Background: Circulating DNA has been reported as prognostic in metastatic colorectal cancer (mCRC) but its correlation with tumor burden has never been clearly established. The aim was to evaluate the correlation between pretreatment levels of circulating tumor DNA (ctDNA), cell-free-DNA (cfDNA), circulating tumor cells (CTC), CEA, CA19.9 with tumor characteristics on CT scan.

Methods: It was a retrospective analysis from a prospective trial on circulating markers (ctDNA, cfDNA, CTC, CEA, CA19.9) at baseline in mCRC patients (NCT01212510). CT scans were centrally reviewed to assess 3 tumor parameters: the diameter using RECIST version 1.1, the total tumor length (TTL) defined as the sum of diameter of all visible lesions, and the volume (Vol) of the main lesion. Relationship between circulating markers and CT scan were analysed as well as progression-free survival (PFS) and overall survival (OS) and prognostic factors using Cox models.

Results: A total of 83 mCRC patients were included. Median baseline ctDNA, cfDNA, CEA, CA19.9 and CTC were 21 (0.12-74) %, 36 (6-2275) ng/mL, 75 (2-64501) ng/mL, 90 (4-70900) UI/mL, and 7 (1-194)/mL, respectively. For CT scan, median value was 81 (11-310) mm for RECIST, 196 (14-1906) mm for TTL and 65 (2-783) mm² for Vol. There was a significant correlation between RECIST and CEA (p = 0.0005), CA19.9 (p = 0.007), cfDNA (p < 0.0001), ctDNA (p = 0.01), between TTL and CEA (p < 0.0001), CA19.9 (p = 0.0008), cfDNA (p < 0.0001), ctDNA (p < 0.0001) and between Vol and CEA (p = 0.008), CA19.9 (p = 0.02), cfDNA (p = 0.0015). The median PFS and OS were significantly increased in patients with low (< vs > to median) CA19.9 (8.8 vs 3.2 m., p = 0.03 and 16.4 vs 9 m., p = 0.01), cfDNA (8 vs 3 m., p = 0.006 and 18.3 vs 8.3 m., p = 0.0001), TTL was only associated with PFS (9 vs 3 m., p = 0.009) and RECIST and Vol with OS (15.3 vs 11.8 m., p = 0.04). In multivariate analysis, RECIST (p = 0.0084), CA19.9 (p = 0.004) and OMS performance status (p = 0.04) were prognostic for OS.

Conclusions: Circulating makers and tumor burden on CT scan were correlated and prognostic. Interventional studies are needed to evaluate the usefulness of circulating makers in decision making.

Clinical trial identification: NCT01212510

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