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Feasibility, acceptability of enteral tube feeding and self-insertion of a nasogastric tube in the nutritional management of digestive cancers, impact on quality of life

Running Head: enteral tube feeding in digestive cancers

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ABSTRACT

No study has evaluated the feasibility of enteral tube feeding (ETF) in undernourished patients with newly diagnosed gastrointestinal (GI) cancer.

Objectives

Evaluate the acceptability of ETF in patients unable to increase their dietary intake and with a weight loss > 10% or albuminemia < 30g/L or BMI < 18.5 before surgery, or a weight loss > 5% during chemotherapy. The feasibility of self-insertion of a nasogastric tube was also assessed.

Results

A total of 308 patients were nutritionally screened during a one-year period. ETF was indicated in 123 cases. Overall acceptability was 78.9% and was higher when weight loss was > 10% ($p<0.0001$) and before surgery ($p<0.0001$), lower during chemotherapy ($p<0.0001$), while not influenced by dietary intake or location of the cancer. Forty patients managed a daily self-insertion of the feeding tube (45.5%) and 48 had a nasogastric tube maintained in place. All Quality of Life (QoL) parameters were significantly improved, notably physical role functioning ($+20.9\% \pm 24.0$, $p<0.005$) and mental health ($+21.0\% \pm 17.7$, $p<0.005$).

Conclusion:

According to the present algorithm, ETF was indicated in 39.9% of cases and accepted in 78.9% of newly diagnosed patients with primary GI cancer while improving QoL. This study strengthens the place of self-insertion of feeding tubes in clinical practice.

Key Words:

Enteral tube feeding, gastrointestinal cancer, chemotherapy, surgery, quality of life

INTRODUCTION

Malnutrition is highly common in patients with gastrointestinal cancer [1]. In these patients, malnutrition plays a major role in the increase in morbidity and mortality observed in operative and perioperative care and during adjuvant therapy[2-4]. Malnutrition, identified by a weight loss >10% and/or low serum albumin concentration (<30 g/L) is a major risk factor of postoperative adverse outcome [5-7]. Treatment of malnutrition, when diagnosed before surgery, can reduce the induced risk of postoperative complications[8]. Furthermore, gastrointestinal cancer patients have been demonstrated to experience a reduction in post-operative infectious complications especially when given oral/enteral “immune-modulating nutrition” in the perioperative period [9, 10].

In medical oncology, malnutrition leads to adverse consequences such as poorer prognosis and treatment outcome [2, 11], reduced functional status [12], reduced quality of life [2, 13], increased risk of chemotherapy- or radiotherapy-induced toxicity [2, 11], and ultimately leads to a lesser chance of survival[6] especially due to failure in completing adjuvant chemotherapy [14] and poor tumour response to therapy [15]. Furthermore, malnutrition is also associated with longer hospital stay, poorer hospitalisation outcomes and higher healthcare costs [16].

For these reasons, screening for malnutrition in patients with gastrointestinal cancer should be initiated immediately at the onset of care, with the aim to maintain or improve nutritional status, maintain skeletal muscle mass and physical performance, reduce the risk of reductions or interruptions of scheduled anticancer treatments, and finally improve patient health-related quality of life (HRQoL)[10].

In a systematic review and meta-analysis, Halfdanarson et al. showed that nutritional support is justified in patients with poor oral intake and weight loss, leading to improved HRQoL in cancer patients [17]. In a second meta-analysis, Balwin et al.[18] also showed that dietary intervention (nutritional counselling, oral supplements, or both) in malnourished or malnutrition risk cancer patients significantly improved their HRQoL although with no effect on survival. The same findings were also observed in other studies with adjuvant radiotherapy[18] in cancer patients. During chemotherapy, weight loss being a common side effect of targeted therapies [19], such loss has been associated with an increased risk of toxicity, impaired quality of life, and shorter

64 survival. Hence, weight stabilisation for patients undergoing chemotherapy for gastrointestinal
65 cancers may be correlated with a significant improvement in survival[20, 21].

66 The type of nutritional intervention in cancer is the subject of much debate [10]. The European
67 Society for Clinical Nutrition and Metabolism (ESPEN) guidelines[10], as well as the French
68 recommendations [22], recommend the use of enteral nutrition or, if the latter is not sufficient or
69 possible, parenteral nutrition in patients undergoing curative anticancer drug treatment, when oral
70 food intake is inadequate despite counselling and oral nutritional supplements. Parenteral
71 nutrition is clearly associated with increased complications and infections and given the lack of
72 data on parenteral nutrition in weight-losing patients receiving targeted therapy, such approach
73 should be avoided. On the other hand, enteral tube feeding can be a source of discomfort and
74 reluctance from patients. For this reason, we developed a specific therapeutic patient education
75 (TPE) programme, the aim of which is to improve the tolerance and acceptability of tube feeding
76 and to show that self-insertion of a nasogastric tube represents an alternative and effective
77 method to gastrostomy and the nasogastric tube maintained in place, and is well tolerated by
78 patients receiving enteral nutrition [23].

79 Given the high prevalence of malnutrition at diagnosis and during cancer treatment (from 20% to
80 70%)[10], we conducted a pilot study to determine the feasibility of proactive enteral tube
81 feeding in patients with newly diagnosed GI cancer [24-26].

83 SUBJECTS AND METHODS

84 The present is a single-arm, interventional, prospective study including all adult (>18 years)
85 patients with newly documented cancer of the gastrointestinal tract (oesophagus, stomach,
86 pancreas, biliary tract or colon cancer), who were candidates for major elective surgery, adjuvant
87 chemotherapy before surgery or for chemotherapy alone and admitted in our institution between
88 April 1st 2015 and March 31st 2016. All were screened for malnutrition and underwent a
89 systematic dietary assessment.

