

Follicular and Hurthle Cell Carcinoma: Comparison of clinicopathological features and clinical outcomes

Danielli Matsuura MD^{1,2}, Avery Yuan¹, Laura Wang MD¹, Rohit Ranganash MD¹, Victoria Harries MD¹, Snehal Patel MD¹, Michael Tuttle, MD³, Bin Xu MD PhD⁴, Ronald Ghossein MD⁴, Ian Ganly MD PhD¹

¹Department of Surgery, Head and Neck Service, Memorial Sloan Kettering Cancer Center, New York, New York; ²Department of Head and Neck Surgery, University of São Paulo Medical School, Brazil; ³Department of Medicine, Endocrinology Service, Memorial Hospital for Cancer and Allied Diseases, Memorial Sloan-Kettering Cancer Center, New York, New York; ⁴Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York

Background

Follicular thyroid carcinoma (FTC) and Hurthle cell carcinoma (HCC) are rare and likely aggressive thyroid cancers. Controversy remains as to which phenotype (FTC or HCC) confers worse outcome and limited data is published regarding their subtypes.^{1,2} The aim of this study was to describe the clinicopathological features and compare the clinical outcomes of patients with FTC and HCC classified based on the 2017 World Health Organization (WHO) classification of tumors of endocrine organs and the extent of vascular invasion (VI).³

Methods

Memorial Sloan Kettering (MSK) Cancer Center Institutional Review Board approval was obtained for this retrospective study with a waiver of informed consent. A total of 201 patients with HCC and FTC primarily treated with surgery at MSK between 1986 and 2015 were included. Head and neck pathologists reviewed and classified each patient into FTC and HCC followed by their subtypes utilizing a modification of the 2017 WHO classification (minimally invasive, encapsulated angioinvasive and widely invasive), stratifying the tumors into 4 groups instead of 3. Although this classification is not mentioned in the Hurthle cell chapter of the latest WHO classification of tumors of endocrine organs, the majority of pathologists follow the WHO classification of FTC. Patients with encapsulated lesion with capsular invasion only, were classified into minimally invasive (MI). Patients with encapsulated lesion, regardless of the capsular invasion status, and presence of vascular invasion were stratified into two groups. If less than 4 foci of vascular invasion were detected, patients were classified into encapsulated angioinvasive with focal vascular invasion (EA-FVI). If presence of more or equal 4 foci of vascular invasion, they were classified into encapsulated angioinvasive with extensive vascular invasion (EA-EVI). Lastly, patients with partial or absent capsule and grossly involving the thyroid were classified into widely invasive (WI).

