REGULAR ARTICLE

Socioeconomic and Social Determinants of Health: Effects on Pulmonary Arterial Hypertension Care

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There is increasing awareness on the significance of socioeconomic status, social determinants of health, and the role of ethnicity and race in clinical outcomes of patients with pulmonary arterial hypertension. However, to date, underrepresentation of minorities in pulmonary hypertension clinical trials and registries remains. In the present review, we summarize the current knowledge on race, ethnicity, traditional and novel socioeconomics and social determinants of health, and its association with clinical outcomes in patients with pulmonary arterial hypertension. We present case examples on the interplay of these factors for specific disease phenotypes and discuss strategies for addressing these variables at the patient care level.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is associated with impaired quality of life and increased cardiovascular morbidity and mortality as well as increased economic burden. Significant progress has been made in the understanding of PAH, and different prognostic models have been developed to better guide its management.[1,2] However, our current approach of disease management relies on data obtained from large registries and clinical trials where there is significant underrepresentation of minorities.[3] Recent years have brought renewed attention to racial and gender disparities in health, highlighted by recent sociopolitical violence as well as the COVID-19 pandemic.[4]

In the present review, we discuss the significance of race or ethnicity and social determinants of health (SDOH) in PAH. We describe 2 case examples displaying the interplay of negative SDOH, and we discuss the steps needed to improve representation of minorities and to overcome the barriers that SDOH imposes on the care of patients with PAH.

DEFINITIONS

Socioeconomic status (SES) refers to an individual's social and economic standing, reflecting his or her social or economic rank within a given social group.[5] SDOH refer to conditions in which individuals are born, grow, live, work, and age[6] and are implicated in health inequalities which disproportionately affect certain groups such as minorities. Health care disparities refer to differences in health care access closely linked with social, economic, and/or environmental disadvantage.[7]

RACE, ETHNICITY, AND SDOH IN PULMONARY HYPERTENSION

Race or Ethnicity

Most studies on the association between race or ethnicity and outcomes in PAH relate to Hispanic and Black patients. In general, Hispanic PAH patients are younger and have a higher frequency of congenital heart disease and portopulmonary hypertension (PoPH) than non-Hispanic Whites.[8] Reasons behind this association include lack of access to proper medical care in early childhood when congenital heart defects could be detected and corrected[8] in addition to a higher frequency of untreated hepatitis B infection[9] increasing risk of PoPH.

Race and ethnicity have been shown to have effects on outcomes in PAH patients. It has been described that healthy Hispanic patients without PAH have a higher right ventricular (RV) mass than non-Hispanic Whites, which has led to the hypothesis that Hispanic patients could have an inherent biologic advantage regarding RV adaptation.[10] Karnes et al[11] used data from the National Biological Sample and Data Repository for PAH (PAH Biobank) to assess differences in outcomes based on race or ethnicity. In their analysis, Hispanic patients had better survival than both non-Hispanic White and Black patients, even after adjusting for age, sex, hemodynamics, and PAH treatment (heart rate [HR] = 0.46, 95% confidence interval [CI] = 0.21–0.99). The authors focused mainly on idio-

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pathic and heritable PAH rather than other subtypes of PAH, limiting the generalizability of these findings. The authors did not account for differences in social, economic, or environmental determinants of health. Medrek et al[12] assessed the effect of race on PAH outcomes using data from the REVEAL registry, and no association was found on the multivariate analysis (which adjusted for age and PAH subtype). In their analysis, they could not account for differences in SES, as this information was not collected in the REVEAL registry. Bernardo et al[13] used data from the Pulmonary Hypertension Association Registry (PHAR) to describe the profile of Hispanic patients with PAH. Of note, PHAR routinely collects information on SDOH,[14] and surveys are available in Spanish. Hispanic patients had suboptimal health care insurance, lower annual income, lower education level, and were more likely to be unemployed as compared with non-Hispanic White patients.[13] While the unadjusted analysis showed better survival in Hispanic individuals, this association was no longer present after adjustment for age, sex, PAH subtype, and SDOH metrics (annual income, health insurance, and education level). Finally, in a recent study in a Hispanic-enriched cohort, authors showed that commonly used risk stratification tools, such as COMPERA and REVEAL 2.0, performed well as risk predictive tools, both with acceptable mortality discrimination.[15]

