Potential role of neuropilin-1 in the prognosis, development and risk of invasion in hepatocellular carcinoma patients

Background
Hepatocellular carcinoma (HCC) represents the third most deadly cancer worldwide with still high therapeutic failure and recurrence rates mainly associated with the late diagnosis and the molecular heterogeneity of this liver tumor. The transmembrane glycoprotein neuropilin-1 (NRP1) has shown a key role in the modulation of tumor-associated signaling pathways and processes by interacting with key receptor tyrosine kinases. Nonetheless, few studies have evaluated the potential value of NRP1 as a tumor biomarker or therapeutic target in HCC. For this reason, we aimed at assessing the clinical significance of the receptor NRP1 in the prognosis, diagnosis and other tumor-associated features in HCC patients.

Methods
We conducted a systematic review with meta-analysis including all the articles published up to May 31st 2022 that evaluated the correlation of NRP1 overexpression with tumor prognosis, development and/or other clinicopathological features in patients diagnosed with HCC. An exhaustive literature search was performed in five online databases, selecting potential papers to be included based on predefined eligibility criteria. Data from included studies were extracted or estimated by Parmar method and meta-analyzed employing the STATA 16 software.

Results
A total of 1,305 patients from seven studies were included in the quantitative analysis, showing approximately 53.81% of patients NRP1 overexpression (Fig. 1). After meta-analysis, higher levels of NRP1 proved to be significantly correlated to poor prognosis, represented by lower overall survival (OS) (Fig. 2). Moreover, a significant association with tumor pathogenesis was also found by observing higher NRP1 expression in tumor tissue samples from 692 HCC patients (Fig. 3). Finally, a marked correlation was obtained between increased NRP1 expression and patient’s age, younger than 50 years old (Fig. 4), and a higher risk of venous invasion (Fig. 5), highlighting the potential of NRP1 as a tumor biomarker in HCC.

Conclusions
Overall, these results suggest that NRP1 has a potential role for prognosis, development and risk of invasion, and, therefore, could constitute a valuable biomarker in patients diagnosed with HCC.

References

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The presenting author has no conflicts of interest to declare

Figure 1. Schematic representation of the percentage of HCC patients with NRP1 overexpression in either tumor tissue or tumor-derived samples.

Figure 2. Meta-analysis of the potential correlation of NRP1 overexpression with OS in HCC patients. Forest plot representing the individual and pooled results from the meta-analysis evaluating the association of NRP1 overexpression with OS in the corresponding articles.

Figure 3. Meta-analysis of the potential correlation of NRP1 overexpression with tumor pathogenesis in HCC patients. Forest plot representing the individual and pooled results from the meta-analysis evaluating the association of NRP1 overexpression with tumor pathogenesis in the corresponding articles.

Figure 4. Meta-analysis of the potential correlation of increased NRP1 expression with tumor prognosis, development and/or other clinicopathological features in patients diagnosed with HCC. An exhaustive literature search was performed in five online databases, selecting potential papers to be included based on predefined eligibility criteria. Data from included studies were extracted or estimated by Parmar method and meta-analyzed employing the STATA 16 software.

Figure 5. Meta-analysis of the potential correlation of increased NRP1 expression with the risk of venous invasion. Forest plot of the pooled overall effect sizes analyzing the correlation of higher NRP1 levels with the clinicopathological parameter of age (> 50 years old) in HCC patients.

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