CHEST

Assessing Differences in Mortality Rates and Risk Factors Between Hispanic and Non-Hispanic Patients With Cystic Fibrosis in California

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BACKGROUND: Over the past 30 years, therapeutic advances have extended the median lifespan of patients with cystic fibrosis (CF). Hispanic patients are a vulnerable subpopulation with a high prevalence of risk factors for worse health outcomes. The consequences of these differences on health outcomes have not been well described. The objective of this study was to characterize the difference in health outcomes, including mortality rate, between Hispanic and non-Hispanic patients with CF.

METHODS: This study is a retrospective analysis of CF Foundation Patient Registry data of California residents with CF, diagnosed during or after 1991, from 1991 to 2010. Ethnicity was self-reported. The primary outcome was mortality. Hazard ratios were estimated from a Cox regression model, stratified by sex, and adjusted for socioeconomic status, clinical risk factors, and year of diagnosis.

RESULTS: Of 1,719 patients, 485 (28.2%) self-identified as Hispanic. Eighty-five deaths occurred, with an overall mortality rate of 4.9%. The unadjusted mortality rate was higher among Hispanic patients than among non-Hispanic patients (9.1% vs 3.3%, $P < .0001$). Compared with non-Hispanic patients, Hispanic patients had a lower survival rate 18 years after diagnosis (75.9% vs 91.5%, $P < .0001$). Adjusted for socioeconomic status and clinical risk factors, Hispanic patients had an increased rate of death compared with non-Hispanic patients (hazard ratio, 2.81; 95% CI, 1.70-4.63).

CONCLUSIONS: Hispanic patients with CF have a higher mortality rate than do non-Hispanic patients, even after adjusting for socioeconomic status and clinical severity. Further investigation into the mechanism for the measured difference in lung function will help inform interventions and improve the health of all patients with CF. CHEST 2016; 149(2):380-389

KEY WORDS: cystic fibrosis; ethnicity; health disparities; pediatric pulmonology

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ABBREVIATIONS: CF = cystic fibrosis; CFFPR = Cystic Fibrosis Foundation Patient Registry; CFRD = cystic fibrosis-related diabetes; CFTR = cystic fibrosis transmembrane conductance regulator; FPL = federal poverty line; HR = hazard ratio; % pred = % predicted value

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This article was presented at the Pediatric Academic Society Meeting, May 5, 2014, Vancouver, BC, Canada.

FUNDING/SUPPORT: This study was supported by the Cystic Fibrosis Foundation, 2nd year Clinical Fellowship [Grant BUU10B0]; the Ernest and Amelia Gallo Endowed Postdoctoral Fellowship; the Lucile Packard Foundation for Children's Health; Stanford National Institutes of Health-National Center for Advancing Translational Sciences-Clinical and Translational Science Award (NIH-NCATS-CTSA [Grant UL1 TR001085]); and the Child Health Research Institute of Stanford University.

The life expectancy of patients with cystic fibrosis (CF) has improved greatly over the last 3 decades, with the median predicted age of survival increasing from 27 years in 1986 to 41 years in 2012.[1-3] This improvement has been attributed in part to the establishment of regionalized care in CF specialty centers.[4-6] CF centers provide coordinated, multidisciplinary care and support services to help patients and their families navigate the labor-intensive and complex therapy regimens required to maintain lung health. However, there remains considerable concern regarding ethnic disparities in health outcomes, which may be related to differential care access or capacity to adhere to these complex regimens.[7-9] For other chronic illnesses, patients of Hispanic ethnicity, particularly those with limited English proficiency or limited health literacy, are particularly susceptible to outcome disparities.[10-12]

The relative proportion of Hispanic patients receiving a diagnosis of CF has been rising over time (7% in 2010),[2] as the size of the general Hispanic population and awareness of the prevalence of CF in Hispanic populations have risen.[13] California has a large Hispanic population (37.6% of the state's population in 2010),[14] and it has the largest number and highest proportion of Hispanic patients with CF, making it an optimal place to study this subpopulation.

Hispanic patients with CF are a potentially vulnerable subpopulation because of an increased prevalence of risk factors associated with worse health outcomes. The health trajectory of Hispanic patients with CF, in contrast to patients of non-Hispanic ethnicity with CF, has not been well described. In this study, we aim to characterize the patterns of mortality and risk factors for poor health outcomes among Hispanic patients with CF over the last 20 years and in comparison with the concurrent non-Hispanic patient population with CF.

