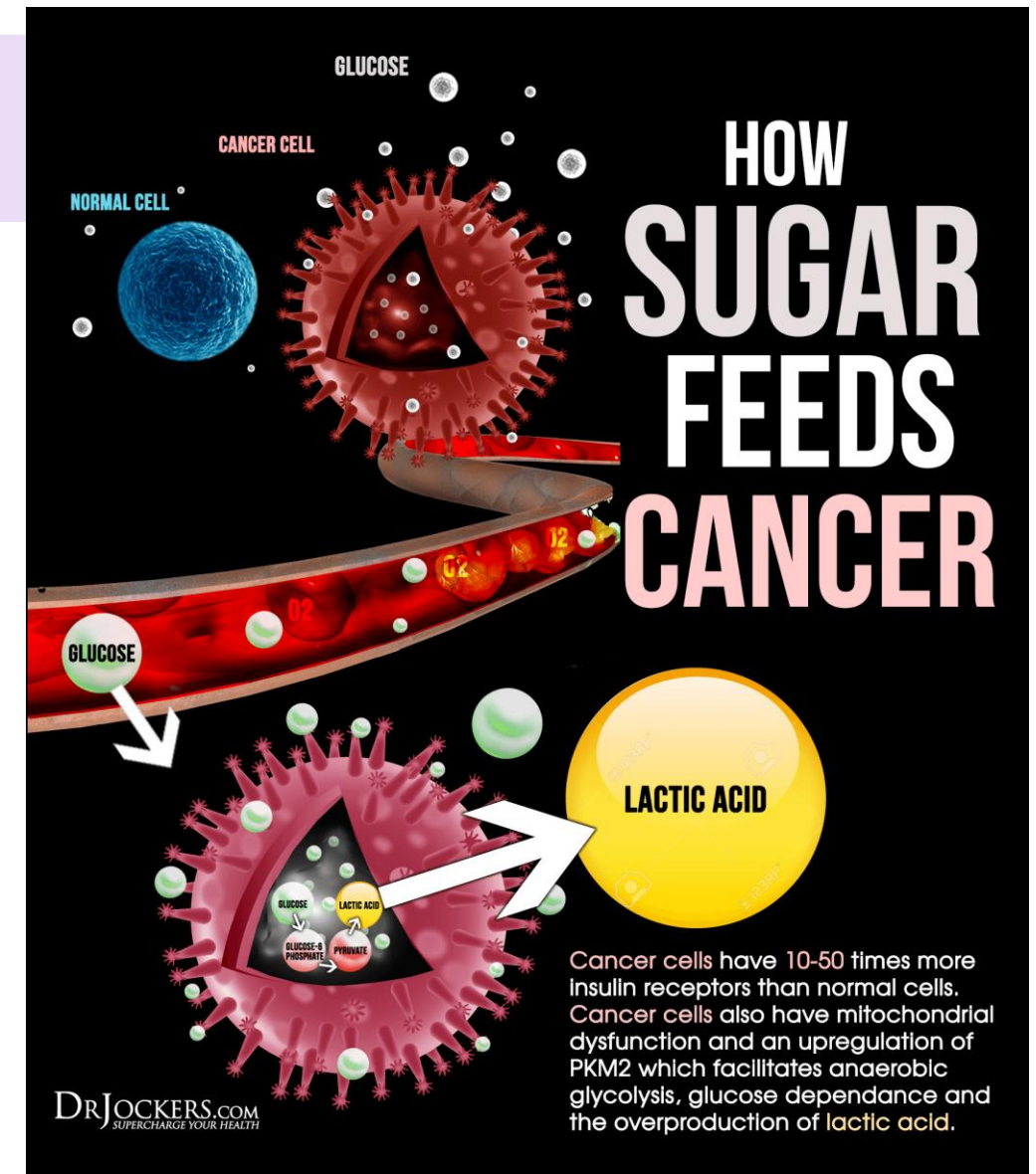
prehabilitation : Nutrition

Nutrition

Deal with stupid ideas

Sugar give cancer

Meat give cancer



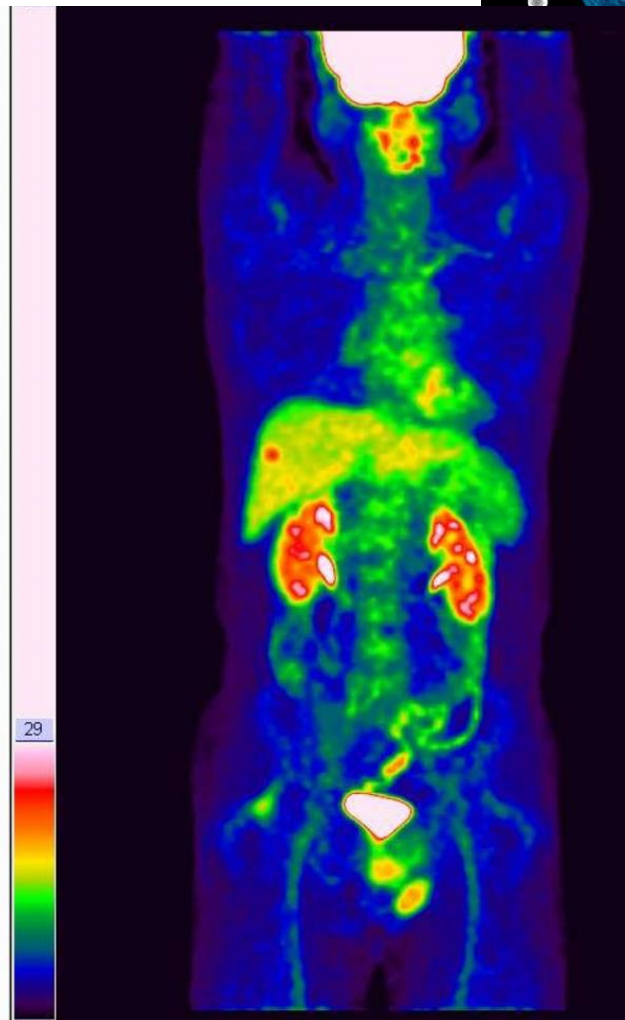
