

ESTIMATING THE SURVIVAL PROGNOSIS OF PATIENTS WITH ADVANCED GASTROINTESTINAL MALIGNANCY ON HOME PARENTERAL NUTRITION: A RETROSPECTIVE, MONOCENTRE STUDY

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BACKGROUND & AIM

The initiation of home parenteral nutrition (HPN) in advanced malignancy patients is a highly controversial topic. Guidelines generally recommend to reserve this therapy for patients with an expected survival longer than 2-3 months.^{1,2} Administering HPN in patients with a shorter survival probably has little benefit, while creating the risk of PN-related complications. Since HPN in advanced cancer patients is becoming increasingly common in our hospital, we wanted to investigate whether current practices are supported by the rational use of HPN.

In this study, we sought to investigate the **proportion of advanced cancer patients receiving HPN in our hospital surviving for longer than 2-3 months**. Furthermore, we wanted to investigate whether the **application of an existing and a de novo developed survival prediction model could improve the estimation of patient survival length**.

MATERIALS & METHODS

2-and 3-month survival proportions with advanced gastro-intestinal malignancy receiving HPN in our hospital during 2008-2016 were examined.

Additionally, agreement (evaluated through the use of Bland-Altman plots) was assessed between observed patient survival times and the current in-hospital survival prediction method (i.e. physician's clinical judgement) or survival estimation by a published prediction nomogram (Figure 1).³

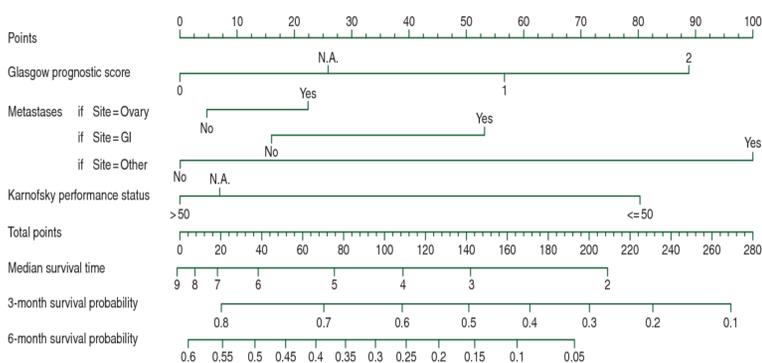


Figure 1: Nomogram developed by Bozzetti et al. for estimating survival length and probabilities of advanced malignancy patients.³

Moreover, through the use of multivariable binary logistic regression analysis (forward stepwise selection method based on Wald coefficient, results considered significant if p-values < 0,05) on clinical and demographic data (e.g. patient age, gender, weight, Karnofsky Performance Score (KPS), Glasgow Prognostic Score (GPS), type of gastro-intestinal tumour, presence of metastatic disease, etc.), as well as biological factors (e.g. CRP, albumin, urea, electrolytes, liver enzymes, etc.) gathered from the studied patient set, both a de novo 2-and 3-month survival prediction model were constructed and externally validated.

RESULTS

The proportion of patients meeting the proposed criteria of **2-and 3-month survival lengths** (n = 250, mean age 60 ± 12 years, 138 (55,2%) men) were **65,2% (n = 163)** and **46,4%, (n = 116)** respectively.

Concerning survival prediction, **clinicians** predominantly tended to **overestimate patient survival** with a proportion of incorrect survival length estimation* for the 2-month cut-off point of **31,7%** (n = 66)** (overestimation of survival in 97,1% (n = 66/68) of patients) and a proportion of **50,0%** (n = 104) (overestimation of survival in 97,1% (n = 101/104) of patients) for the 3-month cut-off point. Furthermore, application of the published **nomogram** did **not improve survival prediction** (proportion of incorrect survival estimation* for 2-and 3-month survival lengths = **29,2%** (n = 73) and **38,4%** (n = 96), respectively). Therefore, using the 250 included patients as a training sample for model construction, de novo 2-and 3-month survival prediction models were developed.