Materials and Methods

This is a retrospective analysis of the CF Foundation Patient Registry (CFFPR) of California residents (N = 4387). The CF Foundation approved the use of the registry data. The Stanford University institutional review board, panel on human subjects in medical research, approved the study protocol (No. 19908).

The CF Foundation has stored health information from patients seen at accredited centers since 1966 and has maintained patient data from 1986.[15] Each patient's ethnicity has been collected by parental or self-report since 1991. Thus, the study period was January 1, 1991, to December 31, 2010. Inclusion criteria included a childhood diagnosis (≤ 18 years of age) of CF during the study period to control for left censoring (events or death prior to entry into the study). Patients who were missing insurance status (n = 5) were excluded (Fig 1).

The primary outcome was death. Subjects were censored at the time of lung transplant, loss to follow-up, or end of the observation period. Other health outcomes included FEV_1, a validated pulmonary health parameter in CF and recorded as the % predicted value (% pred) based on normative data[15-17]; BMI; and *z* score, adjusted for patient's age and sex.

The primary predictor of interest was ethnicity, Hispanic or non-Hispanic, by parental or self-report. Secondary predictors were identified a priori based on a review of previous literature on the clinical, biologic, and social factors most likely to mediate or confound any relationship between ethnicity and health outcomes.

Clinical and biologic factors assessed included age and year of diagnosis,[18] sex,[19,20] CF transmembrane conductance regulator (CFTR) genotype,[19,21] infections with *Pseudomonas aeruginosa* or *Burkholderia cepacia*,[22,23] and CF-related diabetes (CFRD).[24] CFTR genotype severity was categorized into one of five functional classes proposed by Welsh et al.[25] The mutations were further classified into three groups: "high" or "low" disease risk according to the scheme proposed by McKone et al[21] and "unclassified" disease risk for mutations with unknown functional class. Infection with *P aeruginosa* or *B cepacia* was characterized as dichotomous (never/ever) and by age at first acquisition; earlier age at acquisition is associated with worse prognosis.[23,26,27] Diagnosis of CFRD was characterized as dichotomous (never/ever) and age at diagnosis.[24]

Social factors assessed included public insurance status, median household income,[8,19] and access to subspecialty care.[4] Public insurance (Medicare, Medicaid, state special needs program, and/or Indian Health Services) was categorized as dichotomous (never/ever). Neighborhood median household income was estimated by the subject's most frequently reported residential ZIP code using the Claritas, Inc demographic database,[28] and was categorized on the basis of the federal poverty line (FPL) designation for 2004 ($18,850 for a family of four). Access to subspecialty care was defined by the mean number of outpatient visits to CF Foundation-accredited centers per year of observation. Optimal access to subspecialty care was defined as three or more outpatient clinic visits per year.[29,30]

We performed time-to-event (survival) analysis with time as years since diagnosis to avoid left censoring (bias of events/deaths prior to entry into the study), because the study cohort is defined as diagnosis with CF and enrollment in the CFFPR. We estimated cause-specific hazard ratios (HRs) of death in Hispanics vs non-Hispanics using multivariable Cox proportional hazard models, adjusting for the previously mentioned covariates. Assessing the assumption of proportionality for all covariates and time-dependent interaction, we found that sex was in violation and as our final model we present a stratified cox model on sex. Categorical variables were compared by χ^2 or Fisher exact tests. Continuous variables were compared by *t* tests or Mann-Whitney *U* test and

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DOI: http://dx.doi.org/10.1378/chest.14-2189

Wilcoxon two-sample test. To assess whether there was an effect of ethnicity on decline of FEV_1 and BMI by age, we compared random-effects models of FEV_1 and BMI by age and ethnicity with and without interaction of age and ethnicity. Models were compared using sum of squares, corrected Akaike's information criteria, and F test.

Results

A total of 1,719 California residents with CF received the diagnosis during or after 1991 and before 18 years of age. Hispanic patients made up 28.2% (n = 485) (Fig 1). Compared with non-Hispanic patients with CF, a slightly greater proportion (22.9% vs 17.1%, $P = .0056$) of Hispanic patients received the diagnosis after introduction of universal newborn screening in California in June 2007 (Table 1).