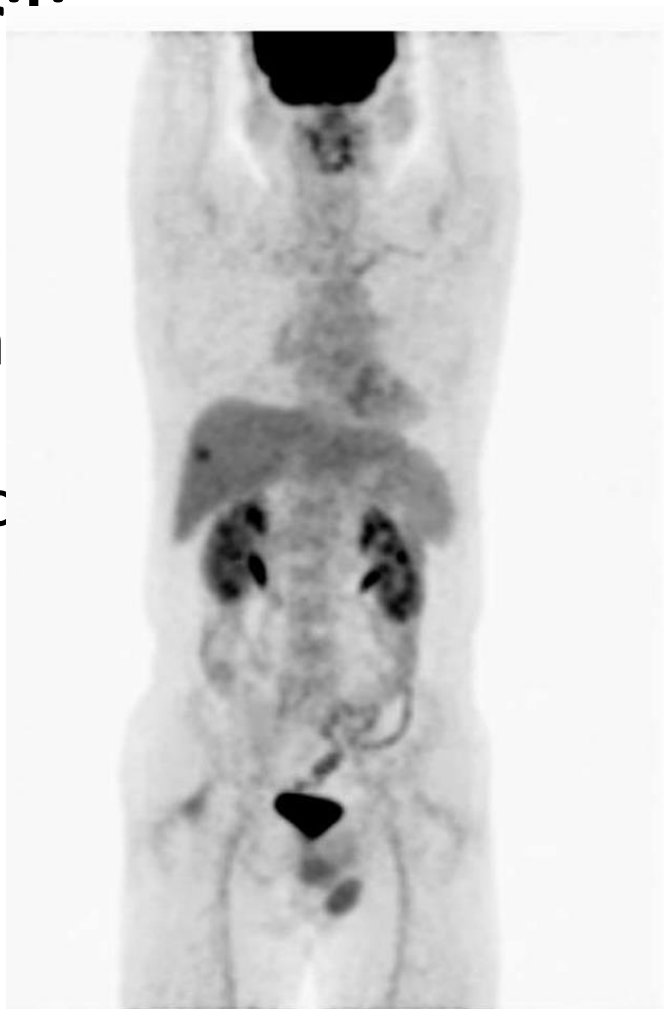
prehabilitation : Nutrition

Nutr...

Deal

Suga

Flesc



prehabilitation : Nutrition

Immuno Nutrition : Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer.

