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Review

Race and contrast-induced nephropathy in patients undergoing coronary angiography and cardiac catheterization

Raveen Chawla [a], Jeremy Turlington [b], Pradeep Arora [a,c], Ion S Jovin [a,b,*]

[a] Department of Medicine, Virginia Commonwealth University Health System and McGuire VAMC, Richmond, VA, United States
[b] Division of Cardiology, Virginia Commonwealth University Health System and McGuire VAMC, Richmond, VA, United States
[c] Division of Nephrology, McGuire VAMC, Richmond, VA, United States

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ABSTRACT

Contrast-induced nephropathy (CIN) is an acute worsening of renal function after receiving intravascular contrast during a procedure. Some of the predisposing factors include underlying diabetes, chronic kidney disease, congestive heart failure, periprocedural hypotension, anemia, contrast volume, and osmolality of contrast; however, it remains unclear if risk varies for CIN with race and ethnicity. There is evidence in the literature showing the link between race/ethnicity and the discrepancies in the utilization of preventive care services and the resources related to cardiovascular and renal health. While these disparities continue to exist and affect some of the predictors of CIN, this review will explore the extent to which race and ethnicity directly affect CIN.

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1. Introduction

Contrast-induced nephropathy (CIN) is a type of acute kidney injury that can occur after any procedure involving the use of intravascular contrast. Although the incidence of CIN is about >2% in the general population, it can be as high as 20%–30% among high-risk patients with diabetes, chronic kidney disease, congestive heart failure and/or older age [1]. Other factors potentially contributing to CIN include periprocedural hypotension, higher contrast media volumes, lower baseline hematocrit and intra-aortic balloon pump use [2]. The need for dialysis due to CIN is rare but has been associated with high in-hospital mortality rate and poor long-term survival [3]. While some of the predictors of CIN have been well documented in the literature, it still remains unclear whether race and ethnicity play a role.

Data on pathogenesis of contrast nephropathy comes from animal models. One of the theories is that acute tubular necrosis (ATN) occurs due to medullary hypoxia, possibly mediated by alterations in nitric oxide, endothelin, and/or adenosine. In humans renal blood flow determined by para-aminohippurate clearance remained 30 % below baseline up to two hours after the administration of contrast. The outer medulla is particularly susceptible to injury due to reductions in renal blood flow. Among diabetics there is impaired nitric oxide generation, which could contribute to the susceptibility to contrast agents. This raises the possibility that the African American population may be more prone to develop CIN due to possible different vascular responses to these mediators or direct toxic effects to the tubule. Indeed, Forman et al. showed that normotensive black and white individuals have different responses to renin-angiotensin system (RAS) blockers in terms of renal flow [4].

Race and ethnicity encompasses more than just one's genetic predisposition to certain diseases; they are also linked with one's socioeconomic status, insurance status, and one's behavior, beliefs, and conceptions toward health care. Understanding these associations is important before further dwelling into how race/ethnicity alone is associated with CIN.

2. Methods

A comprehensive literature search was conducted in PubMed database. The search strategy mainly involved the terms such as ("race" OR "ethnicity") AND ("preventive care" OR "cardiovascular disease" OR "renal disease" OR "contrast-induced nephropathy"). Case series, retrospective studies, review papers were all reviewed. Reference lists of other primary studies were also checked for additional relevant studies. Emphasis was placed on studies looking at the association between race/ethnicity and the utilization of resources pertaining to preventive care, cardiovascular disease, and renal disease. Extramural funding was not used to support this project. The authors are responsible for reviewing other studies, drafting, and editing this paper.

2.1. Race and preventive care

Several health care programs and organizations (e.g. Medicare, Medicaid, Veterans' Administration) now exist in the United States and these programs have helped in partially eliminating the financial strain of using physician services and hospitals, thus partially

* Corresponding author at: Cardiology Section, McGuire VAMC, 1201 Broad Rock Boulevard 111J, Richmond, VA 23249, United States.
E-mail address: isjovin@yahoo.com (I.S. Jovin).