Mortality

During the study period, the overall unadjusted mortality rate for the entire sample was 4.9% (n = 85). Mortality in Hispanic patients was 9.1% (n = 44), whereas mortality in non-Hispanic patients was 3.3% (n = 41) (Table 1). The unadjusted risk ratio for mortality in Hispanic patients was 2.73. The mean age at death for Hispanic patients and non-Hispanic patients was not statistically different (11.7 years [SD, 5.2] years vs 13.4 years [SD, 5.8], $P = .1775$). The leading cause of death in both groups was reported as respiratory or cardiorespiratory. Kaplan-Meier survival analysis showed that Hispanic patients had lower survival rate 18 years after diagnosis (75.9% vs 91.5%, $P < .0001$) (Fig 2).

To assess the potential impact of differing transplant rates, we analyzed cumulative incidence curves for competing events of death and lung transplant, which showed no difference in incidence of lung transplant (data not shown).

Adjusted Analyses

A stratified multivariable Cox proportional hazards model revealed that Hispanic patients had 2.81 times the rate of death of non-Hispanic patients (95% CI,1.70-4.63) after adjusting for year of diagnosis, age at diagnosis, public insurance, neighborhood median household income, bacterial infection, CFRD diagnosis, and CFTR genotype (Table 2). Low neighborhood median household income (two to four times FPL) was also independently associated with a higher rate of death (adjusted HR, 2.93; 95% CI, 1.04-8.24). Compared with patients with two high-risk CFTR mutations, patients who had two CFTR alleles of unclassified disease risk (adjusted HR, 2.61; 95% CI, 1.25-5.43) or were not genotyped at all (adjusted HR, 3.28; 95% CI, 1.68-6.43) had a higher rate of death. Neither *P aeruginosa* or *B cepacia* infection nor CFRD diagnosis was independently associated with an increased rate of death.

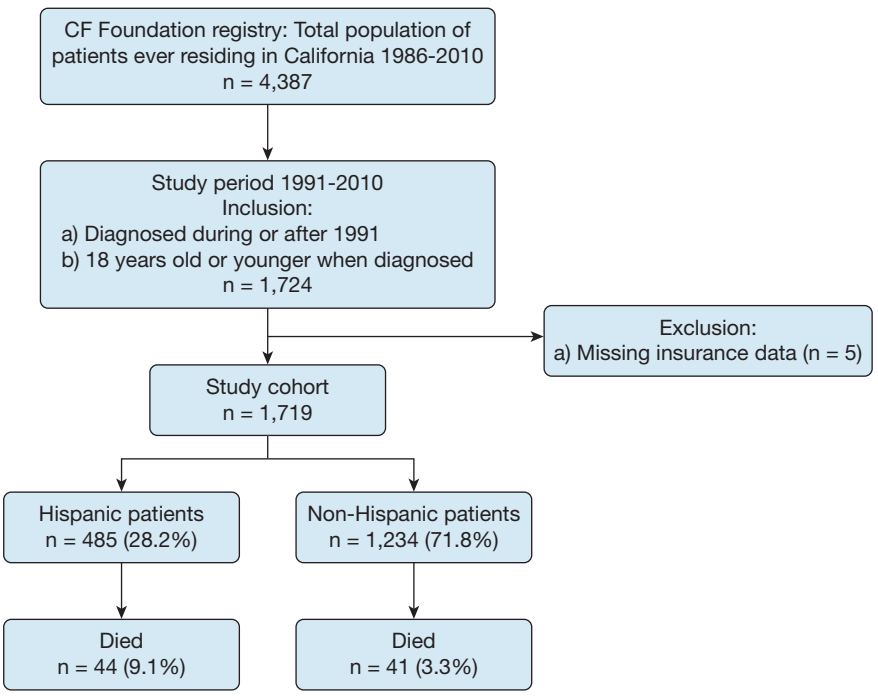

Figure 1 – *Flowchart of study cohort. Of the 4,387 California residents in the CF Foundation Patient Registry, 1,724 received the diagnosis during or after 1991 and before 18 years of age. All had recorded ethnicity. Five patients were excluded because of missing insurance data. The final cohort for analysis was 1,719 patients. Hispanic patients made up 28.2% of the total patient population available for analysis. The unadjusted mortality rate was higher in Hispanic patients. CF = cystic fibrosis.*