Racial variations on etiology of PAH as well as medication responses in non-Hispanic Blacks have also been reported. Black patients with PAH have a higher frequency of connective tissue disease such as scleroderma than White patients[8] and may have a different response pattern to endothelin-receptor antagonists (ERAs).[16] A pooled analysis of randomized clinical trials of ERAs in PAH showed differences in the response pattern of Black patients with placebo-adjusted change in 6-minute walk distance that decreased by 3.5 m, which was in contrast to an increase by 41.5 m in White participants, and this persisted in the adjusted models.[16] It was hypothesized that treatment-response differences could be related to higher endothelin-1 (ET-1) levels in Black patients not sufficiently inhibited by the dose of the ERAs used in the trials.[16,17]

Regarding survival, Parikh et al[18] found that Black patients had increased mortality as compared with Whites (HR = 2.06, 95% CI = 1.18–3.44), but when adding insurance status to the survival model, there were no differences in mortality, suggesting that outcome differences were mostly related to lack of access to care.

Less is known about other minorities with PAH such as Asian patients,[19] Native Americans,[20,21] and Native Hawaiian and other Pacific Islanders. There is limited knowledge about PAH in low- and middle-income countries, which constitutes a significant gap in knowledge.

SOCIOECONOMICS

While effective therapies exist for PAH, economic barriers to proper treatment still exist. The average treatment cost per patient is estimated at $80 000 dollars per year.[22] Deductibles and copayments can lead to substantial out-of-pocket costs, despite active health insurance.[23]

SES has been shown to be an independent predictor for survival in PAH. Wu et al[24] stratified patients with PAH from China in SES tertiles, finding that patients in the lower socioeconomic tertile had increased mortality. Talwar et al[25] used data from a large hospital system in New York and found that patients with lower annual income had higher disease severity on presentation. In a study from Scotland, authors used a geographic index (Scottish Index of Multiple Deprivation) to estimate social deprivation in patients with pulmonary hypertension (PH)[26]; however, unlike the 2 prior studies, no association with mortality or disease severity was found.

RURALITY, HEALTH CARE DESERTS, AND ACCESS TO TECHNOLOGY

Due to the need for specialized care, most patients with PAH receive their treatment at large metropolitan referral centers and frequently must drive long distances for continuity of their care. As such, patients from disadvantaged economic backgrounds could face barriers such as lack of transportation, which leads to missed clinic appointments, inadequate pharmacy access, and delays in medical care.[23,27] Macias et al[28] performed a claims data-based analysis of adults with PH. Mortality risk was significantly higher among those living in small urban counties (HR = 1.48, 95% CI = 1.14–1.92) and rural counties (HR = 2.01, 95% CI = 1.13–3.57), even after adjusting for age, sex, neighborhood poverty rate, race or ethnicity, and disease burden. Efforts to improve access to health care in nonmetropolitan communities include the use of telemedicine. However, successful use of telemedicine relies on having access to proper technology, familiarity with it, and having stable Internet connectivity, which is frequently lacking in rural locations.[29] Lack of access to technology or Internet are considered novel SDOH.[30]

Despite increased numbers of PAH providers in the United States, several states do not have a Pulmonary Hypertension Association (PHA)-certified PH Comprehensive Care Center (PHCCC). Figure 1 displays areas within the United States without an easily accessible PHA-accredited program for PAH care; however, some of these states may have centers with expertise in PAH that are not accredited.

VETERANS

Veterans are considered a vulnerable population, and there is increasing interest in understanding the profile of veterans with PAH. Gillmeyer et al[23] performed a retrospective cohort study of all adult veterans diagnosed with PAH, studying the association between race or ethnicity and SES (including metrics of housing insecurity). This population was predominantly male with only 4% Hispanics. Housing insecurity was found in 3.9%. Patients with lower household income and those without non-VA health insurance experienced significant delays in treatment initiation.