- Braga M, et al. Surgery. 2002 Nov;132(5):805-14.

Some possible randomized study are negative ?

- Did not boost the tumor proliferation (I have tested in nude mice, data not published)

BUT : Help patient to be pro active regarding the disease



7 days before surgery

Prehabilitation : ten times in a row & ten times a day

Teleflex Medical Triflo II Inspiratory Breathing Exerciser

- 5 €
- Use it 7 days before surgery
- Help to use it at day 1 post operative



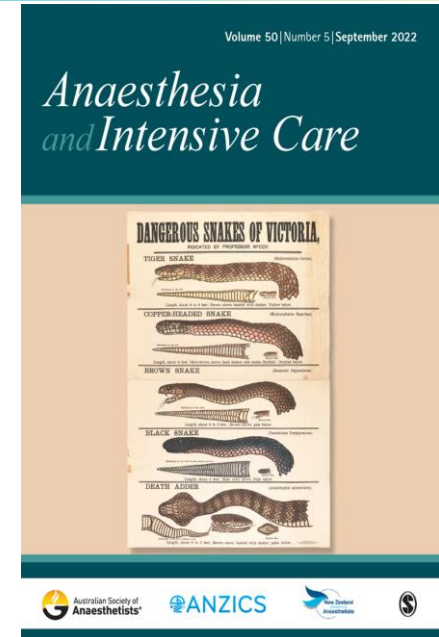
prehabilitation : physical activity

3 times per week
30 minutes

- **Some Negative trials published**
- Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Ausania F, Senra P, Meléndez R, Caballeiro R, Ouviaña R, Casal-Núñez E. Rev Esp Enferm Dig. 2019 Aug;111(8):603-608.
- **Clinical evidence**
- **But need to be prescript by the surgeon**



- **Preoperative cardiopulmonary exercise testing improves risk assessment of morbidity and length of stay following cytoreductive surgery with hyperthermic intraperitoneal chemotherapy.**
- Pillinger NL, Koh CE, Ansari N, Munoz PA, McNamara SG, Steffens D.
- Anaesth Intensive Care. 2022 Aug 3:310057X211064904.



This study explored the associations between preoperative cardiopulmonary exercise testing (CPET) variables and postoperative outcomes following elective CRS and HIPEC.

Preoperative cardiopulmonary exercise testing improves risk assessment of morbidity and length of stay following cytoreductive surgery with hyperthermic intraperitoneal chemotherapy.

This study included patients who underwent routine preoperative CPET prior to elective **CRS and HIPEC**.

CPET was performed using a cycle ergometer and measured peak oxygen uptake (VO_2 peak) and anaerobic threshold (AT).

Patients who did not develop any postoperative complication had slightly higher preoperative AT and VO_2 peak and **shorter length of hospital stay**. Data in this study support the role of CPET prior to CRS and HIPEC as an adjunct to improve risk assessment.

prehabilitation : Psychology

VOLUME 34 • NUMBER 11 • APRIL 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Depressive Symptoms in Patients Scheduled for Hyperthermic Intraperitoneal Chemotherapy With Cytoreductive Surgery: Prospective Associations With Morbidity and Mortality

Carissa A. Low, Dana H. Bovbjerg, Steven Ahrendt, Sara Alhelo, Haroon Choudry, Matthew Holtzman, Heather L. Jones, James F. Pingpank Jr, Lekshmi Ramalingam, Herbert J. Zeh III, Amer H. Zureikat, and David L. Bartlett

prehabilitation : Psychology

Depression is an independent prognosis factor if no post operative complication arrive

- Twenty-eight percent of patients had depression CES-D scores indicative of clinically significant depressive symptoms.
- After adjusting for relevant preoperative demographic and disease-specific factors, depressive symptoms were associated with greater odds of 30-day morbidity (n = 68; odds ratio, 5.50; 95% CI, 1.23 to 24.73; P = .03) and greater likelihood of 30-day readmission (n = 72; odds ratio, 5.92; 95% CI, 1.27 to 27.64; P = .02).

prehabilitation : Psychology

Depression is an independent prognosis factor if no post operative complication arrive