TABLE 1] Mortality and Other Health Characteristics, CF Foundation Patient Registry, California, 1991-2010

Variable	Hispanic (n = 485)	Non-Hispanic (n = 1234)	*P* Value[a]
Mortality			
Outcome during study period			
Died	44 (9.1)	41 (3.3)	< .001[b]
Alive	435 (89.7)	1,174 (95.1)	…
Lung transplant	6 (1.2)	19 (1.5)	…
Age at death			
< 18 y	37 (84.1)	32 (78.1)	.48[b]
> 18 y	7 (15.9)	9 (22)	…
Mean (SD), y	11.7 (5.2)	13.4 (5.8)	.18[c]
Sex			
Male	250 (51.6)	625 (50.7)	.74[b]
Female	235 (48.5)	609 (49.4)	…
Year of CF diagnosis			
1991-2006	374 (77.1)	1,023 (82.9)	.006[b]
2007-2010	111 (22.9)	211 (17.1)	…
Age at diagnosis			
< 6 mo	261 (53.8)	610 (49.4)	.10[b]
≥ 6 mo	224 (46.2)	624 (50.6)	…
Median (IQR), mo	5.3 (1.3-31.3)	6.1 (0.8-41.8)	.41[d]
CFTR genotype risk severity			
High-high	174 (35.9)	745 (60.4)	< .001[e]
High-low	28 (5.8)	69 (5.6)	…
High-unclassified	150 (30.9)	266 (21.6)	…
Low-low	2 (0.4)	3 (0.2)	…
Low-unclassified	8 (1.7)	8 (0.7)	…
Unclassified-unclassified	86 (17.7)	71 (5.8)	…
Not genotyped	37 (7.6)	72 (5.8)	…
Clinical characteristics			
Positive culture for *Pseudomonas aeruginosa*			
Never	133 (27.4)	377 (30.6)	.20[b]
Ever	352 (72.6)	857 (69.5)	…
Age at first acquisition, mean (SD), y	5.2 (4.7)	6.1 (5.0)	.004[c]
Age at first acquisition, median (IQR), y	3.7 (1.7-6.9)	4.6 (2.2-8.8)	…
Positive culture for *Burkholderia cepacia*			
Never	468 (96.5)	1,198 (97.1)	.53[b]
Ever	17 (3.5)	36 (2.9)	…
Age at first acquisition, mean (SD), y	8.4 (5.2)	11.9 (4.2)	.01[c]
Age at first acquisition, median (IQR), y	8.0 (3.9-12.6)	12.2 (9.4-14.0)	…
Diagnosis of CF-related diabetes			
Never	433 (89.3)	1,091 (88.4)	.61[b]
Ever	52 (10.7)	143 (11.6)	…
Age at diagnosis, mean (SD), y	13.4 (4.3)	14.9 (4.4)	.04[c]
Age at diagnosis, median (IQR), y	13.8 (10.1-15.7)	14.6 (12.4-17.4)	…

(Continued)

TABLE 1] *(Continued)*

Variable	Hispanic (n = 485)	Non-Hispanic (n = 1234)	*P* Value[a]
Social factors and health-care access			
Public health insurance[f]			
Never	62 (12.8)	483 (39.1)	< .001[b]
Ever	423 (87.2)	751 (60.9)	…
Percent time with public insurance, mean (SD), % y	78.5 (27.6)	58.5 (34.5)	< .001[c]
Neighborhood median household income			
< 2 times FPL	149 (30.7)	148 (12.0)	< .001[b]
2-4 times FPL	264 (54.4)	645 (52.3)	…
> 4 times FPL	25 (5.2)	235 (19.0)	…
Unable to be determined	47 (9.7)	206 (16.7)	…
Outpatient CF center clinic visits			
No. clinic visits per year, mean (SD)	4.6 (1.4)	4.5 (1.6)	.15[c]
< 3 clinic visits per year	38 (7.8)	129 (10.5)	.10[b]
≥ 3 clinic visits per year	447 (92.2)	1,105 (89.6)	…

Data are shown as No. (%) unless otherwise indicated. CF = cystic fibrosis; CFTR = cystic fibrosis transmembrane conductance regulator; FPL = federal poverty line; IQR = interquartile range.
[a]Comparing Hispanic patients with non-Hispanic patients.
[b]χ^2.
[c]t test.
[d]Wilcoxon two-sample test.
[e]Fisher exact test.
[f]Includes Medicare, Medicaid, state special needs program, and Indian Health Services.