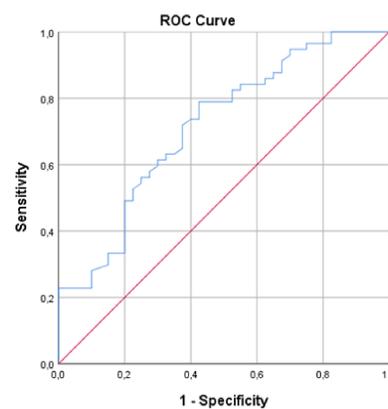
The constructed 2-month prediction model identified KPS, GPS, gender and serum sodium as covariates independently associated with patient survival. However, validation of this model in an independent set of 99 patients (= testing sample) showed a disappointing negative predictive value (NPV) of 0,14 for a survival probability threshold of 0,37°. Therefore, this model was not deemed to be useful for application in clinical practice.

The **constructed 3-month survival prediction model** consisted of **3 covariates: KPS, GPS and serum urea** (see Table 1). **Discriminatory abilities** of this model for a survival probability threshold of **0,25°** in the testing sample were satisfactory and are shown in Figure 2. The proportion of patients with an incorrect 3-month survival estimation (**33,0%, n = 32/99**) was comparable, but not superior to that obtained with the aforementioned published nomogram.

Table 1: Multivariable binary logistic regression analysis for 3-month patient survival of patients with advanced gastro-intestinal malignancy receiving HPN (n = 250)

| Category (reference) | OR (95% CI) | p-value |
|----------------------|---------------------|---------|
| GPS | | |
| - 0 (1 or 2) | 2,436 (1,048-5,665) | 0,039 |
| - 0 or 1 (2) | 2,160 (1,189-3,926) | 0,012 |
| KPS | | |
| - ≤ 50 (> 50) | 0,453 (0,255-0,803) | 0,007 |
| Blood chemistry | | |
| - Urea (mg/dL) | 0,981 (0,966-0,997) | 0,021 |

HPN = home parenteral nutrition, GPS = Glasgow Prognostic Score, KPS = Karnofsky Performance Score, n = number, OR = odds ratio, CI = confidence interval



- Probability threshold value = 0,25
- Sensitivity: 0,96 (n = 57/59)
- Specificity: 0,25 (n = 10/40)
- PPV: 0,65 (n = 55/85)
- NPV: 0,83 (n = 10/12)
- AUC-ROC: 0.716 (SE: 0.053)

PPV = positive predictive value, NPV = negative predictive value, SE = standard error, n = number

Figure 2: Discriminatory abilities of the constructed 3-month survival prediction model with AUC-ROC curve, sensitivity, specificity, positive predictive value and negative predictive value for a survival probability threshold of 0,25

CONCLUSION

This study shows that correct patient survival prediction remains an intrinsically difficult exercise. The discriminatory abilities of the de novo constructed 3-month survival prediction model were promising, but not superior to those obtained through the use of a published nomogram or clinicians survival prediction. In order for these survival prediction models to have clinical utility, further improvement is needed, possibly through a prospective analysis and identification of additional predictors associated with the survival of patients with advanced gastro-intestinal malignancy receiving HPN.

* I.e. patients for which the clinician or nomogram predicted a median survival rate > or < 2-3 months that actually had an observed survival length < or > 2-3 months, respectively.

** Calculated on the total number of patients for which clinicians estimate of survival length was available = 208/250 patients.

° Probability threshold chosen based on a sensitivity level ≥ 0,95 in training sample in order to minimize false negative rate. I.e. if calculated patient survival probability > chosen probability threshold the patient is predicted to survive > 2-3 months and vice versa.

1. Arends J, Bachmann P, Baracos V. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017; 36(1):11-48.

2. Bozzetti F. The role of parenteral nutrition in patients with malignant bowel obstruction. Support Care Cancer. 2019; 27(12):4393-4399.

3. Bozzetti et al. Development and validation of a nomogram to predict survival in incurable cachectic cancer patients on home parenteral nutrition. Ann Oncol. 2015; 26(11): 2335-2340.



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