External validation of a prognostic score for oesophageal cancer (PSOC) for patients treated with palliative intent in a resource-limited setting

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Background. Oesophageal cancer (OC) is common in South Africa (SA), where late presentation limits curative treatment. In resource-constrained settings, staging may not benefit patients with a poor prognosis. The prognostic score for oesophageal cancer (PSOC), based on Eastern Cooperative Oncology Group performance status scale, body mass index and serum albumin, was previously developed to predict short-term survival.
Objective. To externally validate PSOC in an independent cohort.
Methods. We performed a retrospective validation study using prospectively collected data from two public sector hospitals in KwaZulu-Natal Province, SA. Eligible patients had histologically confirmed OC and complete PSOC data, and were treated with palliative intent. The primary endpoint was survival ≥3 months. Logistic regression assessed associations between PSOC and survival. Discrimination was quantified using the area under the receiver operating characteristic curve (AUROC), calibration with the Hosmer-Lemeshow test and accuracy with the Brier score. Secondary analyses evaluated overall survival (OS) with Kaplan-Meier and Cox models.
Results. We included 465 patients (mean age 61 years; male:female ratio 1:1), 97% with squamous cell carcinoma. Higher PSOC scores predicted improved survival (score 4 v. 0: odds ratio 11.87, 95% confidence interval (CI) 4.87 - 28.91; $p<0.001$). AUROC was 0.681 (95% CI 0.630 - 0.732) with good calibration (Hosmer-Lemeshow $p=0.920$). Median OS was 4.8 months, with significant survival differences across score groups (log-rank $p<0.001$). The Brier score was 0.190, indicating good predictive accuracy.
Conclusion. PSOC is a simple, validated tool for predicting short-term survival in OC, and may guide decisions on staging v. palliation in high-incidence, resource-limited settings.

Keywords: oesophageal cancer, palliative care, prognostic score, risk stratification, external validation, survival analysis, AUROC, calibration, Brier score, South Africa

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Oesophageal cancer (OC) is the 11th most common cancer and the seventh leading cause of cancer-related deaths worldwide.[1] South Africa (SA) is a high-incidence area for OC, where the disease is characterised by late presentation and a poor prognosis.[2] The areas with the highest prevalence are the Eastern Cape and KwaZulu-Natal (KZN) provinces – the late stage at presentation results in most patients being suitable for palliative management only. The exact proportion of patients relegated to non-curative management is unknown, but is thought to be between 80% and 95%.[3]

One of the problems faced by clinicians managing patients diagnosed with OC is deciding which patients require staging investigations. While it is desirable, and recommended by international guidelines, to stage all patients, it is not always practical in a resource-constrained environment where it is questionable whether staging investigations would impact the patient's outcome. Many patients, for example, present at a late stage with a poor performance status and signs of malnutrition, and may therefore not tolerate radical treatment modalities such as oesophagectomy, radical radiotherapy, or chemotherapy.[3] Owing to the late stage of presentation, many of these patients are not expected to live beyond 6 - 12 months from the time of diagnosis.[4] It may therefore be prudent to focus on providing optimal palliative care rather than spending time and resources on staging investigations that may not impact the outcome. It may be the case that, in some institutions, many patients with OC are treated palliatively without staging investigations. However, since there are no guidelines on how this should be done, it can only be assumed that the decision is based on individual subjective assessments, like the so-called eyeball test, or institution-based protocols. The eyeball test is used in clinical practice, but its accuracy has been questioned.[5] Attempts have been made to find alternatives to subjective assessments in patients with OC, but only in the context of assessing suitability for radical treatment, such as oesophagectomy, in high-income countries.[6] There is no tool to assess prognosis and guide therapy in patients

with OC in Africa, despite the disproportionately high disease burden and resource constraints.[7]

Previously, we developed and internally validated a clinical prognostic score that can predict the prognosis of patients diagnosed with OC, and therefore aid in decision-making in the clinical context.[8] Building on our preliminary work, the present study aimed to validate the score, called the prognostic score for oesophageal cancer (PSOC), externally, on a new cohort, to assess its accuracy and clinical utility in guiding whether to perform staging investigations or initiate palliative care for patients with OC in high-incidence, resource-limited settings.