90 All eligible patients gave their written informed consent. The study protocol was approved by the
91 ARS (Agence Régionale de Santé) of Lorraine, France (authorisation number
92 J4G9045PRO/2010).

Nutritional Assessment

Nutritional status (NS) was assessed using anthropometric measurements (BMI: body mass index = body weight/height²), weight loss within 6 months, and an index of food intake using 10-point verbal (AVeS) and visual (AViS) analogue scales[26]. Plasma albumin concentration was systematically analysed.

Nutritional counselling and nutritional support (**Figure 1**)

Nutritional counselling was systematically offered. As proposed by ESPEN[10], the nutritionist provided individualised advice to achieve energy and nutrient balance. Critical purposes of nutrition counselling were: (1) to provide the patient with the justifications and goals of nutritional recommendations, and (2) to motivate the patient to adapt to the resulting altered nutritional demand of his or her disease. Oral nutrition support included regular food or fortified food (meals or snacks) and oral nutritional supplements (ONS) to fill nutritional gaps when patients were at nutritional risk. Furthermore, all patients who had a programmed surgery, regardless of their nutritional status, received oral or tube-fed immuno-nutrition (pharmaco-nutrition), containing omega3 fatty acids, nucleotides and arginine, 7 days before the surgery, as recommended by the French and ESPEN recommendations [10, 24]

Dietary intervention (nutritional counselling, oral supplements, or both)

Dietary intervention administered systematically prior to surgery when the delay between the nutritional screening and the surgery was greater than 1 month, as well as during adjuvant chemotherapy or during chemotherapy, was also tested. This intervention was assessed within 1 week, both in terms of evaluation of food intake (reduced food intake less than 30%) and on weight gain.

Enteral tube feeding (ETF) was systematically offered:

- prior to surgery (Figure 1A): in case of a weight loss within 6 months of more than 10% regardless of the daily energy deficit, and regardless of the reduction in food intake [24], or if albuminemia was less than 30g/L, or if BMI < 18.5 (< 21 if age > 70 years) [25, 26], immediately or after testing a dietary intervention (nutritional counselling, oral

supplements, or both) if the delay between the nutritional screening and the surgery was greater than 1 month.

- during adjuvant chemotherapy before surgery (**Figure 1B**): in case of a recent weight loss of more than 10% regardless of the daily energy deficit, or in case of a recent weight loss of more than 5% after testing a dietary intervention (nutritional counselling, oral supplements, or both)
- during chemotherapy (**Figure 1B**): in case of a recent weight loss of more than 5% within 6 months associated with a reduction in food intake corresponding to a daily energy deficit > 30%, immediately or after testing a dietary intervention (nutritional counselling, oral supplements, or both).
- Patients gave their written informed consent for the Therapeutic Patient Education programme (TPE)

Exclusion criteria for ETF

- patients with a diagnosis of terminal malignancy,
- lifespan estimated at less than 60 days.

Exclusion criteria for self-insertion of tube feeding

- swallowing dysfunction, ear-nose-throat (ENT) surgery, anatomical abnormalities of ENT,
- patient with cognitive disability or language barrier restricting therapeutic education.

Enteral nutrition formula,

The objectives were to reach 25 and 30 kcal/kg/day, and above 1 g/kg/day of proteins and if possible, up to 1.5 g/kg/day, including oral and tube feeding nutrition, as recommended by French and ESPEN guidelines. Both hyperenergetic and hyperprotein formulas were used to achieve this goal.

Parenteral Nutrition (PN)

In patients with severe malnutrition and a contraindication for ETF (non-functioning GI, uncontrolled GI side-effects or inability to place an enteral tube), parenteral nutrition was considered and discussed.

Modality of ETF

Cyclic enteral nutrition was administered nocturnally via a nasogastric tube (or jejunostomy for 12 patients); during daytime, patients were able to eat normally and lead their normal life.

Nasogastric tube (NG tube): Fine bore 8 – 10 French gauge silicone NG tubes without guide-wire were used. The first NG tube was placed by an experienced physician or nurse. The position of the NG tube was systematically verified by X-ray and was again verified by injection of air and listening for bubbles with a stethoscope. At this time, the necessary tube length was determined. Next, the patient inserted and tested the NG tube by himself/herself under the surveillance of a nurse. The position of the NG tube was verified after each insertion by injection of air and listening for bubbles with a stethoscope.

Therapeutic Patient Education (TPE) programme ¹⁴

The objective of this programme is to teach the patient the necessary skills and TPE into clinical practice: assessment of disease, treatment, hygiene, adaptability to a new situation, management and control of treatment and ETF technical aspects. An educational diagnosis was first made consisting of spatial and temporal orientation, learning ability, sight and hearing capabilities, adequate housing conditions, and personal hygiene.

These first steps included instructions on indications and principles of Enteral Nutrition (EN). A therapeutic contract between the medical staff and the patient was then established. In a second phase, a personalised TPE programme with learning priorities was defined. Individual or group TPE sessions set during a 3 day-hospitalisation were planned and provided as described in a previous study¹⁴. Throughout this second step, assessment of patient education was based on acquisition of skills (preparation and administration of EN products, role of hydration, administering medications, related care of the NG tube).

Finally, the implementation of skills and TPE into clinical practice was assessed for every patient.

Following the TPE programme, the patient was given a booklet pertaining to self-insertion of the NG tube, including information regarding NG tube positioning, storage and administration conditions of EN, inventory of necessary equipment, installation steps of EN products, screening for complications, course of action in case of adverse events, and contact information of the nutrition medical staff.

