

Qoppa as a new synthetic analytical marker to detect the oncological population at high risk of metastasis during follow-up and optimize the imaging test schedule

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INTRODUCTION & AIM

Advanced cancers release soluble factors into the venous circulation, disrupting systemic homeostasis. These effects are most evident in highly vascularized organs such as the liver, lungs, and brain, which exhibit microvascular and pathophysiological alterations. Circulating biomarkers derived from these responses may thus indicate subclinical tumor activity and metastatic potential.

This study aims to develop an analytical parameter that identifies patients at higher risk of metastasis as an indirect marker of pre-metastatic niche formation. By integrating response-related biomarkers with global inflammatory indices, this tool could improve risk stratification and, in future studies, guide the optimization of radiological monitoring.

METHOD

Study design and population

Prospective observational study with informed consent focus on oncological patients attended at HM CIOCC Málaga (May 2024 – July 2025). Single heterogeneous study group (metastatic and non-metastatic patients).

- Inclusion: confirmed oncological diagnosis (at least one non-hematological malignancy), >18 years old, capacity to consent, written informed consent.
- Exclusion: incapacity to consent, verbal consent only.

Response biomarkers

Prior systematic literature review to identify relevant and technically feasible biomarkers (Table 1). Extraction of 10mL fasting peripheral blood and determination via immunoassay Luminex 200.

Global analytical parameters

20 qualitative and quantitative parameters related to metastasis risk from routine analysis prior to blood sampling up to 190 days before (Table 2).

Creation of synthetical analytical markers

Hierarchical clustering (Ward's method, Euclidean distance) was performed and the optimal cluster number was calculated using elbow method and silhouette coefficient. Synthetic variables were created for each cluster by aggregating parameters via linear models.

Stratified ROC curve analysis by metastatic status evaluated mortality risk, de novo metastasis risk (for non-metastatic patients), and metastasis burden increase (metastatic patients), determining optimal cut-off values of the synthetic cluster variables.

Kaplan-Meier analysis compared overall and progression-free survival between high and low value for synthetic variable groups.

Table 1. Response biomarkers analyzed

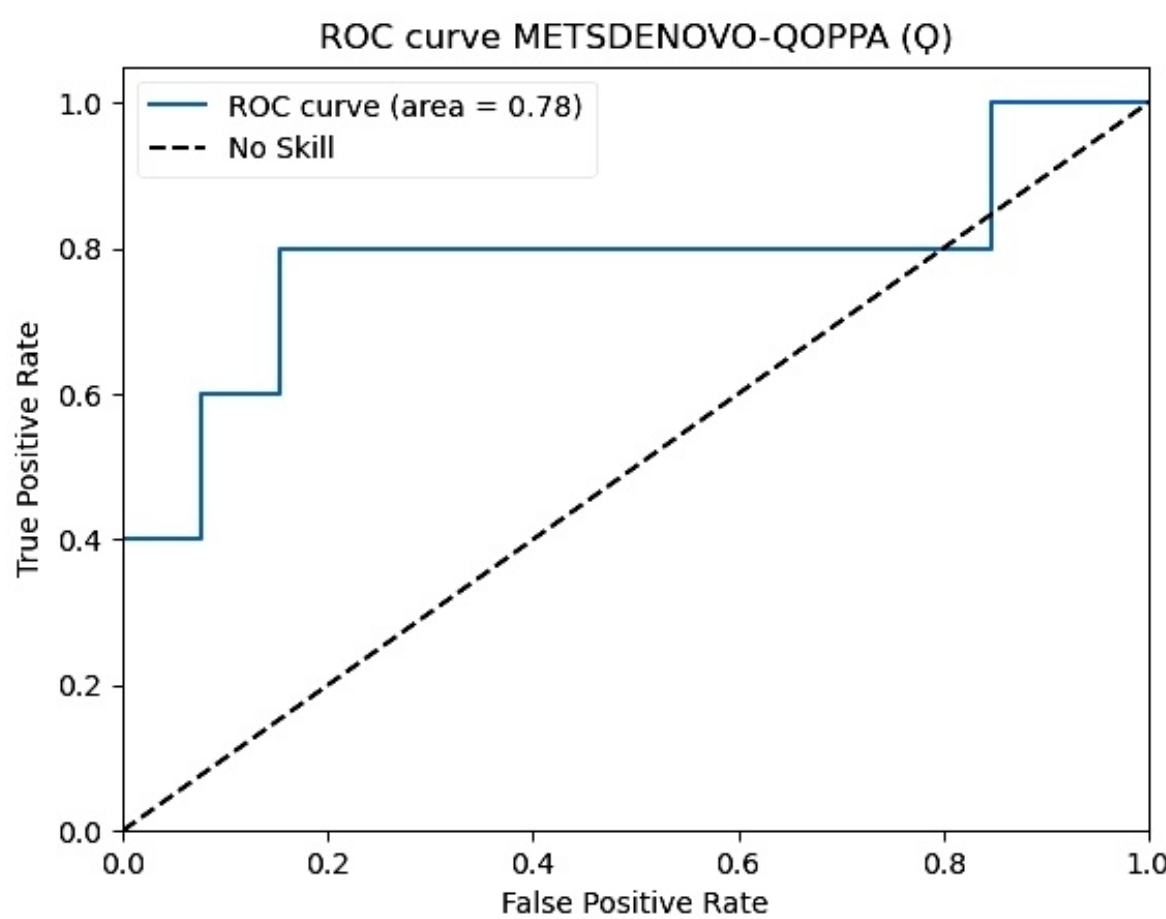
Angiopoietin-like 4	ANGPTL4
Cathepsin D	CATD
Fibroblast growth factor 21	FGF21
Growth/differentiation factor 15	GDF15
Hepatocyte growth factor	HGF
Intercellular Adhesion Molecule 1	ICAM1
Interleukin 6	IL6
Interleukin 10	IL10
Interleukin 18	IL18
Leptin	LEP
Myeloperoxidase	MPO