OTHER AT-RISK GROUPS

Other vulnerable populations in PAH include immigrants, prisoners, refugees, and patients with disabilities and mental health disease. There is a lack of information regarding the frequency of this

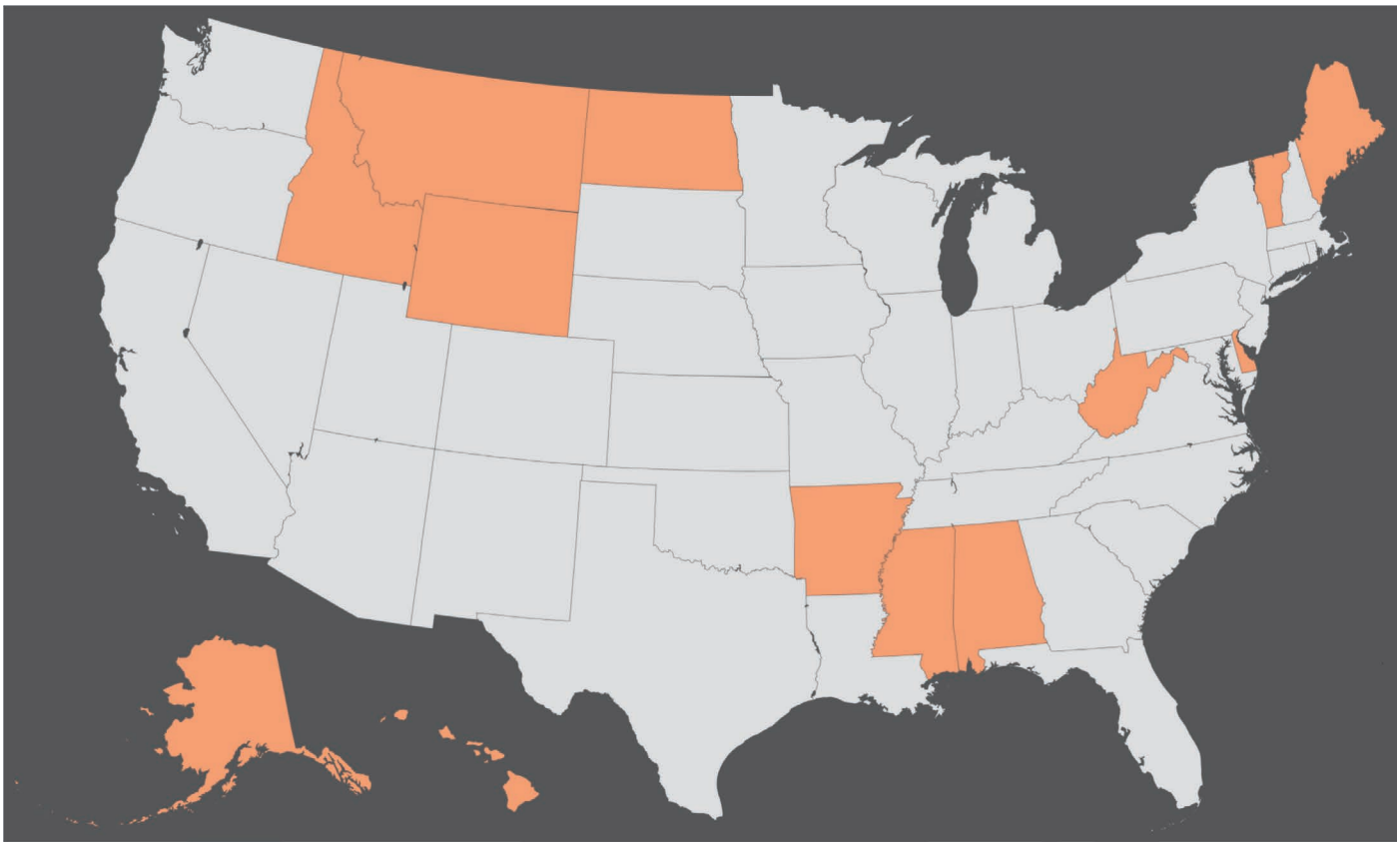

Figure 1: PAH care deserts. Highlighted are the states within the United States without a PHA-accredited center (either Accredited Center of Comprehensive Care or Accredited Regional Clinical Program). Source: phaassociation.org. PAH, pulmonary arterial hypertension; PHA, Pulmonary Hypertension Association.

demographic and prevalence of mental health disorders and the distinct barriers to proper care these patients face. Patients with language barriers could face difficulties with understanding their disease process and treatment options. Patients with disabilities or mental health disorders may face limitations of care related to underestimation of their ability to manage advanced therapies such as parenteral prostacyclins and is yet another area with significant gaps in knowledge.