Outcome measurements:

Patient outcome measures were acceptability, tolerability and health related quality of life (DUKE).

Acceptability of ETF

It represents the proportion of patients who had an indication for enteral nutrition, without contraindication (patients with a diagnosis of terminal malignancy, lifespan estimated at less than 60 days) and who accept the treatment (acceptability = number of patients who accept tube feeding/total number of indication).

Acceptability of self-insertion represents the proportion of patients who accept enteral tube feeding, without contraindication of self-insertion and who accept the latter (acceptability = number of patients who accept self-insertion/ total number of enteral tube feeding patients without contraindication of self-insertion)

Feasibility particularly concerns self-insertion and was measured by the number of eligible patients without contraindication and who acquired the competencies to practice self-insertion of tube feeding relative to the total number of eligible patients who underwent an ETF.

Patients who did not fulfil the programme with regard to the administration of nutrition and insertion of the tube received dietary intervention (nutritional counselling, oral supplements, or both), during each medical consultation

Patient monitoring

After a 3 day-hospitalisation TPE programme, patients were discharged home, at which two types of monitoring were performed:

(1) by service providers of EN products and equipment necessary for home enteral nutrition (per French legislation - Journal officiel de la République Française (JORF) n°0046 of February 24th, 2010, page 3512, text n°33), the objective of this monitoring being to analyse the tolerance, observance and nutritional assessment (weight, BMI) of the patients.

- D1 after hospital discharge: visit at home by the dietician.

- D2, D3: by phone, to analyse the possible difficulties and observance

- D14; followed by every 3 months: visit at home by the dietician

A detailed report regarding adverse events and the use of feed packs was submitted monthly by the service providers to the medical staff.

(2) by the medical staff

- Nurse's phone calls: once weekly, to analyse the possible difficulties and observance.
- D14; D30 and thereafter every 2 to 3 months: Patients were seen in outpatient care. During each consultation, weight gain and adherence to treatment were evaluated and all adverse events were recorded. Adherence to treatment was self-reported by the patient at each medical visit.

ETF complications:

Complications were collected by service providers and by medical staff by phone or in outpatient care. No serious complications were observed; of note, no patient presented ETF intolerance or pneumonia. Feeding tube complications and adverse effects were never responsible for an ETF interruption. Minimal adverse events were observed, including feeding tube clogging in 3 patients although these patients were all educated in managing the clog and in changing the feeding tube. Other complications included vomiting and diarrhoea, mostly in patients during chemotherapy, thus the accountability of enteral tube feeding could not be proven. Most of the above complications were successfully managed outside of hospital. Almost half of the patients experienced sudden displacement of their feeding tube.

Health Related Quality of Life (HRQoL)

HRQoL was assessed both before and at the end of the TPE programme, at the end of the nutrition support period or at 6 months when the enteral tube feeding was continued beyond that time, by use of a French validated version of the DUKE questionnaire, a 17-item generic self-reporting instrument, with responses rated according to a 3-point Likert scale covering a 1-week time frame [27]. The DUKE questionnaire includes 10 scales, six of which pertain to health function: physical health (items 8-12), mental health (items 1, 4, 5, 13, 14), social health (items 2, 6, 7, 15, 16), general health (aggregation of physical, mental and social health measures to indicate overall well-being) (item 15), perceived health (item 3) and self-esteem (items 1, 2, 4, 6, 7), with high scores indicating better HRQoL; while the 4 remaining scales pertain to health dysfunction: anxiety (items 2, 5, 7, 10, 12, 14), depression (items 4, 5, 10, 12, 13), pain (item 11) and disability (item 17), with high scores indicating greater dysfunction.

Statistical analysis

The intent-to-treat (ITT) population included all patients who received at least one day of EN by self-administered NG tube. Results are expressed as percentages, means \pm standard deviation with data tested for normality by skewness and kurtosis tests. Groups of patients were compared using factorial analyses (ANOVA 2 X 2) and a Sheffé's *F* test if the interaction was significant. Chi-square tests were used to compare treatment groups and cancer localisation between the 3 weight loss groups, and the Kruskal-Wallis rank sum test to test ETF acceptability. A Bonferroni correction was adopted for multiple Chi² comparison (0.05/number of analysis).

A multivariate analysis was performed to determine the parameters associated with acceptability using logistic regression analysis. The dependant variable was acceptability, namely yes or no, while the independent variables were weight loss categories (discontinued values, 0, 1, 2), type of treatment (1= surgery alone, 2 chemotherapy alone, 3 = chemotherapy and surgery) and categories of reduction of food intake (0, 1).

All analyses were performed using the Stview statistical software package 5.0 (Los Angeles, CA).

RESULTS

Three hundred and eight patients newly diagnosed with a primary GI cancer and admitted in our institution between April 1st, 2015 and March 31st, 2016 were all screened for malnutrition. Mean age of the patients was 66.8 ± 10.9 years, 61% of whom were male. Cancer sites consisted of pancreatic adenocarcinoma or cholangiocarcinoma (P) (40.6%), stomach, gastric cardia or oesophageal carcinoma (SO) (23.4%), colon and rectum cancers (CR) (25.0%) and other sites (O) (10.7%).

Nutritional Assessment (Table 1)

Mean BMI corresponding to the fitness weight (stable weight before the malignancy) was 27.3 ± 5.3 kg/m² (mean weight 77.1 ± 16.7 kg), mean initial BMI was 23.8 ± 5.1 and mean weight loss within 6 months was -12.7 ± 8.9 % at inclusion.