- Depressive symptoms were associated with shorter survival after adjustment for preoperative demographic and disease-specific factors (n = 87; hazard ratio, 1.88; 95% CI, 1.07 to 3.31; P = .03).
- This association was no longer significant when intraoperative/postoperative prognostic variables were added to the statistical model (n = 87; hazard ratio, 1.31; 95% CI, 0.72 to 2.37; P = .37).

prehabilitation : Psychology

Six times as many

Table 3. Multivariate Logistic Regression Models of Associations With 30-Day Outcomes

Variable	Odds of 30-Day Morbidity (n = 68)		Odds of 30-Day Readmission (n = 72)	
	OR (95% CI)	P	OR (95% CI)	P
Age, years	1.00 (.94 to 1.06)	.96	0.99 (.94 to 1.05)	.81
Diagnosis				
Colorectal	18.60 (2.38 to 145.12)	.01	27.32 (2.46 to 302.98)	.01
Other	10.08 (1.55 to 64.67)	.02	12.74 (1.38 to 117.88)	.03
Appendiceal (referent)	1.00		1.00	
PCI score	1.10 (1.01 to 1.19)	.03	1.10 (.99 to 1.21)	.06
CC score				
2 or 3	0.31 (.04 to 2.69)	.29	0.12 (.01 to 1.48)	.10
0 or 1 (referent)	1.00		1.00	
Hospital LOS, days	1.03 (.98 to 1.09)	.23	1.01 (0.92 to 1.11)	.82
Depression				
CES-D \geq 16	5.50 (1.23 to 24.70)	.03	5.92 (1.27 to 27.64)	.02
CES-D < 16 (referent)	1.00		1.00	

Abbreviations: CC, completeness of cytoreduction; CES-D, Center for Epidemiologic Studies Depression scale; LOS, length of stay; OR, odds ratio; PCI, Peritoneal Cancer Index.

prehabilitation : Psychology

OK so what in practice ?

- Find with the patient what can help him to be more stronger

- Music ?
- Book ?
- Family ?



- In case of massive depression – discuss to delay major abdominal surgery
 - If depression can be partially treated

prehabilitation : questions for practice

- It is scientific Nutrition
- Oral impact
- Physical activity
- Respiration ?
- Psychology
- Stop smoking > 15 days



Guidelines for Perioperative Care in Cytoreductive Surgery (CRS) with or without hyperthermic IntraPeritoneal chemotherapy (HIPEC): Enhanced recovery after surgery (ERAS®) Society Recommendations — Part I: Preoperative and intraoperative management

Martin Hübner ^{a,*,1}, Shigeki Kusamura ^{b,1}, Laurent Villeneuve ^c, Ahmed Al-Niaimi ^d, Mohammad Alyami ^e, Konstantin Balonov ^f, John Bell ^g, Robert Bristow ^h, Delia Cortés Guiral ⁱ, Anna Fagotti ^j, Luiz Fernando R. Falcão ^k, Olivier Glehen ^l, Laura Lambert ^m, Lloyd Mack ⁿ, Tino Muenster ^o, Pompiliu Piso ^p, Marc Pocard ^q, Beate Rau ^r, Olivia Sgarbura ^s, S.P. somashekhar ^t, Anupama Wadhwa ^u, Alon Altman ^v, William Fawcett ^w, Julia Veerapong ^x, Gregg Nelson ^y

Rehabilitation : questions for surgeon

- No drain
- No tube
- Locoregional anesthesia
- Post operative mobilization
 - On the floor
 - On the team targets



Guidelines for Perioperative Care in Cytoreductive Surgery (CRS) with or without hyperthermic IntraPERitoneal chemotherapy (HIPEC): Enhanced Recovery After Surgery (ERAS®) Society Recommendations — Part II: Postoperative management and special considerations

Martin Hübner ^{a,*,1}, Shigeki Kusamura ^{b,1}, Laurent Villeneuve ^{c,d}, Ahmed Al-Niaimi ^e, Mohammad Alyami ^f, Konstantin Balonov ^g, John Bell ^h, Robert Bristow ⁱ, Delia Cortés Guiral ^j, Anna Fagotti ^{k,1}, Luiz Fernando R. Falcão ^m, Olivier Glehen ^{n,d}, Laura Lambert ^o, Lloyd Mack ^p, Tino Muenster ^q, Pompiliu Piso ^r, Marc Pocard ^s, Beate Rau ^t, Olivia Sgarbura ^{u,v}, S.P. Somashekhar ^w, Anupama Wadhwa ^x, Alon Altman ^y, William Fawcett ^z, Jula Veerapong ^{aa}, Gregg Nelson ^{ab}