Methods

Study design and setting

We conducted a retrospective validation study using prospectively collected clinical data from two public sector hospitals in KZN Province, SA: Grey's Hospital (GH, a tertiary referral hospital for Area 2) and Inkosi Albert Luthuli Central Hospital (IALCH, a quaternary referral hospital for Area 1). Consecutive adults with a diagnosis of OC and treated with palliative intent were eligible. Data were collected at first presentation to IALCH (1 January 2016 - 30 September 2022) and GH (1 November 2020 - 30 April 2025). Most patients underwent palliation with self-expanding metal stents; a minority received palliative radiotherapy or serial dilatations.

Participants and data sources

We included patients with: (*i*) histologically confirmed OC; (*ii*) informed consent; and (*iii*) complete data for all variables required to compute the PSOC. We excluded patients lacking any PSOC component, patients in whom informed consent could not be obtained, patients lost to follow-up, and those without a valid death date (for time-to-event analyses). The decision to treat patients palliatively was based on several factors, including the patient's performance status, general clinical condition and stage of disease.

Data were captured at index presentation and harmonised across sites before analysis.

Predictors and score calculation

PSOC was developed and internally validated previously.[8] In brief, three baseline predictors, Eastern Cooperative Oncology Group performance scale status, body mass index (BMI) and serum albumin, were independently associated with survival beyond 3 months in the development cohort. These predictors were combined into a weighted score ranging from 0 to 4 (Table 1). For clinical interpretability, we analysed the PSOC both as a 5-level categorical variable (0 - 4) and as a pragmatic two-group prognostic classification: scores 0 - 2 indicate a lower predicted probability of survival beyond 3 months, and scores 3 - 4 indicate a higher predicted probability of survival beyond 3 months.

Outcomes

The primary endpoint was survival beyond 3 months (binary: ≥3 months v. <3 months), aligned with guidance on short life expectancy in palliative endoscopy. We also evaluated all-cause overall survival (OS) from index presentation to death. The index date (time zero) was the date of the first presentation at GH or IALCH. Where time was displayed in months, we used a standardised conversion of 28 days per month for consistency with reporting.

Sample size

For external validation of discrimination, we based the minimum sample size on an expected area under the receiver operating characteristic curve (AUROC) of 0.67 from the development study, following Obuchowski's[9] AUROC precision framework and the Hanley-McNeil[10] variance approximation. This yielded a minimum of 128 patients to achieve acceptable precision around the AUROC estimate.

Statistical analysis

We performed complete-case analyses. Baseline characteristics are presented overall and by site (counts/percentages for categorical variables, and mean (standard deviation (SD)) or median (interquartile range (IQR)) for continuous variables. The proposed clinical utility of PSOC was examined by cross-tabulating the primary endpoint across score categories, and by estimating odds ratios (ORs) from logistic regression with PSOC as: (*i*) a categorical predictor for ≥3-month survival; (*ii*) a grouped predictor (0 - 2 v. 3 - 4) for ≥3-month survival; and, secondarily, (*iii*) a categorical predictor for death; and (*iv*) a grouped predictor for death.

For the primary endpoint (≥3-month survival), we fitted logistic regression models to obtain predicted probabilities and 95% confidence intervals (CIs) by score. Discrimination was quantified using the AUROC curve with empirical receiver operating characteristic (ROC) methods; we also report operating points across clinically relevant thresholds. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test with four groups, and visualised using a calibration plot comparing mean observed to mean predicted probabilities with a 45° reference line. Overall probabilistic accuracy was summarised by the Brier score (mean squared error of predicted probabilities; lower values indicate better accuracy). We additionally display the relationship between PSOC and the predicted probability of ≥3-month survival.

For time-to-event analyses, we set the time origin at the index presentation and modelled failure as all-cause death. Kaplan-Meier curves were generated by PSOC category (0 - 4) and, in secondary analyses, by the grouped score (0 - 2 v. 3 - 4), with log-rank tests for between-group differences and risk tables at 6-month intervals. We then fitted Cox proportional hazard models with PSOC as a categorical predictor. Discrimination from the Cox model was summarised using Harrell's concordance (C-index). Proportional hazards assumptions were checked graphically and by global tests where appropriate.

Two-sided p-values <0.05 were considered statistically significant. Analyses were performed in Stata 17.0 (StataCorp, USA) using standard procedures (logit, logistic, roctab, lroc, lfit, estat gof, stset, sts, stcox, estat concordance).

Handling of missing data and censoring

Patients missing any PSOC component or with an undeterminable primary endpoint were excluded from analyses of that endpoint. For time-to-event analyses, patients without a valid death date were not included because reliable last-contact dates were unavailable; consequently, Kaplan-Meier and Cox models estimate time-to-death among those with observed events. Palliative modalities used to treat patients were not included in the analysis, but the vast majority were treated with insertion of a self-expanding metal stent.