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minimizing the disparities that existed among racial/ethnic minorities groups. These disparities have also been linked to both health care access and insurance coverage [5,6]. Immigration status and limited English proficiency have also been some of the barriers to access health care [5]. As of 2000, heart disease, cancer, and cerebrovascular disease were among the leading causes of death [7], all of which, to a certain extent, could have been prevented by utilization of the health services. In the past, racial/ethnic minority populations have been found to be less proactive than white populations at utilizing care services [8–10]. However, new data has been emerging that has shown quite the opposite [11,12].

In 2003, Heisler et al. published an observation study of 801 white and 115 black patients who finished the Diabetes Quality Improvement Project survey in 21 Veterans Affairs (VA) facilities. While there was not any difference in the use of a hemoglobin A1c test or foot examination, blacks were shown to be less likely compared to whites to have LDL checked in the previous two years [13]. Over the years, more studies emerged showing the opposite results.

In 2011, Vaidya and colleagues analyzed patterns of utilization of preventive care services impacting cardiovascular (CV) outcomes, i.e. cholesterol and blood pressure checkup. While the trend showed that all minority groups (African Americans, American Indian/Alaska Native, Asian, non-Hawaiian, and multiple races) were found to use cholesterol checkup more than whites, African Americans were found to use this service at almost double the rate of whites [11]. This perhaps could be due to the fact that African Americans are generally at higher risk for CV diseases and have received more counseling than their white counterparts [11,14]. A similar trend was noticed with the blood pressure checkup with the exception of Asians, who had significant lower utilization rate of blood pressure screening compared to whites, which was also consistent with the results of a previous national report [56]. This could perhaps be related to increased use of complementary and alternative medicine (CAM) such as herbal supplements among this set of minority groups [15] or due to the so-called the "healthy immigrant" effect where immigrants, on average, are healthier than the US-born population and do not require health services [16]. Of note, Hispanics were found to do poorly compared to non-Hispanics for cholesterol checkups but better with blood pressure checkup.

A lack of health insurance is also one of the reasons for delayed care and one of the main barriers to accessing services. As of 2011, racial and ethnic minorities were more likely to be uninsured than non-Hispanic whites [12]. More specifically, about 17% of Asians, about 33% of Hispanics, and 20% of African Americans were uninsured compared to 11.1% of non-Hispanic whites [12,55]. Holden et al. shed light on preventive service utilization among uninsured adults by race/ethnicity and income. Among the uninsured population, African Americans and Hispanics were significantly different from whites in many independent variables, i.e. poverty and education levels. In general, they were poorer and less educated compared to uninsured whites. This study ultimately showed that uninsured African Americans did significantly better compared to uninsured whites and Hispanics in seeking preventive services, especially routine checkups, blood pressure checks, Papanicolaou (Pap) smears and mammograms. Uninsured Hispanics also did better than uninsured whites in terms of receiving Pap tests, mammograms, influenza vaccinations, and routine checkups [12]. All in all, this study showed that whites did worse in preventive service utilization than Hispanics or African Americans at most income levels. Similar findings have also been reported in the literature; for instance Jones et al. showed racial and ethnic minorities did better receiving mammograms than whites [17], and Cook et al. showed African Americans and Hispanics were more likely to receive Pap smears than whites [18]. Further research would be needed to better elucidate this pattern. Although it could be attributed to the fact that more people from racial/ethnic minorities live in urban areas that are saturated with healthcare services, therefore, making it easier for them to access those services.

Some older studies have shown that racial/ethnic minority populations are not as proactive as their white counterparts at utilizing health care services [8–10], especially preventive services such as blood pressure checks, cervical cancer screening, and cholesterol screening [19]. However, most recent data is conveying the contrary. This change in paradigm is multi-factorial and needs further investigation, but it could be attributed to more self-awareness, better education provided by health care providers and more accessible healthcare services in urban areas [12].

