Background: Clonal hematopoiesis of indeterminate potential (CHIP) is defined as a clonal accumulation of somatic mutations in hematopoietic stem cells in the absence of hematologic malignancy or other clonal disorders. CHIP has been associated with a higher risk of developing hematologic malignancies. Recently, CHIP has been linked to a family history of lung cancer (FHLC) in lung cancer patients. In the present study, we evaluated the association between clinical factors and CHIP in individuals enrolled in a lung cancer screening program.

Methods: Thirty-two asymptomatic individuals with lung cancer enrolled in the International-Early Lung Cancer Action Program (I-ELCAP) at the Clinica Universidad de Navarra, were matched by sex, age, COPD, smoking history and FHLC with 32 screened controls without lung cancer. CHIP was evaluated with the PMPv2 NGS panel, an in-house panel designed for the evaluation of SNV/INDELs in 56 genes associated with myeloid malignancies. CHIP was defined by the presence of cancer-associated somatic mutations with a minimum of 1000 reads and a variant allele frequency (VAF) ≥ 2% and < 40%. Statistical differences were analyzed with the Fisher’s exact test.

Results: CHIP was found in 13 individuals (20%). Two individuals had two mutations. Mutated genes included DNMT3A (6), TET2 (3), ASXL1 (2), PPM1D (2), BCOR (1) and SH2B3 (1). The presence of CHIP was significantly associated with age (<60 vs. ≥ 60 years; p=0.022) and smoking history (<50 vs. ≥ 50 pack-years; p=0.009), but not with sex, COPD or FHLC. No statistically significant differences in CHIP frequencies were found between lung cancer patients (22%) and controls (19%). Mutated genes in cancer patients included DNMT3A (2), PPM1D (2), ASXL1, TET2, BCOR and SH2B3 (1 each), while control subjects had mutations in DNMT3A (4), TET2 (2) and ASXL1 (1).

Conclusions: CHIP was found in 20% of asymptomatic individuals screened for lung cancer. CHIP was more common in older individuals and in those with greater tobacco exposure. The prevalence of CHIP was similar in screened individuals with or without lung cancer.