Ethical considerations

The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (ref. no. BREC00009028/2025).

Results

Cohort characteristics

A total of 465 patients met the inclusion criteria, comprised of 235 from IALCH and 230 from GH. The mean age at presentation was 61 years, with a male-to-female ratio of 1.02:1. Histologically, 97% had squamous cell carcinoma and 3% had adenocarcinoma, adenosquamous carcinoma, or invasive carcinoma with the type

Table 1. Components of the PSOC and weight of each component

Parameter	β	OR (95% CI)	*p*-value	Weighted score
BMI >18.5 kg/m^2	0.624	1.87 (1.14 - 3.06)	0.013	1
Albumin ≥25 g/L	1.118	3.06 (1.46 - 6.42)	0.003	2
ECOG 0 - 1	0.938	2.56 (1.50 - 4.35)	0.001	1

PSOC = prognostic score for oesophageal cancer; OR = odds ratio; CI = confidence interval; BMI = body mass index; ECOG = Eastern Cooperative Oncology Group.

Table 2. Demographic data (*N*=465)

Characteristic	Value
Mean age, years	61
Male:female ratio	1.02:1
Patients with squamous cell carcinoma, *n* (%)	451 (97)
Median survival, months	4.8

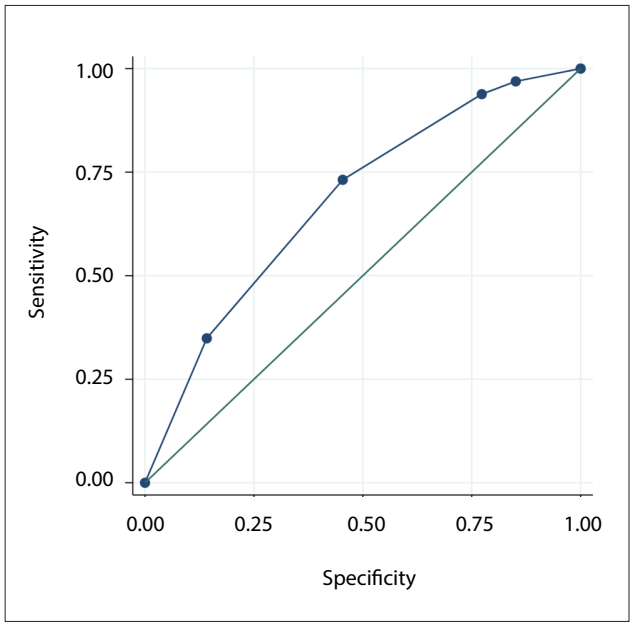

Fig. 1. Area under receiver operating characteristic (AUROC) curve for predicting ≥3-month survival (AUROC curve = 0.6808).

not specified. Median (IQR) survival for the entire cohort was 4.8 (2.5 - 9.1) months, and 71% survived at least 3 months. Baseline demographic and clinical characteristics are summarised in Table 2.

Primary endpoint: ≥3-month survival

When PSOC was modelled as a categorical predictor, the odds of surviving ≥3 months increased progressively with higher scores. Compared with a score of 0, the odds ratios (ORs) for survival ≥3 months were: score 1 = 1.91 (95% CI 0.61 - 5.97, p=0.266), score 2 = 3.13 (95% CI 1.35 - 7.26, p=0.008), score 3 = 5.92 (95% CI 2.59 - 13.54, p<0.001), and score 4 = 11.87 (95% CI 4.87 - 28.91, p<0.001). When grouped into low (0 - 2) v. high (3 - 4) scores, the high-score group had significantly greater odds of surviving ≥3 months (OR=4.59, 95% CI 1.59 - 13.25, p=0.005).

Discrimination

The AUROC for predicting ≥3-month survival in the external validation dataset was 0.681 (standard error = 0.026, 95% CI 0.630 - 0.732), indicating fair discrimination (Fig. 1). This was comparable with the development dataset AUROC of 0.67 (95% CI 0.62 - 0.73).