Prehab and HIPEC

Prehabilitation to improve postoperative outcomes in patients with peritoneal carcinomatosis undergoing hyperthermic intraperitoneal chemotherapy (HIPEC): A scoping review

D. Strijker ^{a, *}, W.J.H.J. Meijerink ^b, A.J.A. Bremers ^a, P. de Reuver ^a, C.J.H.M. van Laarhoven ^a, B. van den Heuvel ^b

Conclusion: No research has been published on the effect of prehabilitation prior to HIPEC. This review demonstrates that preoperative modifiable risk factors for outcomes in patients undergoing HIPEC are multifactorial. A multimodal prehabilitation program prior to HIPEC, including nutritional support, psychical exercise, psychological support and smoking cessation, might therefore be a promising approach to improve postoperative outcomes.

Impact of Muscle Mass Depletion on Surgical Outcomes in Patients with Primary High-grade Serous Ovarian Cancer Undergoing CRS and HIPEC.

- Mercan U, Gulpinar B, Ersen O, Kosmaz K, Durhan A, Unal AE.
- J Coll Physicians Surg Pak. 2021 Nov;31(11):1314-1319.



The presence of sarcopenia (OR: 0.050 95% CI: 0.004-0.675; $p=0.024$) was found to be independent predictor of serious postoperative complications.

Sarcopenia can easily be diagnosed without additional cost or radiation exposure with routine preoperative staging CT images.

- **Prehabilitation to improve postoperative outcomes in patients with peritoneal carcinomatosis undergoing hyperthermic intraperitoneal chemotherapy (HIPEC): A scoping review.**

- Strijker D, et al. Eur J Surg Oncol. 2022 Mar;48(3):657-665.



Fourteen studies identify the following preoperative factors: poor nutritional status, poor performance status, low health related quality of life and an history of smoking.

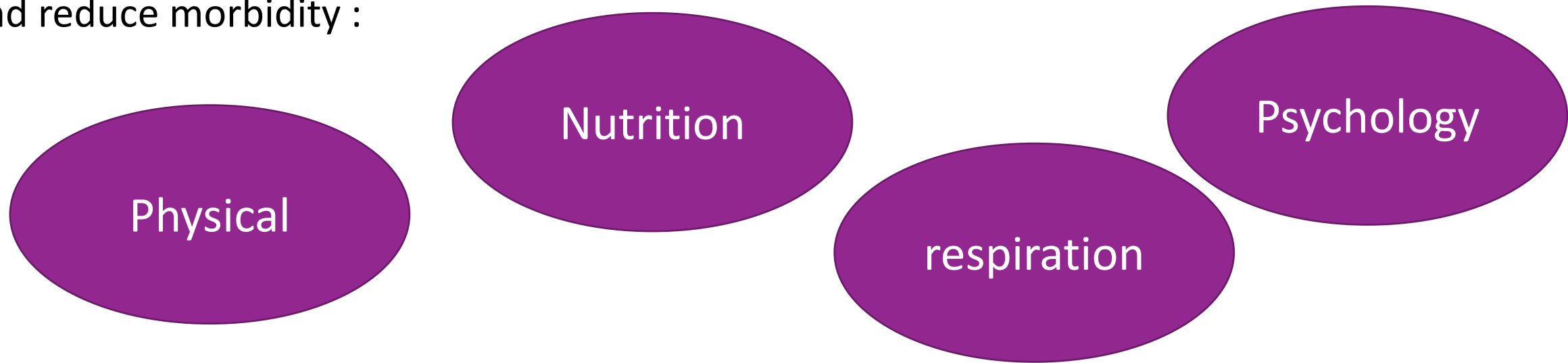
A multimodal prehabilitation program prior to HIPEC, including nutritional support, psychical exercise, psychological support and smoking cessation, might therefore be a promising approach to improve postoperative outcomes.

Prehabilitation of patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal malignancy.

Cortés-Guiral D, Mohamed F, Glehen O, Passot G. Eur J Surg Oncol. 2021;47(1):60-64.