The majority of patients (59.7%) were in the “severe malnutrition” group with a weight loss > 10%, among whom 59.8% had a reduction in food intake greater than 30%. Twenty-one percent of patients had “moderate malnutrition” with a weight loss between 5 -10%, among whom 51% had a reduction in food intake greater than 30%, while only 18.5% of patients had a weight loss

less than 5%, among whom 28% had a reduction in food intake greater than 30%. As presented in **Table 1**, among each group, a recent reduction in food intake was observed, the latter of which was significantly greater in the severe malnutrition group ($p=0.0002$).

As described in Table 1, pancreatic cancers and gastric cardia or oesophageal carcinoma were more frequent in the $> 10\%$ weight loss group, $p=0.0371$.

Nutritional supports were significantly different between the groups, with a higher prevalence of enteral tube feeding in the severe malnutrition group ($p<0.0001$).

Acceptability of ETF (Table 2)

Overall acceptability was 78.9%. According to the initial algorithm, 30 patients had no indication due to a palliative care situation, 27 were able to efficiently increase their food intake. Five additional patients received an ETF as a result of personal choice. The clinical characteristics of subjects who refused tube feeding did not differ from those who accepted tube feeding support. Cancer sites did not influence acceptability ($p=NS$).

Acceptability of enteral tube feeding according to the treatment groups (surgery, chemotherapy before or after surgery, and chemotherapy alone) was as follows:

In the “surgery only” group ($n=130$), 35 patients had a tube feeding. Thirty-eight efficiently increased their food intake and 14 refused, among whom 8 were overweight or obese. In this group, acceptability of enteral tube feeding was $35/49 = 71\%$.

In the group of patients with chemotherapy before or after surgery ($n=109$), 39 had a tube feeding. Twelve patients were in palliative care, 26 efficiently increased their food intake and 8 refused, among whom 4 were overweight or obese. In this group, acceptability of enteral tube feeding was $39/47 = 83\%$. Three additional patients had an ETF prior to surgery by personal choice, since they were unable to efficiently increase their food intake sufficiently to take oral immune-nutrition before surgery.

In the group of patients with chemotherapy alone ($n=57$), 21 had a tube feeding. Two patients were in palliative care, 11 efficiently increased their food intake among whom 4 were overweight or obese and 3 refused. In this group, acceptability of enteral tube feeding was $21/24 = 87.5\%$. Two patients in palliative care, without indication for ETF, preferred to receive this treatment. Overall, the acceptability was not statistically different between these groups.

Acceptability of ETF according to nutritional status

In the severe malnutrition group with a reduction in food intake (RFI) greater than 30% (n=110), 7 were in palliative care, 26 efficiently increased their food intake; most of these patients were overweight or obese prior to surgery (n=12, BMI= 28.6 ± 3.2). Fifty-eight patients accepted a tube feeding support immediately or following testing a dietary intervention (nutritional counselling, oral supplements, or both) (n=5) and 14 refused (30%). In this group, acceptability was 63/77 (82.0%).

In the severe malnutrition group with an RFI of less than 30%, 4 were in palliative care and 15 increased their food intake efficiently. In this group, there were 28 indications for ETF (38.3%) and 10 refused (21.3%). Acceptability was 64.3% (18/28) in this group.

Among the moderate malnutrition group with an RFI greater than 30% (n=24), 3 patients efficiently increased their food intake and 3 were in palliative treatment. There was a theoretical indication for tube feeding for 12 patients due to a persistent weight loss during chemotherapy (n=8), or before surgery due to a hypoalbuminemia lower than 30g/L (n=4). Five patients had a tube feeding and one patient refused. Finally, 5/6 (83.3%) patients accepted the ETF. In this group, 3 additional patients had an ETF prior to surgery by personal choice, since they were unable to efficiently increase their food intake sufficiently to take oral immune-nutrition before surgery.

Among the moderate malnutrition group with an RFI lower than 30% (n=43), 9 had an indication for ETF prior to surgery due to a hypoalbuminemia lower than 30g/L (n=4), 2 due to a BMI lower than 18.5 kg/m², and 2 due to a persistent weight loss during chemotherapy. Eight of 9 patients accepted the ETF (89.0%). Two additional patients received ETF despite palliative care by personal choice.

Among the stable weight group, 7 patients had a hypoalbuminemia lower than 30g/L prior to a scheduled surgery. Four patients efficiently increased their food intake and 3 had an indication for ETF and accepted the latter. Finally, 3/3 (100%) accepted ETF in this group.

In the stable weight group with a food intake greater than 70%, there was no indication for ETF.

Finally, ETF was significantly more frequent in patients with a weight loss greater than 10% ($p < 0.001$) while the acceptability was higher in patients with a reduction in food intake greater than 30%.

Multivariate analysis

Multivariate analysis (**Table 3**) revealed that acceptability was significantly increased in patients with a weight loss greater than 10% and was conversely less acceptable in patients during chemotherapy alone or before or after surgery.

Enteral tube feeding and daily self-insertion of the feeding tube

Eighty-eight patients had a nasogastric feeding tube and 12 patients had a jejunostomy feeding tube for a mean period of 102 ± 90 days (range 7 – 330 days). Seven patients had long-term enteral tube feeding. All of these patients were included in a Therapeutic Patient Education programme. Sixty-three subjects (63%) in this cohort were men. The mean ages for men and women were $67.0 \text{ years} \pm 9.6$ (range=37-88).

Among the group who had a nasogastric feeding tube (n= 88 patients), 38 (43%) had a contraindication for feeding tube self-insertion due to a physical or cognitive incapacity, and 10 out of 50 patients refused self-insertion. Forty patients managed a daily self-insertion of the feeding tube and 48 had a nasogastric tube maintained in place. The acceptability of feeding tube self-insertion was 80% (40/50) and feasibility was 45.5% (40/88).

