

## Consensus guidelines are required for the peri-operative nutritional assessment and management of patients who undergo surgical resection for suspected pancreatic cancer

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### Abstract

Surgical resection remains the only treatment option for patients with pancreatic cancer who wish to achieve long-term survival. Despite recent advances, this is associated with considerable morbidity and mortality. Surgical candidates are frequently malnourished, and this is known to negatively affect outcomes. Despite this, the nutritional assessment and management of pancreatic cancer patients remains highly variable and there is no consensus. We argue that a specialist nutrition professional should be involved pre-operatively to optimise outcomes and to identify patients who require additional support. Micronutrient deficiencies are common amongst surgical candidates; it is unknown whether this affects outcomes. Furthermore, it is unknown if correcting deficiencies is of benefit. Robust studies are required to investigate this. Finally, there is limited evidence to support the use of prehabilitation in pancreatic surgery, but this is starting to emerge. The present short communication aims to review the recent literature and comment on the above issues.

**Keywords:** Pancreatic cancer, Pancreatic ductal adenocarcinoma, Pancreatico-duodenectomy, Resection, Nutrition, Dietitian, Micro-nutrient, Prehabilitation

### Abbreviations:

PC = pancreatic cancer  
USA = United States of America  
UK = United Kingdom  
PEI = pancreatic exocrine insufficiency  
PERT = pancreatic exocrine replacement therapy

### Introduction

Pancreatic cancer (PC) is the most lethal common cancer, globally it resulted in over 432,000 deaths in 2018 and this figure is set to rise [1]. It is predicted that, by 2040, PC will be the second biggest cancer killer in the United States of America (USA) [2]. Treatment options are limited since the disease often presents at a late stage. Surgery remains the only treatment option that offers a potential cure for patients who are fit and have localised disease. Unfortunately, only about 10-20% of newly diagnosed patients are suitable surgical candidates [3]. Despite advances to surgical techniques and peri-operative care, surgical resection remains high-risk and overall survival is poor [4].

Patients who undergo resection for suspected PC are frequently malnourished, this is a known poor prognostic indicator [5]. It has recently become apparent that the nutritional assessment and management of this group of patients is highly variable across the United Kingdom (UK). In addition, micronutrient deficiencies are common in surgical candidates and it is unknown whether correcting these would improve outcomes [6]. Finally, there are proven benefits to the use of prehabilitation programmes in colorectal surgery yet their use remains inconsistent in pancreatic surgery [7,8]. Since pancreatic resection is associated with such high morbidity and mortality, we argue every effort should be made to optimise outcomes. The present article aims to review the recent literature and comment on these issues.

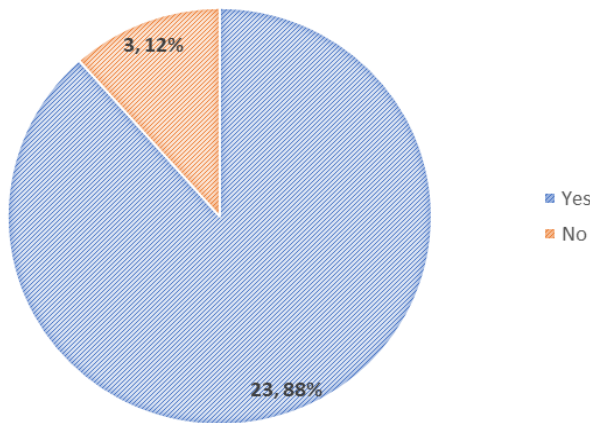
### Nutritional assessment

Over half of all patients who present for PC surgery are at moderate-to-severe risk of malnutrition [9]. All patients are likely malnourished to some degree. The reasons behind this are multiple. Firstly, these patients have an underlying cancer; the association between malignancy and malnutrition is well described [10]. Sec-

only, most PC patients have a degree of pancreatic exocrine insufficiency (PEI) at diagnosis [11]. The fibrosed pancreatic ducts secrete less pancreatic juice and less of this reaches the duodenum due to obstruction of the main duct, this results in maldigestion and malabsorption [12]. In addition, PC also affects the endocrine pancreas and up to half of patients are insulin deficient at diagnosis [13]. Malnutrition is associated with increased overall morbidity and mortality following surgery for PC [5]. Furthermore, malnourished patients are more likely to experience post-operative pancreatic fistula, surgical site infection, and prolonged length of stay [5].

Since 2009, UK guidelines have recommended that pancreatic resection teams include a specialist nutrition professional. Formal nutritional assessment allows for patient optimisation as well as identifying those who require additional support. Whilst the number of UK units with a specialist dietitian has increased since 2009, some units still do not have access to one (Figure 1). Recent international surveys have highlighted that specialist dietitian involvement may be even less frequent in Spain and Korea[14,15]. It is difficult to prove the value a specialist dietitian brings since the evidence is of low quality. However, there are surely benefits to these high-risk patients who are almost always malnourished and then undergo major surgery which has a profound impact on the gastrointestinal tract.

Among the UK units that do have access to a specialist nutrition professional, nutritional assessment and dietetic practice varies considerably. Half of UK units do not perform nutrition risk screening. Again, there is no high-quality evidence which suggests this leads to adverse outcomes, but it would seem a practical and low-cost way of rapidly identifying patients who require additional input. Among UK units there are also huge differences regarding the components of a nutritional assessment and the use of pancreatic exocrine replacement therapy (PERT). No formal recommendations exist to guide clinicians on these issues, and it would seem a consensus is required.