Prehabilitation is a multimodal approach that helps optimize postoperative recovery and reduce morbidity :

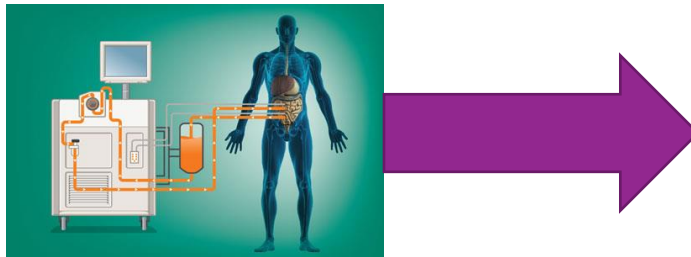


Pre – Re habilitation : patient – team – surgeon actions



Quality of life and surgical palliation

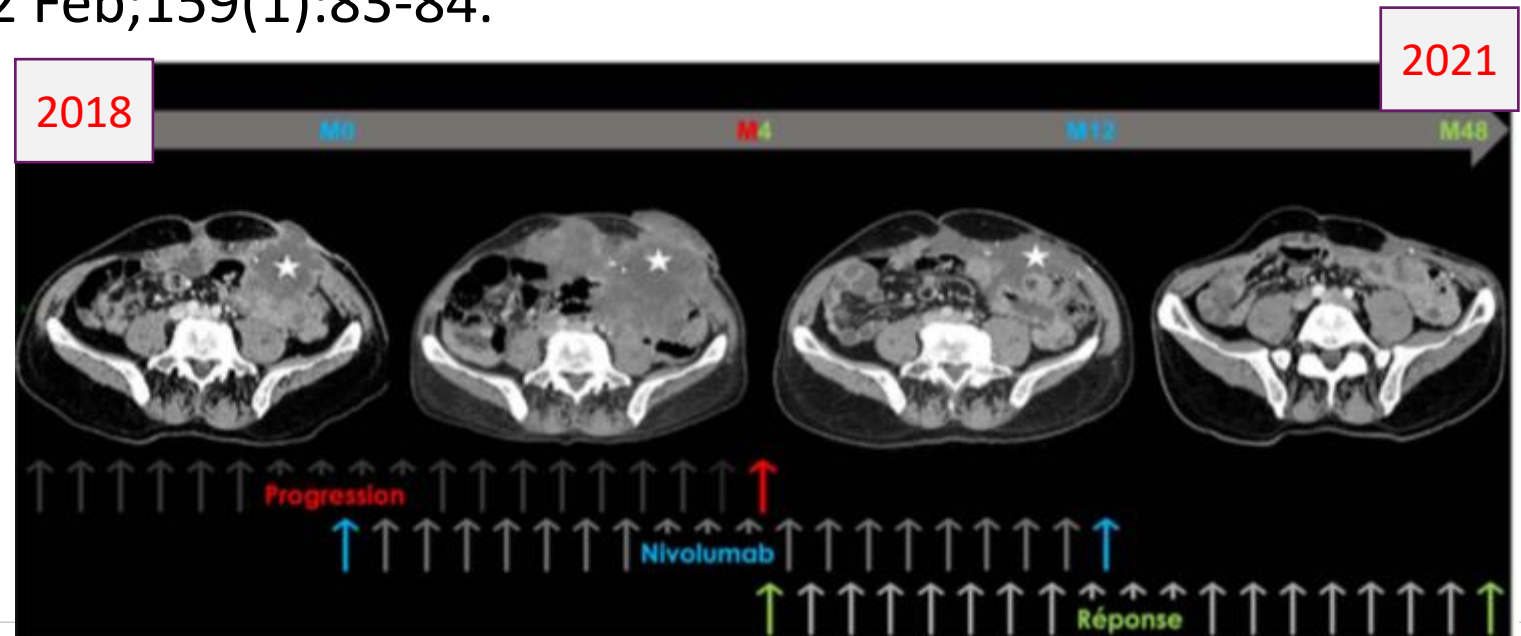
- **My best case :**
- [Selected Patients With Peritoneal Metastases From Breast Cancer May Benefit From Cytoreductive Surgery: The Results of a Multicenter Survey.](#) Cardi M, Pocard M, Dico RL, Fiorentini G, Valle M, Gelmini R, Vaira M, Pasqual EM, Asero S, Baiocchi G, Di Giorgio A, Spagnoli A, Di Marzo F, Sollazzo B, D'Ermo G, Biacchi D, Iafrate F, Sammartino P. Front Oncol. 2022 May 11;12:822550.
- In case of hormonal positive receptor : offer anti-hormonal therapy with a positive result on ascitis and tumor growth during 24 months – no pain, no ascitis, no secondary effect