~~Overall acceptability was 79.4%. According to the initial algorithm, 30 patients had no indication due to a palliative care situation, 27 were able to efficiently increase their food intake. Five additional patients received an ETF as a result of personal choice. The clinical characteristics of subjects who refused tube feeding did not differ from those who accepted tube feeding support. Cancer sites did not influence acceptability (p=NS).~~

Impact of ETF and the Therapeutic Patient Education programme on quality of life

At the end of the study, among the 88 patients who underwent nasogastric tube feeding, 7 patients died during the study, 1 interrupted his follow-up, 9 were in terminal palliative care and 10 had not finished their TPE programme at the end of the study. Patients with a jejunostomy were excluded from this specific analysis. Sixty patients completed the TPE and were investigated using QoL questionnaire prior to as well as at the end of the nutrition support or at 6 months when the enteral tube feeding was continued beyond that time. The mean delay between the 2 questionnaires was 73 ± 63 days (median= 48.5 days).

All QoL parameters were significantly improved following the TPE programme, the most notable of which were physical role functioning (mean $+20.9 \pm 24.0$ %, $p < 0.005$) and mental health (mean $+21.0 \pm 17.7$ %, $p < 0.005$).

Other improved parameters were social health (mean $+6.4 \pm 16.7$ %, $p < 0.05$), general health (combination of physical, mental and social health measures to indicate overall well-being) (mean $+12.8 \pm 13.6$ %, $p < 0.005$), perceived health (mean $+30.4 \pm 57.9$ %, $p < 0.05$), self-esteem (mean $+13.4 \pm 18.2$ %, $p < 0.005$), health dysfunction: anxiety (mean $+15.0 \pm 17.7$ %, $p < 0.005$), depression (mean $+20.1 \pm 18.8$ %, $p < 0.005$), pain (mean $+19.6 \pm 49.7$ %, $p < 0.05$) and disability (mean $+37.0 \pm 65.9$ %, $p < 0.05$).

Parenteral nutrition

In the present cohort, all of the patients had a functional bowel, hence there was no indication for parenteral nutrition.

Discussion

To our knowledge, this is the first study testing the feasibility and acceptability of enteral tube feeding according to the European guidelines of nutritional support in cancer patients in an outpatient setting. The present study shows that enteral tube feeding can be very well accepted by patients with digestive cancer and was able improve their quality of life. Management via a TPE programme allowed attaining an acceptability of 82%, especially for patients with severe malnutrition. Overall, ETF was accepted by 79.4% of patients in need of nutritional support. Furthermore, 80% of these patients, in the absence of contraindication of self-insertion, placed their feeding tube on their own every evening. Most importantly, if patients had the choice between the self-inserted NG tube and a long-term NG tube, all would prefer self-insertion of the NG tube [23]. The optimal tutoring conditions with the help of a specialised clinical nurse as well as a specific therapeutic patient education programme are potential reasons explaining these results. This programme was indeed specifically developed to enable self-management in enteral nutrition owing to experienced health professionals cooperating with patient representatives to strengthen patients' approach and ensure feasibility.

Acceptability of tube feeding has not previously been explored in a systematic patient cohort study. In Crohn's disease, one questionnaire-based study showed that the majority of patients would prefer a solid food diet alternative [28], while many studies mainly analysed the potential barriers to the acceptance of gastrostomy tube feeding (reviewed in [29]). Only half of the reviewed studies reported positive perceptions towards percutaneous endoscopic gastrostomy (PEG) feeding. Both the present study as well as our previous study [23] show that daily self-insertion of the feeding tube may represent an appealing alternative to PEG. European guidelines on artificial enteral nutrition recommend a nasogastric tube for short periods and a PEG or a jejunostomy for a period exceeding 2–3 weeks [30]. We propose a safe alternative to enteral nutrition with the daily self-inserted nasogastric tube for home enteral nutrition. Self-insertion of a nasogastric tube can only be achieved, however, through a therapeutic education programme, after careful assessment of the patient's skills. Such approach can be effective and well tolerated in patients eligible for this programme and who require EN at home. In this study, many patients resumed enteral tube feeding after surgery or after a chemotherapy cycle, when anorexia increased and food intake decreased. However, in both the present as well as in our previous study [23], we exclusively selected patients who could safely self-insert their nasogastric tube. Patients were ineligible if they had a swallowing disorder; ear, nose or throat surgery; anatomical abnormalities of the ears, nose or throat; cognitive disability; or a language barrier preventing therapeutic education. The proportion of ineligibility herein was nevertheless high, considering there were 38/88 (43%) patients who had a contraindication to tube self-insertion, similarly that that observed in our previous study (37/66, 56%)[23].

The indications for enteral tube feeding may seem excessive, especially in patients undergoing curative anticancer drug treatment. In this situation, ESPEN guidelines [9] recommend supplemental enteral nutrition or, if not sufficient or possible, parenteral nutrition if oral food intake is inadequate despite counselling and oral nutritional supplements (ONS). Malnourished or weight-losing cancer patients receiving anticancer treatment who are anticipated to be unable to ingest and/or absorb adequate nutrients for more than 1-2 weeks are candidates for artificial nutrition, preferably by the enteral route. French recommendations [21] and ASPEN guidelines [31] recommend enteral tube feeding in case of malnutrition and/or an incapacity to eat during 7-14 days. Moreover, according to these recommendations, the weight loss thresholds associated with an increased risk of morbidity and mortality in medical oncology is 5%.