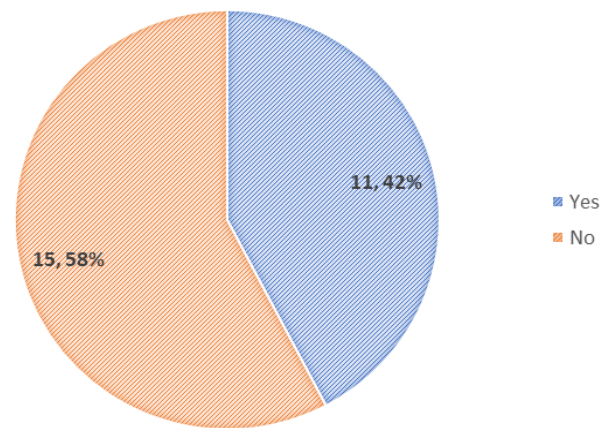
**Figure 1:** Do your patients receive input from a specialist dietitian?

Not all UK pancreatic resection units have access to a specialist nutrition professional despite recommendations from 2009.

### Micronutrients

Micronutrients, often referred to as vitamins and minerals, have numerous important functions e.g., zinc is required for cell and enzyme production, vitamin D is essential in calcium homeostasis, selenium optimises immune cell functioning, and iron is central to erythrocyte production. Much of these functions are directly involved in the processes which are necessary for a successful recovery from major surgery. A recent single-centre study highlighted that, among those who underwent pancreatic resection for suspected cancer, 79% were zinc deficient, 58% were vitamin D deficient, 38% were selenium deficient, and 35% were iron deficient[6]. It is likely that deficiencies in these micronutrients, as well as others, correlate with poor outcomes although this remains unproven. Whether correcting micronutrient levels would improve outcomes is also unknown. Interestingly, there are UK guidelines which advise checking micronutrient levels prior to bariatric surgery but no such guidelines exist for pancreatic resection [16].

A recent UK-wide survey highlighted that most units do not check micronutrient levels either pre- or post-operatively (Figure 2). In those who do, the components of a screen vary wildly between units. We argue that further studies are required to investigate the prevalence of micronutrient deficiency, and borderline deficiency, in the pre- and post-operative period, and to study the impact on correcting deficiencies on short- and long-term outcomes following pancreatic resection, as this may result in subtle benefits.



**Figure 2:** Do you check micronutrient levels in those who undergo pancreatic resection?

Most UK units do not check micronutrient levels. The relevance of this is unknown.

### Prehabilitation

Prehabilitation is a relatively new concept. It refers to the pre-operative optimisation of a patient's general condition to enable them to withstand a stressor i.e., surgery [17]. Prehabilitation should be patient-centred and aspects can focus on exercise, nutrition, smoking status, alcohol consumption, and psychology, and can involve various members of the multi-disciplinary team[17]. It can include interventions such as prescribed exercise plans, specialist dietitian dietary advice, counselling, and occupational therapy. There is good evidence to suggest that structured prehabilitation programmes can improve outcomes following surgery for colorectal cancer [18].

Whilst still limited, data is beginning to emerge which supports the use of prehabilitation prior to pancreatic resection [8]. Bundred et al carried out a recent meta-analysis which included six studies and 193 patients who underwent pancreatic resection for suspected cancer. All studies showed either improved muscle mass or markers of muscle function following prehabilitation [19]. The authors concluded that a structured and supervised programme was required to maximise adherence and that further studies are required to standardise programmes and obtain a consensus on the optimum length and timing of prehabilitation [19]. Ausania et al, in a randomised trial, compared the outcomes of 18 patients who received prehabilitation prior to pancreatic resection, to 22 who went straight to surgery. Although overall morbidity and mortality was similar between the two groups, delayed gastric emptying was less common in those who received prehabilitation and long-term outcomes were not studied [8].

In another small study, Baimas-George et al demonstrated that pre-operative frailty scores could be improved after prehabilitation in hepatopancreaticobiliary surgical patients[20]. Also, van Beijsterveld et al report the case of a 75-year-old co-morbid female who underwent pancreatoduodenectomy. A personalised community-based four-week prehabilitation programme was shown to significantly improve her pre-operative functional mobility and she made an uneventful recovery following surgery [21]. A recent UK-wide survey confirmed that almost half of UK units have no prehabilitation program. In those who do, what is provided varies hugely between units. Structured guidelines would arguably increase uptake and result in subtle gains for patients. Further studies are required to advise on the composition of prehabilitation programmes.

## Conclusion

Most patients who undergo surgery for suspected pancreatic cancer are malnourished yet there is no consensus on how patients should be assessed and managed. Micronutrient deficiencies are common in PC patients, and it is unknown if correcting these would improve outcomes. Structured prehabilitation programmes would likely optimise patients and improve outcomes but there is limited evidence to support this, and current practice is highly variable. Consensus guidelines are required on these topics so that subtle gains can be made to morbidity and mortality rates.

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## Disclosure statement

TR and SA declare that there are no conflicts of interest.

## Authorship statement

TR: investigation, writing – original draft, writing – review and editing, project administration. SA: conceptualisation, writing – review and editing, supervision.

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