Lung Function and BMI

At 6 years of age (the first age at which lung function can be measured and collected reliably), the mean FEV_1 for Hispanic patients was lower than for non-Hispanic patients (77% pred [SD 23% pred] vs 89% pred [SD 20% pred], $P < .0001$). However, the yearly rate of decline in FEV_1 between Hispanic and non-Hispanic patients was not different (Fig 3A). BMI as a proxy for nutrition plotted by age was not different between Hispanic and non-Hispanic patients (Fig 3B).

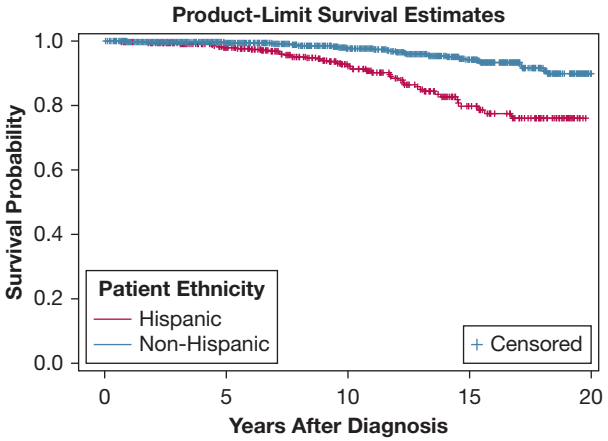

Figure 2 – *Kaplan-Meier plot shows a difference in survival rates between Hispanic and non-Hispanic patients with CF. Hispanic patients (red): n = 485 (44 failed, 441 censored). Non-Hispanic patients (blue): n = 1,234 (41 failed, 1,193 censored). Log-rank χ^2, 35.0647; df = 1; P < .0001. CF Foundation Patient Registry, California, 1991-2010. See Figure 1 legend for expansion of abbreviation.*

Clinical and Biologic Factors

There were no significant differences in age at diagnosis and distribution of sex between Hispanic and non-Hispanic patients. The median age at diagnosis for the entire cohort was 5.8 months (interquartile range, 0.9-38.3).

Different CFTR genotype patterns were observed between Hispanic and non-Hispanic patients (Table 3). The top 15 CFTR alleles by frequency accounted for 80% of the CFTR alleles for non-Hispanic patients, but only 64% for the Hispanic patients, indicating greater heterogeneity of CFTR mutations in the Hispanic population. Although all the top 15 mutations have been verified as causing CF,[31] Hispanic patients had more mutations that have not been classified by CFTR functional class. Hispanic patients had a high percentage (50.3%) of at least one CFTR allele of unclassified risk, compared with 28.1% in non-Hispanic patients (Table 1). Of note, 6.3% of patients in the registry did not have CFTR genotype data, and this was not significantly different between groups (χ^2 $P = .19$).

TABLE 2] Multivariable Proportional Hazards Model for the Risk of Death Stratified by Sex, CF Foundation Patient Registry, 1991-2010 (n = 1,719)

Covariate	HR (95% CI)
Ethnicity	
Hispanic	2.81 (1.70-4.63)
Non-Hispanic	Reference
Neighborhood median household income	
< 2 times FPL	2.13 (0.69-6.53)
2-4 times FPL	2.93 (1.04-8.24)
> 4 times FPL	Reference
Missing	2.19 (0.68-7.05)
CFTR genotype risk severity	
High-high	Reference
High-low	1.23 (0.35-4.31)
High-unclassified	1.12 (0.63-1.98)
Low-low	0
Low-unclassified	3.33 (0.66-16.83)
Unclassified	2.61 (1.25-5.43)
Not genotyped	3.28 (1.68-6.43)

Stratified by sex. Model is adjusted for ethnicity, CFTR risk severity, *Pseudomonas aeruginosa* infection, *Burkholderia cepacia* infection, CF-related diabetes, year of diagnosis, age at diagnosis (mo), public insurance, and neighborhood median household income. HR = hazard ratio. See Table 1 legend for expansion of other abbreviations.