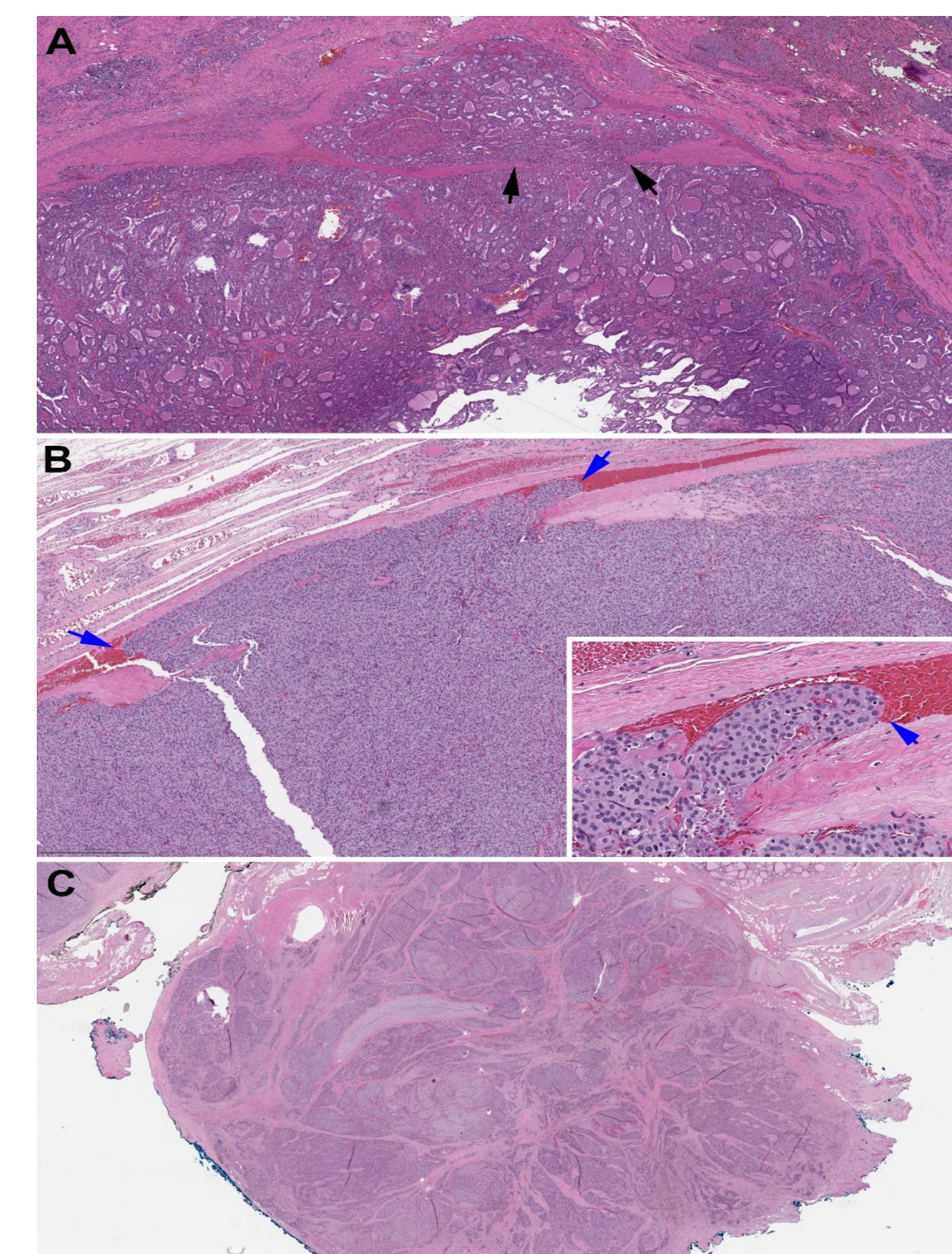


Figure 1. Minimally invasive, encapsulated angioinvasive and widely invasive carcinoma. (A) A minimally invasive follicular carcinoma has one focus of capsular invasion (black arrows), in which a mushroom-shaped tumor bud penetrates through the tumor capsule extending beyond its contours. (B) An encapsulated angioinvasive Hurthle cell carcinoma. Vascular invasion (blue arrows) is present as a tumor embolus covered by endothelial cells and attached to the wall of an intracapsular vessel. Insert: high power view. (C) A widely invasive Hurthle cell carcinoma demonstrates widely invasive multinodular and infiltrative growth with extensive extrathyroidal extension.

Results

Patients with HCC (n=120) had a greater percentage of patients older than 55 years old (59% vs 26%, p<0.001) and with extensive vascular invasion (32% vs 19%, p<0.001) compared to FTC (n=81). Of 81 patients with FTC, there were 42 FTC-MI, 23 FTC EA-FVI, 15 FTC EA-EVI and 1 FTC-WI. In all FTC groups, the majority of patients were younger than 55 years-old, female, had T1/T2 tumors and no ETE. Of 120 HCC, there were 48 HCC-MI, 31 HCC EA-FVI, 32HCC EA-EVI and 9 HCC-WI. In the first three HCC groups, most patients were older than 55 years-old, female, had T1/T2 tumors and no ETE. In the HCC-WI subgroup, the majority of patients were male (78%), had T4 tumors (33%), extensive vascular invasion (67%) and metastases to the central and lateral neck (55%). Our entire cohort had a median follow-up of 84 months (IQR 36-126) and a median survival of 85 months (IQR 42-129). Comparing groups 1,2,3 and 4 (figure 2), group 4 patients (HCC-WI and HCC EA-EVI) had a poorer 10 year OS (95% , 94%, 82% vs 78%, respectively, p =0.026), DSS (100%, 94%, 97% vs 88%,