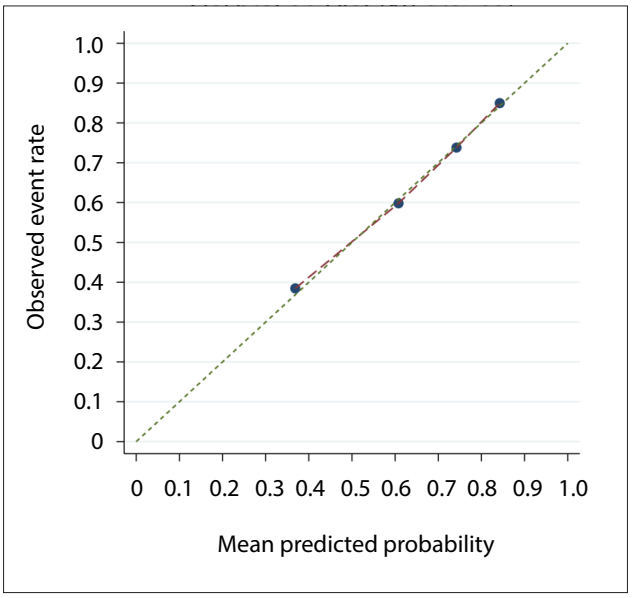

Fig. 2. Calibration curve comparing observed and predicted probabilities (10 groups).

Calibration

The Hosmer-Lemeshow goodness-of-fit test (four risk groups) yielded χ^2 = 0.17, p=0.920, indicating no evidence of lack of fit. The calibration plot (Fig. 2 demonstrated close agreement between observed and predicted probabilities across the risk range. The relationship between PSOC and the predicted probability of ≥3-month survival is shown in Fig. 3, demonstrating an approximately linear increase in predicted survival probability with higher scores.

Survival analysis

Kaplan-Meier curves stratified by PSOC category (0 - 4) showed progressively longer survival with increasing score (Fig. 4). The log-rank test demonstrated a statistically significant difference in survival distributions across score groups ($\chi^2(4)$ = 80.95; p<0.001).

In the Cox proportional hazards model (Appendix Table S1), hazard ratios (HRs) for death compared with score 4 (reference) were: score 0 = 4.76 (95% CI 3.16 - 7.18, p<0.001), score 1 = 2.87 (95% CI 1.77 - 4.64, p<0.001), score 2 = 2.32 (95% CI 1.77 - 3.04, p<0.001), and score 3 = 1.61 (95% CI 1.26 - 2.05, p<0.001).

Overall model performance

The Brier score for the primary endpoint was 0.190 (SD 0.201), indicating good accuracy of predicted probabilities. Model concordance from the Cox model further supported acceptable discriminatory ability.

Discussion

To our knowledge, this is the first prognostic score for OC that has been developed and validated in an African population. The need for a prognostic score validated in the context of African patients with

Table 3. Proposed clinical utility of the PSOC

PSOC	Survival probability, %*	95% CI	Proposed management
0 - 2	50.6	42.7 - 58.5	Palliate
3 - 4	74.8	69.4 - 79.6	Staging investigations

PSOC = prognostic score for oesophageal cancer; CI = confidence interval.
*Probability of surviving ≥3 months.

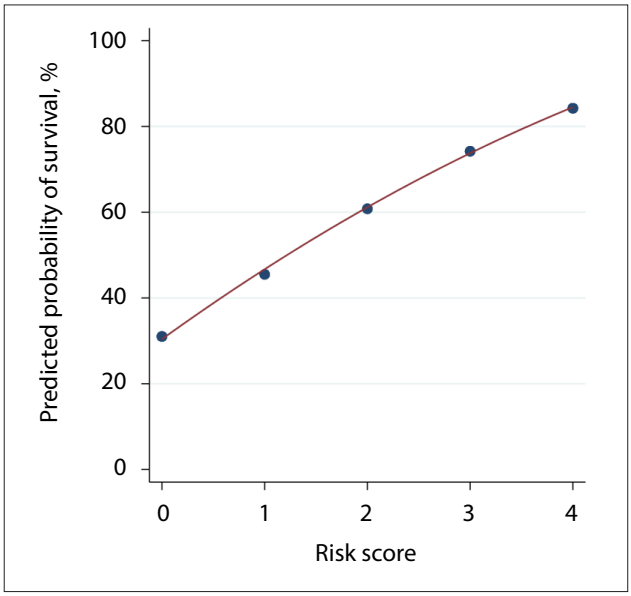

Fig. 3. Risk score and predicted probability of survival.