Quality of life and surgical palliation

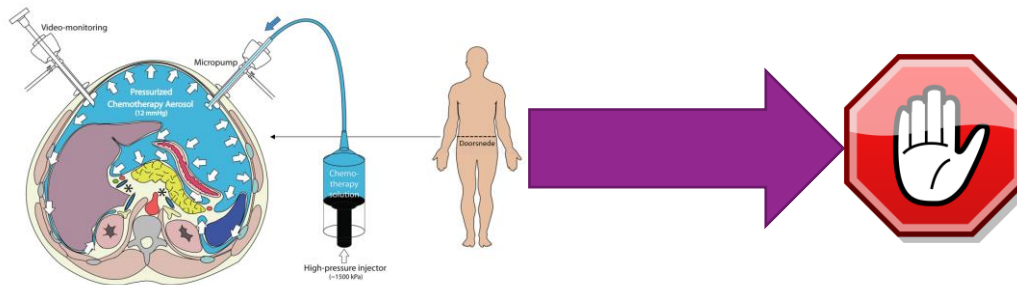
- **My second best case :**
- [Peritoneal recurrence of colorectal cancer with microsatellite instability: Is immunotherapy alone more effective than surgery?](#) Gavignet C, Hobeika C, André T, Pocard M. J Visc Surg. 2022 Feb;159(1):83-84.

- MSI >>> Immunotherapy
- Offer complete response



Quality of life and surgical palliation

- **My worst case :**
- [A severe oxaliplatin immune-induced syndrome after oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy \(PIPAC\).](#) Ezanno AC, Malgras B, Aoun O, Delarge A, Doreille A, Pocard M. Pleura Peritoneum. 2022 Jan 31;7(1):35-38.
- In case of major secondary effect it is hard to obtain from colleague working in Intensive care unit a care implication.



Frailty : HIPEC or PIPAC or IP any treatment

- **Frailty is of major impact in two situations : HIPEC or bowel accident with ip treatment**
- 1 Performing a cytoreductive surgery and HIPEC procedure for a patient > 70 years
 - Gastric cancer & CRS & HIPEC : Total gastrectomy - Major weight loss – even in absence of any complication the fatigue is of major impact, more than 3 months in postoperative days
- 2 IP antibody drug delivery for gastric cancer peritoneal meta (Catumaxomab / CD3 EpCAM)
 - One patient : ascites infection after the second injection : death
- 2 Failure to rescue in case of postoperative complication
 - 250 PIPAC procedures and 2 small bowel fistulas : 2 deaths

Frailty : gastric cancer specificity

- Major nutritional alteration
 - Difficult to evaluate with obese patient, or ascites that increase the weight
 - Difficult to evaluate with young patient able to stay OMS 1 or doing professional activity
- Intra venous chemotherapy protocols highly toxic as first line proposal
 - But hematologic results are conserved
- Sub occlusion is strong to evaluate
 - patient are able to take limited food or liquid spontaneously, and report nothing
 - Some patient know that occlusion is a contraindication and did not report recent alteration
 - Small bowel is affected by distension and easy to traumatize
 - Small bowel infiltration is difficult to identify on the CT

Frailty : peritoneal mesothelioma specificity

- Tumor progression could be very quick ?
- Major nutritional alteration could be present
 - Difficult to evaluate with obese patient , or ascites that increase the weight COMSEL
- Pulmonary association could increase frailty
 - Pleural involvement could be associated
- Inflammatory situation
 - Fever could be induce by the disease



Frailty, Prehab and HIPEC/PIPAC

- Selection of patient that could have an interest and no toxicity with PIPAC :
 - Results of PIPAC Estok01
 - Some abstract presented with patient receiving only 2 PIPAC
- Offer a pre habilitation process
 - for every patient having cytoreductive surgery & HIPEC
 - Mortality after cytoreductive surgery and HIPEC should be less than 1%