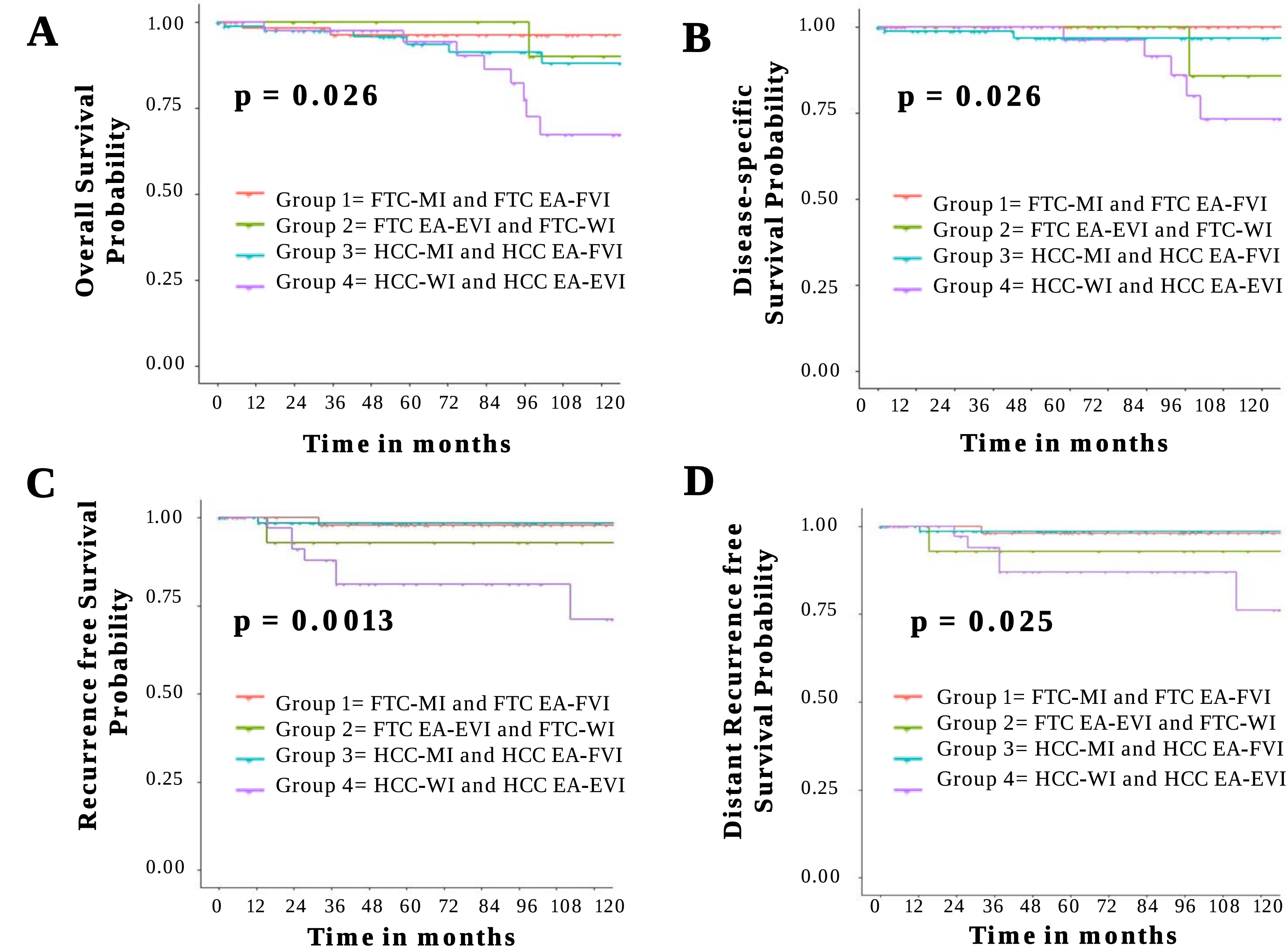


Figure 2. Kaplan-Meier estimates of overall survival(A), disease specific survival(B), recurrence free survival(C) and distant recurrence free survival(D) probabilities, stratified by Group 1= FTC-MI and FTC EA-FVI, Group 2= FTC EA-EVI and FTC-WI, Group 3= HCC-MI and HCC EA-FVI, Group 4= HCC-WI and HCC EA-EVI.

p=0.026), RFS(98%, 93%, 98% vs 71%, p=0.0013) and DRFS (98%, 93%, 98% vs 76%, p=0.025 There was no difference in LRRFS. There was no difference in LRRFS. Stratified by extent of vascular invasion (extensive, focal and no VI), patients with extensive vascular invasion had poorer distant control (DRFS: 79%, 95%, 100%, p=0.005), and poorer DSS (74%, 97%, 99%, p=0.014) compared to patients with focal or absent VI.