Although there was no difference in the overall incidence of infection with *P aeruginosa* or *B cepacia* between Hispanic and non-Hispanic patients, Hispanic patients reported a younger age at first acquisition for both organisms (Table 1). There was no difference in incidence of CFRD between the two groups, but the mean age at diagnosis with CFRD was 1 year younger in Hispanic patients than in non-Hispanic patients (13.4 years (SD, 4.3) and 14.9 years (SD, 4.4), respectively; $P = .04$).

Social Factors and Health-care Access

Hispanic patients were more likely to ever have public health insurance and a greater average percent time with public insurance per time in the registry (Table 1). Nearly a third of the Hispanic patients lived in neighborhoods with high rates of poverty (estimated neighborhood median household income of less than two times FPL). There was no difference in health-care access (mean number of clinic visits per 12 months or suboptimal use) at outpatient CF centers between Hispanic and non-Hispanic patients (Table 1).

Discussion

Although the median lifespan for CF has improved over the last 20 years, we found significantly higher rates of mortality among patients of Hispanic ethnicity with CF. By Cox proportional hazards modeling, Hispanic patients had 2.81 times the mortality rate of death compared with non-Hispanic patients, and this remained significant and independent of the biologic, diagnostic, clinical, and social factors that are known to be associated with mortality in CF. This finding is congruent with prior published data of mortality rates

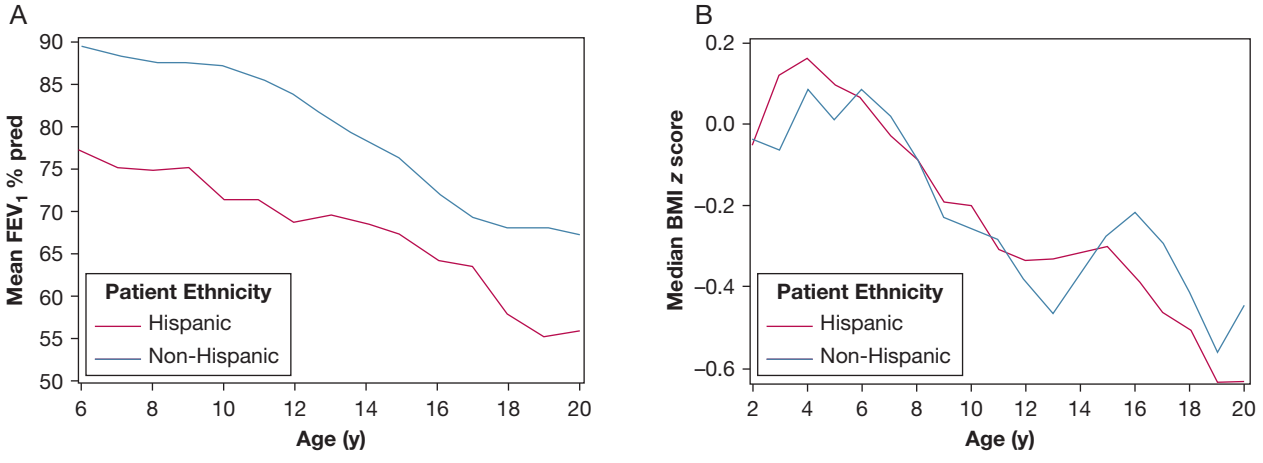

Figure 3 – *A, B, Plots of mean FEV_1 % pred by age and median BMI z score by age from all clinical encounters stratified by ethnicity. A, At 6 years of age, the mean FEV_1 for Hispanic patients (red) is lower than for non-Hispanic patients (blue), (77% pred [SD, 23% pred] and 89% pred [SD, 20% pred], respectively, $P < .0001$). The yearly rate of decline in mean FEV_1 % pred is not different between the two groups. FEV_1 was best predicted by a random-effects model without interaction of age and ethnicity. (Difference in corrected Akaike's information criteria (AICc), 1.85; information ratio, 2.53; F test 0.7026) B, The yearly rate of decline in median BMI z score is not different between the two groups. BMI was best predicted by a random-effects model without interaction of age and ethnicity. (Difference in AICc, 3.5; information ratio, 5.76. Sum of squares was lower for less complicated model.) CF Foundation Patient Registry, California, 1991-2010. % pred = % predicted value. See Figure 1 legend for expansion of other abbreviation.*

