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Review Article

NUTRITION FOR PANCREATIC SURGERY

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Introduction

The American novelist Leo Rosten (1908-1997) once said: "Some things are so unexpected that no one is prepared for them". This statement probably epitomizes what pancreatic cancer is. This highly aggressive malignancy is characterized by early malnutrition, cachexia, and early metastasis. With no reliable method for early detection when carcinoma pancreas is usually diagnosed, it has already advanced and less than 20 % of patients are candidates for surgery. Patients affected with pancreatic cancer have a dismal survival (1- and 5-year relative survival rates are 29% and 7%, respectively).

Hence it becomes imperative to ensure appropriate and optimal nutritional support for the patient getting treated for carcinoma pancreas in order to ensure the least morbidity and try to provide good quality of life. There are many reasons why a patient of carcinoma pancreas does poorly on the nutritional front which include neuro behavioral changes and cachexia

How does pancreatic cancer become malnourished?

The neurobehavioral changes are independent (no relation to chemotherapy or size or histopathology of tumor) irreversible processes (with no effect with medicine or supplementation) that manifest as a loss of desire to consume food thus is directly responsible for weight loss and poor nutritional status. The excessive release of cytokines particularly TNF –alpha (apart from transforming growth factor β, IL-1, and IL-6) may be related to the behavioral manifestations via central (hypothalamic food control deregulation)and peripheral mechanisms(by release of lactate, oligonucleotides, ketones, islet amyloid polypeptide, reduction of zinc, etc)[3,4,5]. There may also be a false sense of satiety in some patient due to the invasion of the tumor into the gastrointestinal tract. Another reason for the anorexia might be the reduced release of ghrelin (growth hormone releasing peptide) which might have appetite stimulant properties, probably something like a hunger signal that increases the tendency to eat[1]. This reduced release of

ghrelin was demonstrated in a study by Corbetta and colleagues[2] compared to other malignancies where there was an augmented release.[6]This might be related to the fact that the extremely fast progression of the disease itself. All this put together in pancreatic cancer also results in loss of muscle and adipose tissue resulting in the phenomenon of cancer cachexia. Lipid mobilizing factors and proteolysis inducing factors also cause lipolysis and proteolysis contributing to protein and fat tissue loss. The neural invasion and astrocyte activation also cause proteolysis and lipolysis.

Does this malnourishment lead to significant effect?

Severely malnourished pancreatic cancer patients who are subjected to surgeries have prolonged length of stay.[7]They are also known to have increased chances of surgical site infections, increased length of ICU stay, pancreatic fistula and associated deep space infection. Pancreatic fistula, one of the most dreaded complication post pancreatic surgeries is closely linked to malnutrition, specifically a nutritional risk index (NRI) score of 100 or less (OR =8.12, 95% CI: 1.06-22.30; P<0.05).[8]Patients with low albumins when subjected to surgery are also associated with an increased incidence of pancreatic fistulas.[9]

Nutritional management of patients for pancreatic surgery.

Screening

The management should start with an adequate screening programme. All patients posted for pancreatic surgery should be first referred to a nutritional support team for screening for malnutrition.

There are numerous scores that have been studied. The Onderas prognostic nutrition risk index (10 × serum albumin value (g/dL) + 0.005 × total lymphocyte count in the peripheral blood (per mm^3))(PNI)and the MUST(using BMI, weight loss and acute disease effect) are two tools that were studied retrospectively in 268 patients who underwent surgery for pancreatic adenocarcinoma. A low PNI score was linked to increased perioperative and postoperative complications that included pancreatic fistulas. The nutrition risk index is another toll to study pre-operative malnutrition risk. [Nutritional Risk Index= (1.519 X serum albumin, g/L) + 0.417 X (present weight/usual weight x 100). A Nutritional Risk Index>100 indicates that the patient is not malnourished, 97.5-100 indicates mild malnourishment, 83.5-<97.5 indicates moderate malnourishment and <83.5 indicates severe malnourishment]. The MUST and the nutrition risk index showed a good level of agreement in the prediction of overall morbidity, SSI rate, and length of hospital stay. The MUST and SGA agree well on the SSI rates. The Nutrition risk index, however, does not pick out those patients who were at high risk for malnutrition. The BMI as proven in many studies was again proven to be a poor tool to asses nutritional status and prediction of postoperative morbidity pre pancreatic surgery. However something as simple as the loss of weight of greater than 5 % in the preceding 3 to 6 months correlated well to increase the length of stay and increased surgical site infections.[10,11]

Do we need Preoperative nutritional support?