At the end of the present study, 60 patients completed the TPE programme, the benefits of which were investigated through a health-related QoL questionnaire: improvements in home activities, social activities, family relationships, physical well-being, and mental well-being were the major benefits reported by the patients. Furthermore, all patients who performed self-insertion of the feeding tube were able to remove their feeding tubes for a good portion of the day.

The present findings furthermore showed that enteral tube feeding included in a TPE programme was able to significantly improve the quality of life in patients undergoing chemotherapy, or before or after surgery. In the systematic review by Baldwin et al. [18], quality of life was significantly improved on the global QoL scale. However, unlike the present study, positive results were observed only in those studies in which patients received adjuvant radiotherapy, whereas negative results were obtained in the studies that included patients undergoing systemic chemotherapy. In the systematic review and meta-analysis by Halfdanarson et al., the authors studied the effect of nutritional counselling on quality of life [17]. Five randomised clinical trials with a total of 488 patients were included. The standardised mean difference in QoL scores between those who received nutritional counselling versus no nutritional counselling was 0.56 (0.01-1.14, $p < 0.06$). ESPEN guidelines concluded that this borderline statistical significance, in combination with a point estimate in favour of the intervention, suggests that nutritional counselling may be justified in select patients suffering from especially poor oral intake and weight loss.

Nutritional therapy in cancer patients who are malnourished or at risk of malnutrition has been shown to improve body weight and energy intake but not survival [18, 32]. However, in patients undergoing adjuvant radiotherapy, there is strong evidence that nutritional support improves intake and weight, as well as some aspects of quality of life [33-35].

Our study has several important limitations, the most noteworthy being its observational nature. This study was not intended to analyse the effects of management on nutritional efficiency and survival, but rather to analyse the feasibility of enteral tube feeding. Only long-term outcome analysis will show whether enteral tube feeding has an impact on survival. The conclusion on the impact of ETF on quality of life should moreover be interpreted with caution given that this observational study does not assess the impact of the type of care on quality of life. Quality of life can be improved due to the very regular and close follow-up of patients who have

accepted enteral nutrition. Lastly, the proportion of ineligibility herein was nevertheless high, ranging from 43% - 56% [23]

CONCLUSION

The present study shows the clear feasibility of introducing enteral nutrition in patients with digestive cancer when it is not possible to increase food intake, or for weight loss from, 5% during chemotherapy and 10% before surgery. According to the present algorithm, enteral nutrition was indicated in 39.9% of cases and accepted in 78.9% of cases. Acceptability was higher in patients with >10% weight loss and during chemotherapy. While the place of self-insertion remains to be conclusively established, such approach was successfully used in 45.5% of patients who accepted ETF.

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AUTHORS CONTRIBUTION

Didier Quilliot : design of the study, practical performance, preparation of the manuscript

Niasha Michot : practical performance

Justine Krier : practical performance

Lucie Germain : design of the study

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Aurélie Malgras : design of the study, practical performance

487 Phi-Linh Nguyen-Thi : design of the study, data analysis

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489 **CONFLICT OF INTEREST STATEMENT**