Patients with substance abuse and addiction are a particularly vulnerable population and will be described later (see Populations at Risk). The significance of SES, SDOH, and medical literacy on trust in the medical care system, medication adherence, and treatment compliance is an area in need of further investigation.

REPRODUCTIVE HEALTH CARE

Unequal access to reproductive health care across the United States affects women of reproductive age. Female patients with PAH are counseled against pregnancy based on international consensus guidelines,[31,32] and pregnant patients with PAH are often counseled to pursue termination. With the recent Supreme Court decision to overturn Roe v. Wade, pregnant patients with PH face several challenges affecting their care including the possibility of having to relocate to a different state to pursue termination with its associated logistic costs. This is a significant challenge to all women but may be more pronounced in women of minority communities and lower SES.[33]

SPECIAL POPULATIONS AT RISK

Although SDOH are important outcome modifiers across the spectrum of PH, disease-specific considerations may uniquely elevate the significance, effect, and implications of SDOH in certain subtypes of PAH. Two specific populations, PoPH and methamphetamine-associated PAH (meth-PAH), present a particular challenge of intersecting social and biological factors that may influence patient outcomes in a compounded fashion (Figure 2).

PoPH is a type of PAH that uniquely occurs in patients with portal hypertensive liver disease.[34,35] Patients with PoPH demonstrate worse treatment responses than those with idiopathic PAH (IPAH) despite comparable hemodynamic disease severity at time of diagnosis, and PoPH patients have among the worst survival outcomes of any PAH subtype, with a 5-year mortality in excess of 60%.[34–36] In a recent analysis of PHAR, PoPH patients were less likely to be college graduates and more likely to have annual incomes below the poverty level and to be on Medicare or Medicaid insurance than IPAH patients.[37] Additionally, PoPH patients were prescribed fewer PAH therapies and were less likely to be treated with combination therapy than IPAH patients at time of registry enrollment, despite similar or worse