After screening patients for malnourishment that patient who warrant pre and perioperative support need to be channelized into optimal nutritional support. It does seem that those patients who are moderately or severely malnourished may benefit from perioperative nutritional support. In a prospective study conducted by Wu et al 468 moderate to severely malnourished patients who were being operated electively for cancers of the GI tract were randomized to 8 odd days of pre operative and 8 days of postoperative nutritional support versus control receiving standard oral hospital diet preoperatively

with hypocaloric nutritional support postoperatively. twofold reduction in complications (P =0.012) , a three-fold reduction in death (P =0.003), lesser major septic complications (14.9% vs. 27.9%, P =0.011) was noted all in favor of the perioperative specialized nutritional support group. They also demonstrated a lower mortality (2.1% vs. 6.0%, P =0.003).[12]In another small pilot study in a patient undergoing Whipple's surgery preoperative nutritional support for 4 days translated to decrease the length of hospital stay and cost savings.[13]In another prospective randomized multicenter trial for preoperative nutritional support in major upper GI surgery in 154 patient preopnutrtiona was studied. Preoperatively, patients received 5 days of oral immunonutrition (an arginine-, RNA-, and omega3 fatty acid-supplemented diet) or an isoenergetic control diet (1 L/d). Again the use of perioperative administration enteral immunonutrition reduced postoperative infections and treatment costs.[14]in a metanalysis using 17 studies which studied the use of perioperative enteral nutrition with supplementation with immunonutrtion using the IMPACT formula similar outcomes were reported.[15]

How to deliver pre-operative nutrition for pancreatic surgeries?

Combating anorexia-cachexia of pancreatic carcinoma:

Drugs used in combating anorexia are slow to show the effect and may result in effective weight gain anywhere between 4 weeks to 6 months. However meaningful weight gain would be seen only at 5 to 6 months. Hence for immediate preoperative nutrition, the use of these agents like megesteroletc maybe not very helpful if introduced de novo. However, if these drugs are being taken by the patient it seems prudent to continue the same weighing the benefits versus the risks as abrupt stoppage could result in unwanted side effects. However psychological counseling and psychiatric help in combating depression along with appropriate medications would help in improving enteral nutrition intake which may ultimately help in preoperative nutrition.

Enteral nutrition:

As mentioned above pre-operative enteral nutrition supplemented with arginine in moderate to severely malnourished patients may help in reducing the length of stay and postoperative infectious complications. the ESPN recommends preoperative nutritional support for 10 – 14 days even if this needs delaying surgery in severely malnourished patients.

Addition of immune enhancing nutritional formulae especially arginine may help in reducing postoperative infectious morbidity.[14, 15]. This specialized nutritional support has to consumed orally. However, there would be subsets of a patient who refuse to consume orally in view of extreme anorexia and satiety. In such states, it makes it imperative to pass a nasogastric tube for enteral feeding. At times the tumor itself causes obstruction and prevention of enteral nutrition. In such cases passage of a nasojejunal tube if possible may help.

Parenteral nutrition:

Parenteral nutrition should be resorted to in cases of severe malnourishment where usual enteral nutrition is not able to achieve target goals. In parenteral nutrition, a high fat to glucose ratio can be used in the formula as the ability in cachexia to utilize fat is much higher. In such patient use of TPN is shown to reduce postoperative stress response of surgery by increasing protein synthesis and immune function, resulting in a decrease in postoperative infectious complications**.**[16]In another study of 90 patient for elective gastric or colorectal surgeries with severe malnourishment use of TPN reduced complication rate by approximately one third and also showed a reduction in mortality as compared to usual care.[17]When providing parenteral nutrition we have to ensure strict aseptic precautions and be very

careful in avoiding an early diagnosis of refeeding syndrome.

Immune modulating nutrition:

Ina trial of 212 patient undergoing pancreatic-duodenectomy patients were randomized to receive enteral formula enriched with arginine, omega 3 fatty acids, and RNA, standard nutrition and TPN. The study went on to report that early postoperative enteral nutrition is safe and provision on immunonutrition reduces immunometabolic response and improves outcomes compared to parenteral nutrition.[18]similar findings were reported by other studies using ecosapentoic acidsenterally, and omega 3 fatty acids reducing the overall length of stay and postoperative morbidity as compared to standard enteral nutrition.[19,20,21]In another study 167 malnourished cancer patients posted for surgery were randomized to receive parenteral nutrition for 14 days preoperatively.post operatively the patient were divided into 4 groups, standard, enteral, parenteral, and immunomodulating. Results of this study did not demonstrate any superiority of immunomodulatory formula over the others in the PN arm.[22]In view of a small number of studies done in this aspect it is not very clear whether immune modulating should be routinely used in the care of surgical cases of ca pancreas and more studies are warranted in this field.