490 The authors declare no conflict of interest for this study.

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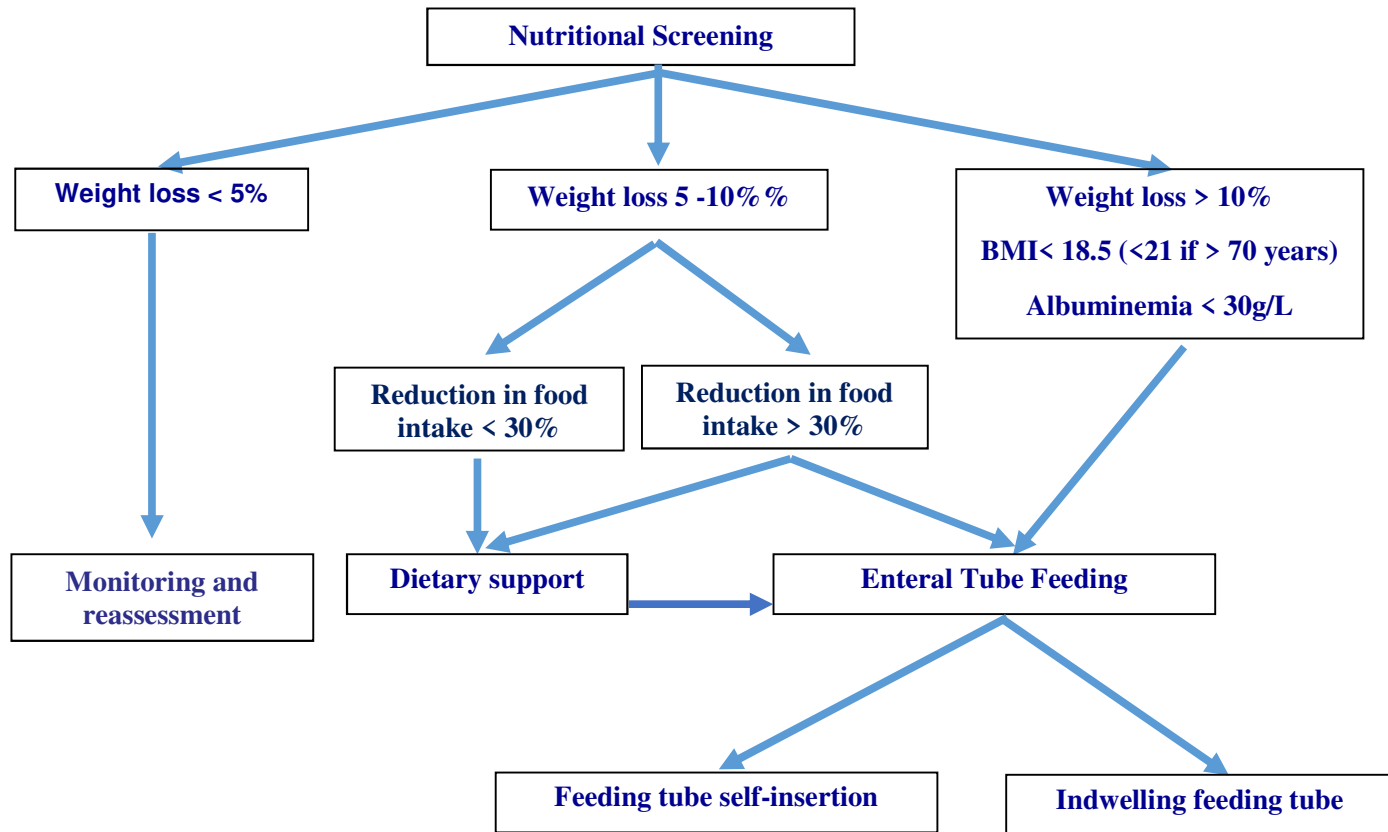
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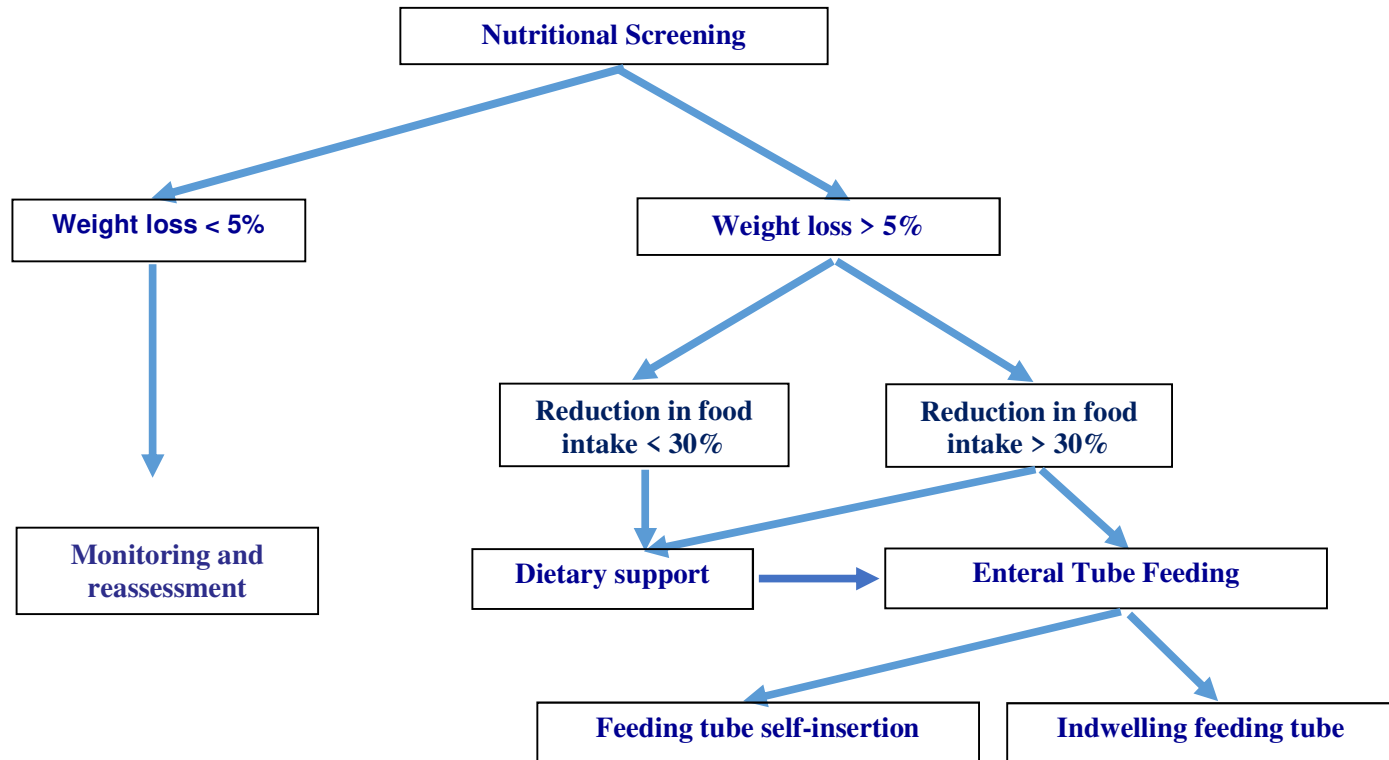
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- 1 **Figure 1:** Nutrition management algorithm, **1A:** before surgery for digestive cancer, **1 B:** Nutrition
- 2 management algorithm during chemotherapy for digestive cancer
- 3