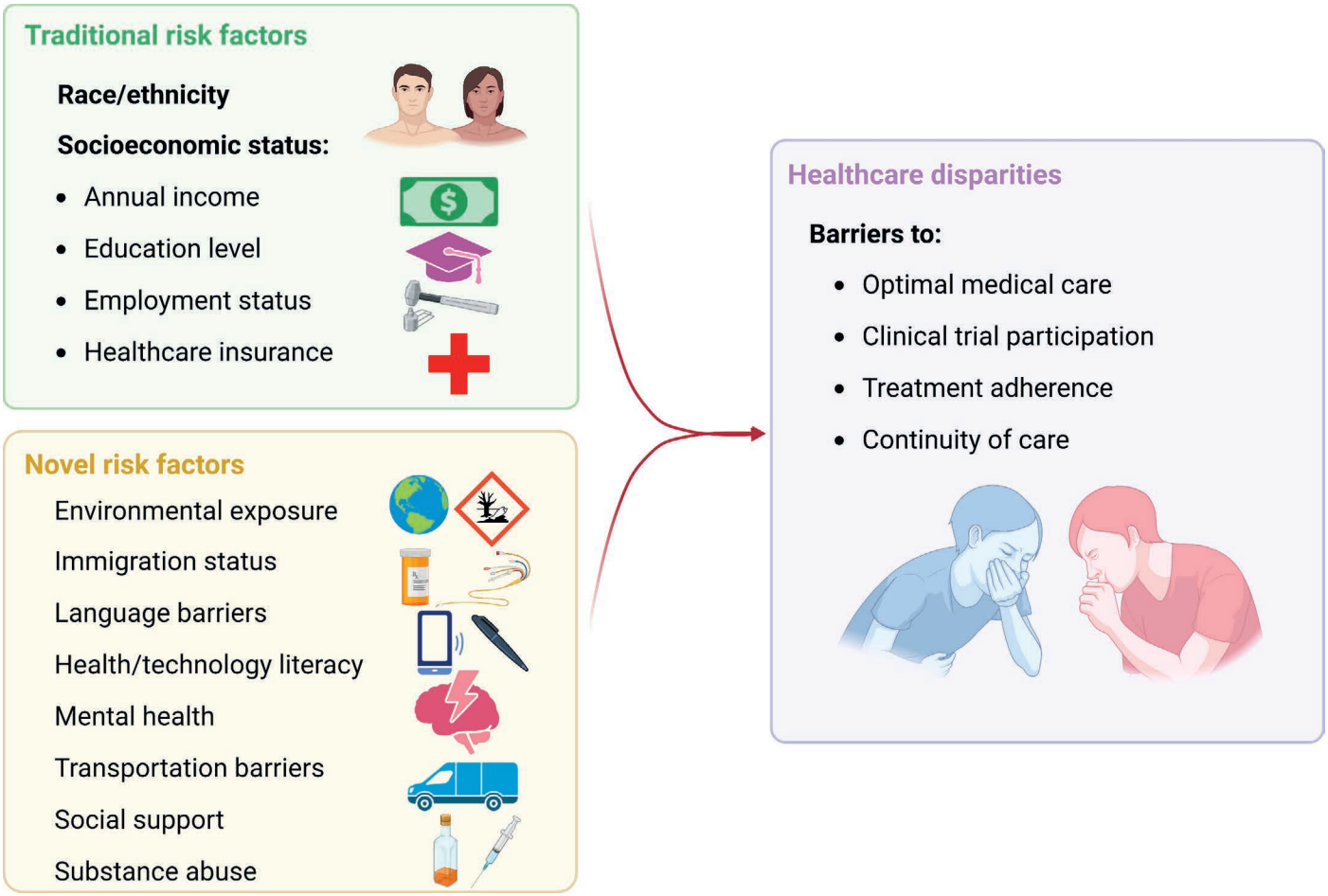

Figure 2: Interplay between biologic, socioeconomic, and racial or ethnic factors in PAH. Traditional and novel risk factors contribute to health care disparities in PAH. These factors usually coexist and exponentially affect outcome care in these patients. Created with BioRender.com. PAH, pulmonary arterial hypertension.

PAH disease severity. When examining health care usage, PoPH patients were significantly more likely to seek care at an emergency department than IPAH patients even after adjustment for age and measures of disease severity.[37] PoPH patients may be particularly vulnerable to the influence of SDOH by both their underlying PAH and their comorbid portal hypertensive liver disease.[38,39] Social deprivation, financial instability, and education level have been linked to both mortality and lower rates of liver transplantation in patients with cirrhosis.[40,41] Disentangling the links between pulmonary vascular disease, portal hypertensive disease, SDOH, and clinical outcomes has the potential to favorably affect outcomes in this high-risk population.

Meth-PAH is defined as PAH associated with significant exposure to amphetamines, predominantly methamphetamine, and is associated with more severe disease, poorer treatment responses, and lower survival than IPAH.[42,43] Meth-PAH patients tend to have suboptimal insurance coverage, lack of education, lower annual income, increased employment instability, and are less likely to receive parenteral prostacyclins than IPAH patients.[42,44] Meth-PAH patients also suffer from worse mental health quality of life scores, and coexisting mental health challenges not only place these individuals at risk for specific SDOH disparities but additionally play a pernicious role in dictating clinical care and patient outcomes.[45] A concerted effort to understand the unique mental health challenges faced by meth-PAH patients and how these difficulties may aggravate existing SDOH disparities and precipitate morbidity, mortality, and care disparities will be necessary to address and ameliorate the effect of these factors on patient outcomes.

