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THE IMPACT OF CLASS ONE MUTATIONS ON THE MEDIAN AGE OF DEATH OF PWCF IN THE UK

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Background

Disease severity as indicated by pancreatic and pulmonary function is related to genotype. People with cystic fibrosis (PWCF) homozygous for F508del as compared to heterozygous F508del or no F508del mutation have more severe disease manifestations.(Kerem E, et al. N Engl J Med. 1990;323:1517-22). An association between 'mild genotypes' and increased age of death has been reported (Hoo Z, et al. J Resp med. 2014:108(5);716-21).

Studies defining the impact of class I mutations on disease severity are often limited by small numbers (Geborek A, Hjelte L. J Cyst Fibros. 2011; 187-192). Mckone reported no significant difference in mortality rate of class I: F508del heterozygote combinations when compared to patients homozygous for F508del. (McKone, et al. Lancet. 2003;361:1671-76).

Aims

To compare the median age of death of PWCF with class I mutations to those homozygous for F508del mutation.

Methods

Age at and year of death, sex and presence of meconium ileus of PWCF with at least one class I mutation or homozygous F508 registered on the Cystic Fibrosis Trust UK CF Registry (2007-2015) was requested. Multiple linear regression was used to assess the effects on age at death.

Results

Mutations	**Number**	**Median age of death**
Homozygous F508del	387	27
F508del:Class 1	85	25
Homozygous Class 1	7	24

After adjusting for sex, age at diagnosis and the presence of meconium ileus, the median age of death for PWCF with at least one class 1 mutation was 2.45 years less than those homozygous for F508del, p=0.029, (CI-4.66, -0.25)

Conclusions

The median age of death for PWCF with a class 1 mutation combined with either F508del or another class I mutation was significantly younger than those homozygous for F508del.