Table 2. Global analytical parameters analyzed

Naples prognostic score	nps
Lymphocyte – monocyte ratio]	lmr
Albumin	alb
Hemoglobin	hb
Prognostic nutritional index	pni
Combined platelet – NLR score	copnlr
Platelet – lymphocyte ratio	plr
Neutrophil – platelet – lymphocyte – hemoglobin ratio	nplhb
Systemic immune inflammation index	sii
Systemic inflammation response index	siri
Neutrophil – lymphocyte ratio	nlr
Leukocyte – lymphocyte ratio	llr
Aspartate aminotransferase – neutrophil ratio	anri
Protein C reactive	pcr
Aspartate aminotransferase – platelet count ratio	apri
Novel prognostic model	npm
Lactate dehydrogenase – albumin ratio	lar
Serum iron	si
Hemoglobin – albumin – lymphocyte – platelet	halp
Vitamin B12	vitb12

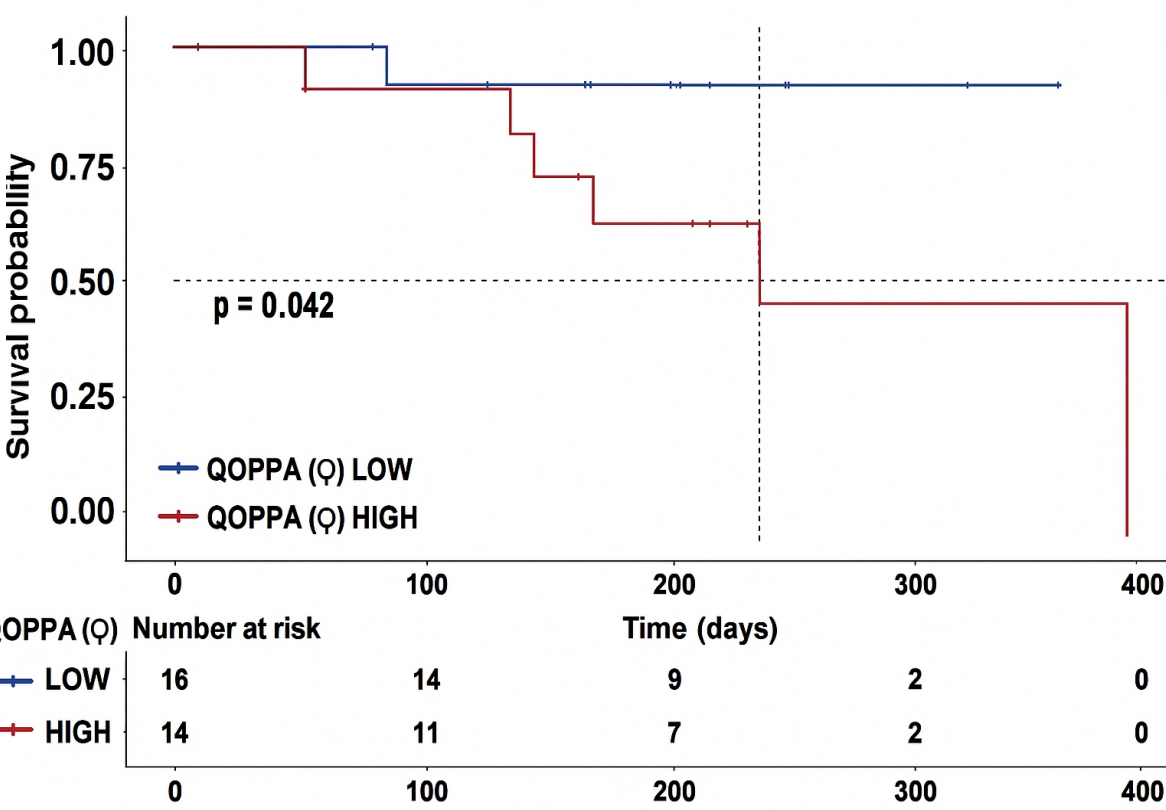
RESULTS & DISCUSSION

Figure 1. ROC curve for de novo metastases development in initially non-metastatic patients



A total of 30 patients were recruited, with 12 non-metastatic and 18 metastatic at enrollment. Hierarchical clustering of analytical parameters and response biomarkers yielded two distinct clusters generating two synthetic variables: STIGMA (nps, lmr, alb, hb, pni) and QOPPA (copnlr, plr, nplhb, sii, siri, nlr, llr, anri, pcr, apri, npm, lar, si, halp, vitb12, ANGPTL4, CATD, FGF21, GDF15, HGF, ICAM, IL6, IL10, IL18, LEP, MPO).

Figure 2. Kaplan-Meier curve for survival probability in the total population according to Qoppa value



ROC analysis showed STIGMA was not a good predictor, whereas QOPPA demonstrated strong predictive value for metastatic progression risk in initially non-metastatic patients (AUC=0.78, Fig. 1). Additionally, QOPPA was an acceptable predictor for mortality risk in the total population and exclusively metastatic subgroup, confirmed by Kaplan-Meier analysis (Fig. 2).

CONCLUSION

QOPPA is a novel synthetic biomarker that identifies high-risk patients for metastatic debut (AUC=0.78). This risk-stratification tool could optimize radiological surveillance by intensifying monitoring in high-risk patients while de-escalating in low-risk individuals. Further prospective studies are needed to validate clinical implementation.

FUTURE WORK / REFERENCES

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