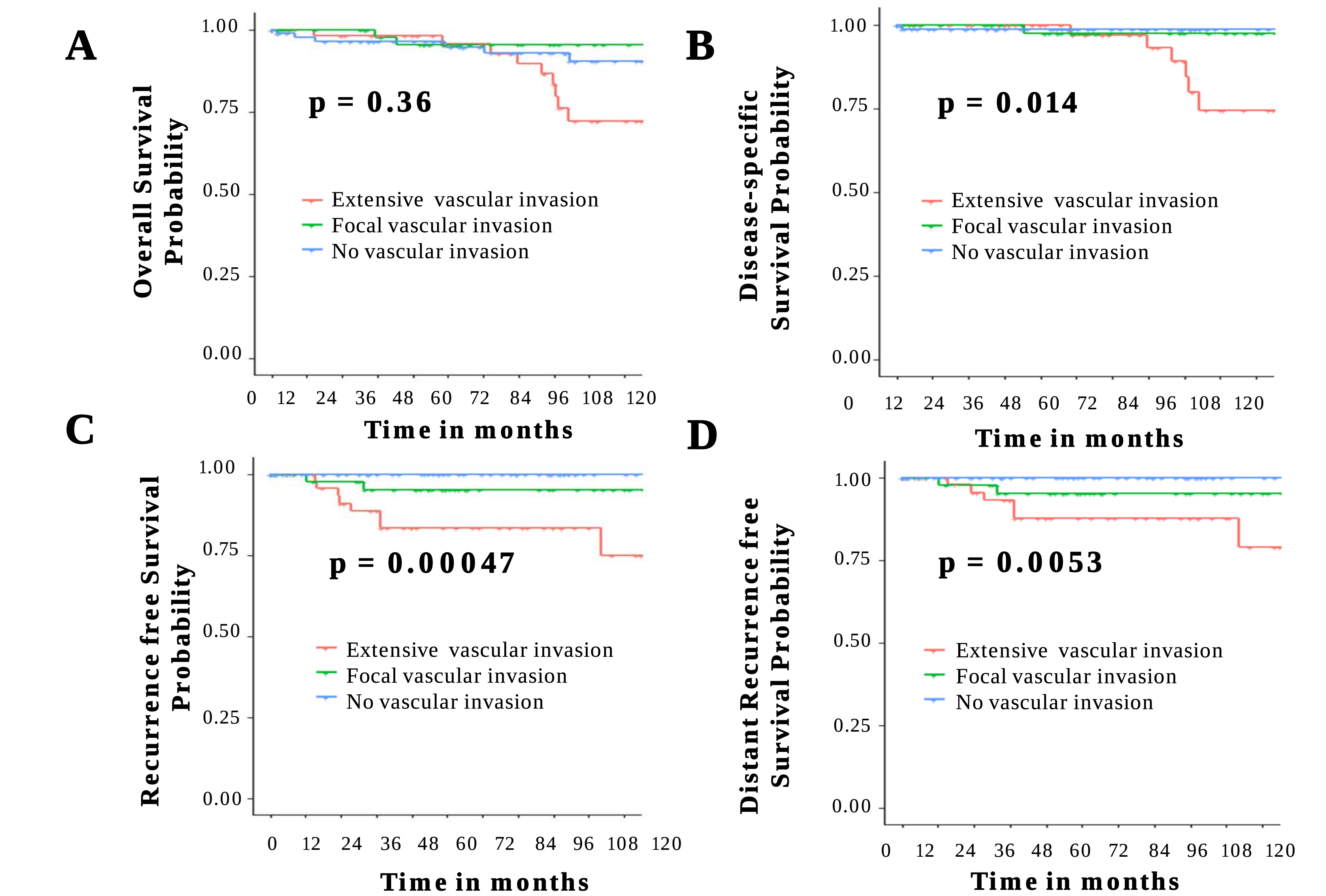


Figure 3. Kaplan-Meier estimates of overall survival (A), disease specific survival (B), recurrence free survival (C) and distant recurrence free survival (D) probabilities stratified by extent of vascular invasion.

Conclusions

Patients with widely invasive HCC and encapsulated HCC with extensive vascular invasion have poorer distant control and are more likely to die compared to other subtypes of HCC and FTC. Accurate pathological assessment of vascular invasion is essential to identify patients at higher risk of recurrence and death.

References: **1.** Ghossein RA, Hiltzik DH, Carlson DL, Patel S, Shaha A, Shah JP, Tuttle RM, Singh B 2006 Prognostic factors of recurrence in encapsulated Hurthle cell carcinoma of the thyroid gland: a clinicopathologic study of 50 cases. *Cancer* **106**:1669-1676. **2** Xu B, Wang L, Tuttle RM, Ganly I, Ghossein R 2015 Prognostic impact of extent of vascular invasion in low-grade encapsulated follicular cell-derived thyroid carcinomas: a clinicopathologic study of 276 cases. *Human pathology* **46**:1789-1798; **3.** 2017 WHO Classification of Tumours of Endocrine Organs. Vol 10. 4th ed, Lyon