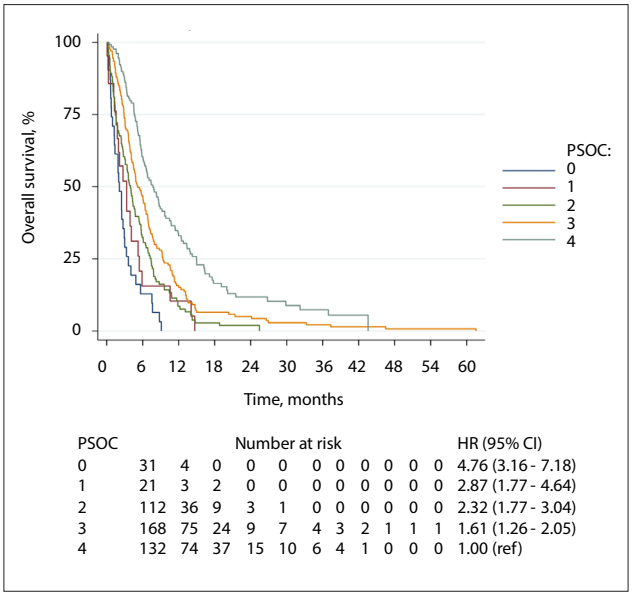

Fig. 4. Kaplan-Meier Curve by prognostic score for oesophageal cancer (PSOC): Kaplan-Meier estimates of overall survival. (HR = hazard ratio; CI = confidence interval; ref = reference.)

OC cannot be overstated, since the continent has a high incidence of OC, and countries face significant resource constraints.[11,12] In our cohort of patients treated palliatively, the PSOC demonstrated fair discrimination, good calibration and acceptable overall predictive accuracy for short-term survival. These findings confirm its potential as a pragmatic and objective tool for guiding initial management decisions in resource-limited settings, where most patients are treated palliatively.

Most internationally accepted guidelines on the management of OC are based on data from high-income countries, resulting in under-representation of African patients during the process of guideline development.[13] Current guidelines require patients to be staged before receiving palliative care for OC, but the delay caused by waiting times for staging investigations in low- and middle-income countries may negatively impact patients' quality of life.

Previously performed studies that investigated prognostic factors in patients with OC and devised scores to stratify patients included variables requiring computed tomography staging, such as the presence of metastases.[14-16] Other scores require multiple laboratory tests that may be expensive, unavailable, or time-consuming.[17-19] A recent systematic review found 17 prognostication tools for OC. Only one tool was designed for patients treated palliatively, only six were externally validated, and none were developed in Africa, underscoring the novelty of our study.[7]

Our score, which uses three simple, easily obtained variables, can be applied in a resource-challenged institution and does not require staging investigations or costly laboratory tests. The cut-off value of 3 months for survival was chosen based on the definition of a short life expectancy according to the European Society of Gastrointestinal Endoscopy.[20] The score adequately discriminated between the two groups in the original study, and this has been validated on the independent cohort in this study.

This study has several limitations. Although the data were prospectively collected, the retrospective data analysis and the exclusion of patients with missing data may have influenced the results. The inclusion of only two centres from one province may limit the general applicability of the score. Access to palliative modalities beyond self-expanding metal stents was inconsistent, which may have influenced survival outcomes. Specific palliative treatment modalities such as chemotherapy and radiotherapy were not specified in our cohort, and this may have influenced outcomes. As the PSOC was developed for use at diagnosis to guide staging and palliative decisions, treatment variables (such as stenting or radiotherapy) were not included in the model. However, all patients received palliative-intent management consistent with institutional protocols, and survival outcomes reflect this context.

We believe that the PSOC would be a valuable tool to add to the armamentarium of clinicians in any resource-constrained area with a high incidence of OC , where the majority of patients are treated with palliative intent. The clinical utility of the score is shown in Table 3.

Conclusion

The PSOC is a clinically relevant, validated prognostic score that reliably discriminates patients according to predicted prognoses, and can therefore be used by clinicians in resource-constrained environments to decide whether to treat patients palliatively from the time of diagnosis, or subject them to staging investigations and possibly more radical treatment.

Data availability. All statistical results are reported in this publication. Stata do-files and datasets used in the analyses are available from the corresponding author upon reasonable request.

Declaration. None.

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Author contributions. LF was responsible for conceptualisation, methodology, data collection and analysis, writing and editing of the manuscript. WCC was responsible for methodology data analysis, statistical analysis, writing and editing of the manuscript. SB was responsible for data collection and editing of the manuscript.

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Conflicts of interest. None.

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