Post-operative nutrition for pancreatic surgeries:

Postoperative nutrition: Maximal evidence involves the prescription of postoperative enteral nutrition. The ERAS suggests the use of early fast-track oral feeding which would result in reduced delayed gastric emptying. In a systematic review of 15 studies with 3474 patients data on five feeding routes were studied which included oral diet, NJ tube feeding, gj tube feeding, at feeding, and TPN. normal oral intake was established most quickly in the oral diet group with delayed gastric emptying maximal in the feeding group. This systematic review considered oral diet as the preferred feeding route after pancreaticoduodenectomy.[23]The use of Feeding jejunostomy tubes should be individualized especially in those patients who have gross hypoalbuminemia ,as such patient known to have increased morbidity, reoperation rates, and higher rates of readmission.[24]Use of a nasojejunal feeding is also shrouded with controversies with studies demonstrating increased incidence of postoperative pancreatic fistulas with no changes in infections and length of stay when compared to TPN. In fact, in the TPN group, average energy intake was significantly higher and patients went on to oral feeding much faster.[25]

However, the ESPEN groups advise against the introduction of enteral nutrition in the first 24 hours and in fact recommends feeding beyond the anastomosis if at least 60% target goals are not achieved by enteral nutrition within the first 10 days or if there was obvious undernutrition at surgery. This may stem from the fact that patients following the ERAS post-pancreatic-duodenectomy very rarely achieve full target goals per os within the first couple of days. Those patients who fail to achieve the targets have an increase in the postoperative complication rate[26]. However, it is important to understand there are a couple of risks involved with the use of feeding tubes.

"Food at will" seems to be quite easy and safe to implement. Such practices are commonplace in bariatric surgery for a very long time. Lassen et al investigated in a group of 447 patients who underwent major abdominal surgery(82 patients of these underwent Whipple surgery) into two groups, one having food at will versus another group who were fed with needle catheter jejunostomy from the very first day. a larger number of patients had complications among the tube fed group. In fact, time to resumed bowel function was in favor of allowing normal food at will, length of stay and rate of post-discharge

complications were much lesser among patients fed at will.[27]

Conclusion

It seems that eating at will orally seems the ideal way to go about postoperatively for pancreatic surgeries. However, whether this provides optimal nutrition is a question. Specialised Enteral nutrition should be provided rather selectively. The use of feeding via tubs should be discouraged and if the need should be done via the nasojejunal route which has demonstrated to be fraught with the better benefits and lesser risks compared to the other tube routes.TPN should be reserved only for those patients that have failed all enteral routes of nutrition. There are many questions that still warrant answers. Large multicenter randomized controlled trials will help in answering those.

References:

1. Leidy HJ, Williams NI: Meal energy content is related to features of meal-related ghrelin profiles across a typical day of eating in non-obese premenopausal women. Horm Metab Res *38*(5): 317-322, 2006.
2. Corbetta S, Peracchi M, Cappiello V, Lana , Lauri E, Vago L, and Beck-Peccoz P, Spada A: Circulating ghrelin levels in patients with pancreatic and gastrointestinal neuroendocrine tumors: identification of one pancreatic ghrelinoma. J Clin Endocrinol Metab *88*: 3117-3120, 200.
3. Ezeoke CC, Morley JE. Pathophysiology of anorexia in the cancer cachexia syndrome. J Cachexia Sarcopenia Muscle. 2015; 6: 287-302.
4. Andersson R, Ch D, Leveau P, Haraldsen P. Nutritional aspects in the management of pancreatic cancer. Annals of Gastroenterology.2007; 13.
5. Tan CR, Yaffee PM, Jamil LH, Lo SK, Nissen N, Pandol SJ, et al. Pancreatic cancer cache
6. Shimizu Y, Nagaya N, Isobe T, Imazu M, Okumura H, Hosoda H, Kujima M,Kang awa K, Kehno N: Increased plasma ghrelin level in lung cancer cachexia.Clin Cancer Res *9*: 774-778, 2003.
7. Wakahara T, Shiraki M, MuraseK, et al. Nutritional screening with Subjective Global Assessment predicts hospital stay in patients with digestive diseases. *Nutrition*. 2007;23:634-639.
8. Sierzega M, Niekowal B, Kulig J, et al. Nutritional status affects the rate of pancreatic fistula after distal pancreatectomy: a multivariate analysis of 132 patients. JAm CollSurg 2007;205:52-9.
9. Schnelldorfer T, Mauldin PD, Lewin DN, et al. Distal pancreatectomy for chronic pancreatitis: risk factors for postoperative pancreatic fistula. J GastrointestSurg2007;11:991-7.
10. Kanda, M.; Fujii, T.; Kodera, Y.; Nagai, S.; Takeda, S.; Nakao, A. Nutritional predictors of postoperative outcome in pancreatic cancer. Br. J. Surg. 2011, 98, 268–274.
11. La Torre M, Ziparo V, Nigri G, et al. Malnutrition and Pancreatic Surgery: Prevalence and Outcomes. J Surg Oncol 2013;107:702-8.
12. Wu GH, Liu ZH, Wu ZH, et al. Perioperative artificial nutrition in malnourished gastrointestinal cancer patients. World J Gastroenterol 2006;12:2441-4.
13. Ward-Boahen D, Wallace-Kazer M. Improving Surgical Outcomes in Pancreatic Surgery With Preoperative Nutrition. *Journal of the Advanced Practitioner in Oncology*. 2014;5(2):100-106.
14. Senkal M, Zumtobel V, Bauer K H, Marpe B, Wolfram G, Frei A, Eickhoff U, Kemen M. Outcome and cost-effectiveness of perioperative enteral immunonutrition in patients undergoing elective upper gastrointestinal tract