TABLE 3] Top 15 CFTR Alleles by Frequency Stratified by Ethnicity, CF Foundation Patient Registry, California, 1991-2010

CFTR Genotype (Legacy Name)	Mutation Type	CFTR Functional Class	Allele Frequency, No. (%)
Hispanic patients			
F508del	Deletion	II	390 (43.5)
G542X	Nonsense	I	49 (5.5)
3849+10kbC->T	Splice	V	22 (2.5)
N1303K	Missense	II	14 (1.6)
3120+1G->A	Splice	Unclassified	12 (1.3)
R75X	Nonsense	I	11 (1.2)
3876delA	Frameshift	Unclassified	10 (1.1)
663delT	Frameshift	Unclassified	10 (1.1)
1288insTA	Frameshift	Unclassified	9 (1)
I507del	Deletion	II	9 (1)
H199Y	Missense	Unclassified	7 (0.8)
S549N	Missense	II	7 (0.8)
406-1G->A	mRNA splice	Unclassified	6 (0.7)
R1162X	Nonsense	I	6 (0.7)
W1089X	Nonsense	I	6 (0.7)
W1204X	Nonsense	Unclassified	6 (0.7)
Non-Hispanic patients			
F508del	Deletion	II	1,505 (64.8)
G542X	Nonsense	I	51 (2.2)
G551D	Missense	III	47 (2.0)
W1282X	Nonsense	I	46 (2.0)
R117H	Missense	IV[a]	34 (1.5)
1717-1G->A	Splice	I	31 (1.3)
N1303K	Missense	II	31 (1.3)
3849+10kbC->T	Splice	V	21 (0.9)
5T[b]	Splice	V[a]	19 (0.8)
I507del	Deletion	II	19 (0.8)
R1162X	Nonsense	I	14 (0.6)
R553X	Nonsense	I	13 (0.6)
3120+1G->A	mRNA splice	Unclassified	12 (0.5)
621+1G->T	mRNA splice	I	12 (0.5)
2183delAA	Frameshift	I	10 (0.4)

mRNA = messenger RNA. See Table 1 legend for expansion of other abbreviations.
[a]Varying clinical consequence.
[b]Associated TG tract not reported.

in ethnic minority groups,[19] but this study further explores the specific risk factors associated with mortality.

Disease severity and mortality is a result of complex relationships among multiple factors along a patient's life course.[32,33] In this study, we attempted to investigate these complex mechanisms using the data available in the CFFPR. Hispanic and non-Hispanic patients have different CFTR genotype patterns. Many of the CFTR genotypes seen in Hispanic patients do not have functional or risk classifications. This has future implications because new therapies in CF are based on biologic function or protein trafficking of the CFTR molecule, which is based on predictions from the CFTR genotype.[34] Unknown CFTR genotype was independently associated with increased mortality risk. This finding may be due to more severe clinical phenotype in patients diagnosed by clinical criteria without CFTR genotype.

A higher proportion of Hispanic patients than non-Hispanic patients lived in poor neighborhoods. Prior research has shown that median family income is independently associated with mortality.[8] The adjusted analysis included neighborhood median household income and did not completely attenuate the residual difference in mortality rate observed for Hispanic patients. Poverty and social class likely contribute to the differences in health outcomes but could not be completely accounted for in the data available.[35-37]

Although there was no difference in access and use of CF center care, age at diagnosis, and nutritional status, lung function measured by FEV_1 was significantly lower for Hispanic patients than for non-Hispanic patients at 6 years of age, which is compatible with the one cross-sectional study of Hispanic patients with CF.[38] However, we observed no ethnic differences in yearly rate of decline of FEV_1 or BMI. It is not clear if the 12% predicted point difference in FEV_1 between the two groups is adequate to explain the difference in mortality rates observed. Future studies will need to investigate the causes of the difference in lung function at first measurement between the two groups, which may be a result of differences in normative data for ethnicity, care in the first 6 years of life, severity of pulmonary exacerbations, inherent CF disease severity, or a combination of these factors.