ASSESSMENT TOOLS FOR SDOH

Despite increasing awareness of the effects of SES, SDOH, and health care disparities on clinical outcomes, these issues remain an area of patient care not routinely assessed nor acted upon in routine daily medical practice. In 2019, Fraze et al[46] completed a cross-sectional study of US hospitals and physician practices and found that most health care organizations and providers were not assessing for social effects on care, with only 24% of hospitals and 16% of physicians reporting screening for all 5 of the traditional SDOH. In a focused assessment of PAH care centers, Nadipelli et al[47] conducted semistructured interviews of 17 providers and 1 patient advocate and found a high level of awareness of the importance and effects of SDOH on PAH patient outcomes, but the interviewees voiced challenges

regarding routine screening for these factors. There was no consensus on optimal screening strategies, but there was agreement on the importance of this assessment.

There are multiple screening tools for SDOH which are geared for simplicity and can be completed quickly by patients of varying education levels and are available in multiple languages. A few of the available tools are as follows: The Centers for Medicare & Medicaid Services Accountable Health Communities Health-Related Social Needs Screening Tool (AHC-HRSN) survey consists of 10 brief core and 4 supplemental questions.[48,49] The American Academy of Family Physicians has developed an assessment tool through The EveryONE Project that is available in both English and Spanish and includes 11 focused questions that can be completed by patients independently or with assistance of nonclinical staff.[50] Additionally, the Montefiore Social Needs Assessment is an available tool which is a simplified 1-page assessment with 10 binary questions that can be implemented in daily patient care.[51] Further studies are needed to understand which screening tools are most applicable for the PAH population.

INTERVENTIONS FOR AT-RISK PATIENT POPULATIONS

Tackling the often difficult and challenging risk factors for poor outcomes related to SDOH, SES, and health care disparities is a far greater task than identification alone. Action plans need to be in place, and support systems must exist to act on the social, economic, and resource issues that are uncovered by screening. Because of the complexity of this task, the National Association of Community Health Centers, the Association of Asian Pacific Community Health Organizations, and the Oregon Primary Care Association collaborated to create a patient-centered assessment tool which is available in 30 languages, integrated in electronic medical records, and has a companion implementation and action toolkit known as PRAPARE (Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences) which provides a guide to address negative SDOH.[52] Addressing these unique patient needs requires trained and experienced staff. Nadipelli et al[47] reported that PAH providers surveyed stress the importance of social work support in PAH centers to adequately address patient needs. However, this resource is not routinely available in many PAH centers, resulting in the PAH center coordinators and providers taking on the shared responsibility of addressing barriers to care.

IMPROVING ACCESS AND UNDERSTANDING OF PAH SUBGROUPS IN CLINICAL TRIALS AND REGISTRIES

Currently, PAH clinical trials lack diversity and are not representative of the total patient population, thus limiting the understanding of the spectrum of PAH patients and impeding the development of optimal treatment strategies for all patients. Min et al[53] performed a pooled cohort analysis using harmonized datasets from phase 3 clinical trials and found that PAH research participants from 18 trials (1998–2013) were 78% female and 85% non-Hispanic Whites. Additionally, 97% of Asians and 74% of Hispanics in the sample were recruited from Asia and Latin America, respectively. Registry data also significantly underrepresent many PAH subpopulations. There was a predominance of White patients in REVEAL (72.8%), US National Institutes of Health registry (85.4%), as well as in the Surveillance of Pulmonary Hypertension in America Registry (81.5%). Black, Hispanic, and Asian or Pacific Islander patients enrolled at lower numbers than expected based on census data at that time.[3] Increasing awareness of the lack of diversity of enrollment in clinical trials and registries should prompt reevaluation of our screening and recruitment strategies with goals to shift to increasing opportunities for all patients cared for in PAH centers.

CONCLUSIONS

In health care, patients from every walk of life with varied backgrounds, experiences, and cultures seek medical care. Patients come to health care with expectations of equal opportunity for best outcomes. There are multiple barriers that patients can experience in achieving that goal. SES, race, ethnicity, education level, health care literacy, language, and communication barriers can affect successful treatment and quality of experience.

Change needs to occur at the patient care level and must start with identification of modifiable issues through standardized screening with tools to address factors that are negatively affecting patient care and successful treatment. A deep understanding of how to identify, discuss, and address SDOH is imperative to improve the likelihood of positive outcomes for all patients cared for in PAH centers.

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