surgery: a prospective randomized study. *Archives of surgery (Chicago, Ill. : 1960)*1999;134:1309–1316.

15. Waitzberg Dan L, Saito Hideaki, Plank Lindsay D, Jamieson Glyn G, JagannathPalepu, Hwang Tsann-Long, Mijares Juan M, Bihari David. Postsurgical infections are reduced with specialized nutrition support. *World journal of surgery*. 2006;30:1592–1604.
16. Karagianni, V.T.; Papalois, A.E.; Triantafillidis, J.K. Nutritional status and nutritional support before and after pancreatectomy for pancreatic cancer and chronic pancreatitis. *Indian J. Surg. Oncol*. **2012**, *3*, 348–359.
17. Bozetti et al, perioperative total pareneteralnutrtion in malnourished gastrointestinal cancer patients: a randomized, clinical trial. jpenvol 24,issue 1,pp.7-14
18. Gianotti L, Braga M, Gentilini O, Balzano G, Zerbi A, Di Carlo V (2000) Artificial nutrition after pancreaticoduodenectomy. Pancreas 21: 344–351.
19. Giger U, Büchler M, Farhadi J, Berger D, Hüsler J, Schneider H, Krähenbühl S, Krähenbühl L (2007) Preoperative immunonutrition suppresses perioperative inflammatory response in patients with major abdominal surgery-a randomized controlled pilot study. Ann Surg Oncol 14:2798–2806
20. Xue H, Sawyer MB, Wischmeyer PE, Baracos VE (2011) Nutrition modulation of gastrointestinal toxicity related to cancer chemotherapy: from preclinical findings to clinical strategy. JPEN J Parenter Enteral Nutr 35:74–90
21. Barber MD, Ross JA, Voss AC, Tisdale MJ, Fearon KC (1999)The effect of an oral nutritional supplement enriched with fish oil on weight-loss in patients with pancreatic cancer. Br J Cancer81:80–86
22. Klek S, Sierzega M, Szybinski P, et al. Perioperative nutrition in malnourished surgical cancer patients- a prospective randomized, controlled, clinical trial. Clin Nutr 2011;30:708-13.
23. Gerritsen A, Besselink MGH, Gouma DJ, et al. Systematic review of five feeding routes after pancreatoduodenectomy.Br J Surg 2013;100:589-98; discussion 599.
24. Nussbaum, D.P.; Zani, S.; Penne, K.; Speicher, P.J.; Stinnett, S.S.; Clary, B.M.; White, R.R.; Tyler, D.S.; Blazer III, D.G. Feeding Jejunostomy Tube Placement in Patients Undergoing Pancreaticoduodenectomy: An Ongoing Dilemma. J. Gastrointest. Surg. **2014**, 18, 1752–1759.
25. Perineal, J.; Mariette, C.; Dousset, B.; Sielezneff, I.; Gainant, A.; Marbut, J.Y.; Bin-Dorel, S.; Bechwaty, M.E.; Delaunay, D.; Bernard, L.; et al. Early Enteral Versus Total Parenteral Nutrition in Patients Undergoing Pancreaticoduodenectomy: A Randomized Multicenter Controlled Trial (Nutri-DPC). Ann. Surg. **2016**, 264,731–737.
26. Braga M, Pecorelli N, Ariotti R, et al. Enhanced Recovery After Surgery Pathway in Patients Undergoing Pancreaticoduodenectomy. World J Surg 2014;38:2960-6.
27. Lassen K, Kjaeve J, Fetveit T, et al. Allowing normal food at will after major upper gastrointestinal surgery does not increase morbidity a randomized multicenter trial. AnnSurg 2008; 247:721-9.