Although there was no difference in the prevalence of CF complications, Hispanic patients were diagnosed with *P aeruginosa* or *B cepacia* infection or CFRD 1-3 years before their non-Hispanic counterparts. Lower lung function and earlier incidence of CF complications are likely important contributors to the increased rate of mortality observed in Hispanic patients. Future studies are necessary to investigate this further. Although there was no difference in access to CF centers, there may be contributing individual factors such as adherence to treatment regimens, self-management, culture, health literacy, and English proficiency.[11,12,39-41]

Patients with shared ethnicity, language, and/or culture provide a unique opportunity for targeted intervention to improve health outcomes. Our findings of increased mortality in Hispanic patients, differences in baseline lung function, and early incidence of CF complications suggest a promising opportunity for the development of preventative and management strategies that can be both cost effective and more culturally appropriate for Hispanic patients and families living with CF.

Limitations

This study and its findings are subject to the biases common to studies of clinical registries. Selection bias results from studying the CFFPR, which requires subjects to have access to CF subspecialty care. Misclassification bias can occur from self-reported ethnicity. Measurement bias may have affected assessment of social factors, particularly family income, which was estimated ecologically by ZIP code. As a result, we are unable to capture all the determinants of health, such as discrimination and bias, quality of care, physical environment, and individual factors (health literacy, English proficiency).

Hispanic ethnicity is a sociopolitical construct, heavily confounded by socioeconomic status and cultural identity.[42,43] Social and biomedical scientists have cautioned against the classification of patients by ethnicity and race in biomedical research because of reifying race.[42-45] However, patients of Hispanic ethnicity have been described as experiencing a variety of other health disparities, often related to differences in health-care access, acculturation, and language-related barriers to care.[10-12] This study adds to the literature supporting the existence of health disparities for patients of Hispanic ethnicity; however, the generalizability is limited because of the specific disease progression and management experienced by patients with CF.

Accuracy of age at first detection of airway organisms in the CFFPR is dependent on the sensitivity of detection and diagnosis of organisms in individual subjects, which is affected by culture type and microbiology techniques.[46] However, there is no reason for differential sensitivity of microbiology diagnosis between the two study groups.

Implications

This study demonstrates that Hispanic ethnicity is a risk factor for increased mortality among patients with CF. In addition, neighborhood poverty and unclassified or unknown CFTR genotype are associated with an increased rate of mortality. The key strength of this study was the size and time period covered by this first effort to understand the ethnic, social, and biologic epidemiology of CF-related mortality. As mentioned, the relationship of ethnicity and mortality is likely multifactorial and complex. Some health policies adopted in the last 10 years, such as universal newborn screening, have the potential to

positively affect the health of patients with CF. Future analyses should also consider the impact of these programs on the observed ethnic disparities in health outcomes.

Conclusions

The Hispanic ethnicity-specific disparity in mortality rates among people with CF has persisted despite improvements in the care of all patients with CF. With anticipated continued growth in the overall Hispanic population and the disproportionate growth of the Hispanic population within the CF community, this ethnic disparity in mortality rates should give us pause. Understanding the mechanisms for the increased mortality rate among Hispanics is necessary to improve the health of all patients with CF.

Acknowledgments

Author contributions: M. C. B. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. M. C. B., C. E. M., and P. H. W. contributed to the study design; M. C. B. and C. E. M. contributed to the data collection; M. C. B., L. M. S., and C. E. M. contributed to the data analysis and interpretation; J. A. M. contributed to the data management and analysis; M. C. B. contributed to the writing of the manuscript; and L. M. S., J. A. M., C. E. M., and P. H. W. contributed to the review and approval of the manuscript.

Conflict of interest: C. E. M. has received grant funding support from the National Institutes of Health and the CF Foundation; clinical trials research funding support from KaloBios and Vertex Pharmaceuticals Inc; and funding from Gilead Sciences, Inc for acting in an ad hoc advisory capacity. None declared (M. C. B., L. M. S., J. A. M., P. H. W.).

Role of sponsors: The sponsors had no role in the design of the study, the analysis of the data, or in the preparation of the manuscript. The CF Foundation and CFFPR collected and provided the data analyzed in this study.

Other contributions: The authors thank the CFFPR for review of the manuscript prior to publishing and the CF Foundation for the use of CFFPR data to conduct this study. Additionally, the authors thank the patients, care providers, and clinic coordinators at CF Centers throughout the United States for their contributions to the CFFPR.

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