1A: before surgery for digestive cancer



1B: Nutrition management algorithm during chemotherapy for digestive cancer



1 **Table 1: Patient characteristics (screening) and final nutritional support**

Weight loss group	No malnutrition weight loss <5% n=57		Moderate malnutrition weight loss 5% – 10% n= 67		Severe malnutrition weight loss >10% n= 184		Total	ANOVA (2X2) p interaction and p Chi²
Sex ratio	20/37		25/42		75/109		120/308	P=NS
Cancer location (most frequent to least frequent)	38% CR/ 29.8 % P/ 24.5% SO/ 7% O		46.3%P/ 26.9%CR/ 13.4% SO / 13.4% O		42.1 P/ 26.8% SO / 20.2%CR/ 10.9% O		40.6% P, 25.0% CR, 23.4% SO, 10.7% O.	p= 0.0371
Reduction in food intake (% , n)	< 30% 72% (41)	> 30% 28% (16)	< 30% 64.2% (43)	> 30% 35.8% (24)	< 30% 40.2% (74)	> 30% 59.8% (110)		p Chi²= 0.0002
Sex ratio	13/28	7/9	15/28	10/14	30/44	46/64		p Chi² = NS
Age (mean ± SD)	68.7 ± 9.7	68.8 ± 6.7	68.7 ± 14.0	67.7 ± 10.2	65.6 ± 10.5	65.6±10.9	66.8 ± 10.9	NS
Weight loss % (mean ± SD)	-1.35±2.7	-0.62±4.3	-7.5±1.5	-7.3±1.4	-16.9±6.6	-19.2±7.1	12.7 ± 8.9	p Maln < 0.0001 p Rfi = NS p interac = NS
BMI (mean ± SD)	26.3±5.1	29.2±9.0	23.3±3.5	23.2±4.3	22.9±4.5	22.8±4.6	23.8 ± 5.1	p Maln < 0.0001 p Rfi = NS p interac = NS
Nutr. support (% , n)								
Nutr. Couns.	70.7% (29)	25% (4)	41.9 (18)	20.8% (5)	31.1% (23)	10.1% (11)	Total n= 90	Chi²: p<0.0001
Nutr. Couns. + ONS	29.3% (12)	56.2% (9)	37.2% (16)	50% (12)	44.6% (33)	33.0% (36)	Total n= 118	
Nutr. Couns. + ETF	0	18.7% (3)	20.9% (9)	29.2% (7)	24.3% (18)	57.8% (63)	Total n= 100	

2 Cancer sites included pancreatic adenocarcinoma or cholangiocarcinoma (P), stomach, gastric cardia or oesophageal carcinoma (SO),
3 colon and rectum cancers (CR) as well as other sites (O). BMI: body mass index = body weight/length², weight loss (fitness weight-
4 initial weight)*100/fitness weight; reduction in food intake was evaluated according to the index of food intake using 10-point verbal
5 (AVeS) and visual (AViS) analogue scales²⁵. ONS: Oral Nutritional Supplement, Nutr. Couns: Nutritional Counselling. Maln=
6 malnutrition group effect; Rfi=reduction food intake effect

7

8 Table 2: Indication and acceptability of tube feeding, when indicated, according to nutritional status and cancer treatment.

Weight loss group	<5% n=57		Moderate malnutrition 5% – 10% n= 67		Severe malnutrition >10% n= 184		Indication	p (Kruskal-Wallis rank sum test)
Reduction in food intake	< 30% n= 41	> 30% n= 16	< 30% n= 43	> 30% n= 24	< 30% n= 74	> 30% n= 110		
Treatment							Total	Acceptability of ETF
None	0	0	7% (3)	4.1% (1)	1.3% (1)	6.4% (7)	-	
Surgery	48.7% (20)	50% (8)	35.0% (15)	62.5% (15)	31.1% (23)	45.0% (49)	n= 49/130 (37.7)	35/49 (71%)
Chemotherapy	14.6 % (6)	25% (4)	21.0% (9)	12.5% (3)	21.6% (16)	17.4% (19)	n= 24/57 (42.1%)	21/24 (87.5%)
Surgery and adjuvant chemotherapy	36.6 % (15)	25% (4)	37.2% (16)	20.8% (5)	45.9% (34)	32.1% (35)	n= 47/109 (43.1%) p = NS	39/47 (83%) P = NS
Indications		18.7% (3)	21% (9)	25% (6)	37.8% (28)	70% (77)	39.9% (123) p < 0.001	
Acceptability		100% (3)	89.0% (8)	83.3% (5)	64.3% (18)	82.0% (63)	78.9% (97)	p = 0.0207

9 ETF: enteral tube feeding

Table 3: Normalised coefficients of Enteral Tube Feeding (ETF) acceptability level

	Coeff.	SD	P
Treatment			
Adjuvant			
chemotherapy	-0.211	0.056	< 0.0001
Chemotherapy	-0.351	0.056	< 0.0001
Surgery	0	0	
Weight loss			
> 10%	0.401	0.068	< 0.0001
5-10%	0.050	0.067	0.460
<5%	0	0	

Reduction in food intake and cancer site had no significant effect on acceptability level

The dependant variable is acceptability: yes or no, the independent variables were weight loss categories (discontinued values, 0, 1, 2), type of treatment (1= surgery alone, 2 chemotherapy alone, 3 = chemotherapy and surgery) and categories of reduction of food intake (0, 1).

**Table 4: Characteristics of patients accepting Enteral Tube Feeding (ETF) intervention
(mean \pm SD or percentage)**

	Enteral Tube Feeding n=100
Tube feeding duration	123 \pm 126 days (7—550)
Cancer %	54% pancreatic adenocarcinoma or cholangiocarcinoma (P) 25% stomach, gastric cardia or oesophageal carcinoma (SO) 11% colon and rectum cancers (CR) 10% other sites (O)
Age (years)	67.0 \pm 9.6
Weight loss %	-17.3 \pm 8.6
BMI before cancer	26.8 \pm 5.1
BMI when screening	22.1 \pm 4.6
Decrease in food intake (visual analogue scale)	48.6% \pm 27.8%
Albuminemia g/dL	3.00 \pm 0.81
Treatment	
None	6%
Surgery	35%
Chemotherapy	20%
Surgery+ Chemotherapy	39%
Nasogastric tube	88
Jejunostomy	12

BMI: body mass index