2.2. Race and differences in cardiovascular disease resource utilization and outcomes

Racial and ethnic differences in utilization of cardiovascular disease resources have also been well documented in the literature. Farmer et al. looked at the nationwide ICD registry in 2007 and concluded that blacks and Hispanics were less likely to receive cardiac resynchronization therapy with defibrillator (CRT-D) compared to whites, perhaps due to insurance issues or other factors in our health system [20]. In 2012, Eapen et al. reported similar findings, again demonstrating racial/ethnic disparities in the use of guideline-recommended device therapies for heart failure care [21].

Similar disparities have been shown for other cardiovascular interventions as well, including aortic valve replacement, dual-chambered pacemaker placement, coronary bypass grafting, and percutaneous transluminal coronary angioplasty (PTCA) [22–26]. Ford et al. examined racial/ethnic differences in the use of invasive and several noninvasive procedures among elderly population admitted for acute myocardial infarction (AMI) using the data from the California Cooperative Cardiovascular Project (CCP), which was initially designed to collect data to improve the quality of care for AMI among Medicare beneficiaries. They too came to the conclusion that African Americans were less likely to undergo cardiac catheterization and CABG surgery compare to whites [27]. Hispanics also followed a similar trend in regards to catheterization [27]. Similar studies among Medicare patients had shown the same trend of African Americans being less likely to receive invasive cardiac procedures compared to whites [28–31]. Interestingly, African Americans were somewhat more likely to have received a stress test or an echocardiogram than whites and Hispanics. However, there is mixed data on this topic [32]. Peterson et al. also reported African Americans received significantly fewer cardiac procedures after AMI compared to their white counterparts in the Veterans' Administration [33], a health care system designed to provide equal care to all eligible patients.

Some of the reasons to account for these racial differences have been well documented [27]. They include differences in disease severity, disease prevalence, socioeconomic or insurance status, noninvasive test results, the medical decision-making process, access to health services, physician's beliefs regarding CABG surgery outcomes, cultural or racial biases of the treating physicians, and potentially lower referral rates for cardiac procedures [27]. Furthermore, patients' acceptance of invasive procedures and higher refusal/reluctance rates among African Americans [34,35] are also contributors to these differences. Since these studies were done among veterans and Medicare beneficiaries, economic issues should be less likely to contribute to these differences, although the ability to make copayments or cover other-related expenses could potentially play a role.

Despite receiving fewer invasive cardiac procedures, African Americans who experienced AMI have been shown to have similar, if not better, 30-day [27], 1-year, and 2-year mortality rates compared to whites [28,33]. Udvarhelyi et al. showed improved 30-day survival and equivalent 2-year survival rates for African Americans on Medicare who had AMI compared to whites [28]. Perterson et al. reported similar findings among the veteran population. In their study, Keil et al. analyzed data from a 30-year period in the Charleston Heart Study and reported that black men had an insignificant lower mortality rate from coronary artery disease compared to white men [36]. Conflicting data also exists in the literature regarding racial differences in prognosis after AMI. For example, Castaner et al. reported that 249 black patients who were discharged after having a myocardial infarction had increased mortality rates at the 1-year and 2-year marks compared to the previous reports of survival among white patients [37]. Furthermore, Roig et al., using the National Hospital Discharge Survey data, reported in-hospital mortality following AMI to be higher among African Americans compared to whites until the age of 70; after 70 years, African Americans had lower mortality rates [38].

2.3. Race and differences in renal disease resource utilization and outcomes

Similarly, racial/ethnic disparities also exist in the optimal delivery of care to nephrology patients. An extensive body of literature suggests that patients from minority groups receive less hemodialysis access, both arteriovenous grafts and/or catheters [39–41]. Furthermore, African Americans have also been shown to receive less intensive maintenance hemodialysis compared to whites [39]. Another issue may be that ethnic minorities have less access to renal care [42], which may put them at higher risk for developing CIN.

Arteriovenous fistulas (AVFs) have been shown to have superior outcomes in regards to survival benefit compared to intravascular hemodialysis catheters [43]. Zarkowsky et al. reviewed the U.S. Renal Data System (USRDS) database to study the trends in incident hemodialysis access in regards to race/ethnicity, receipt of nephrology care and medical insurance status. They reported that African Americans and Hispanics compared to their white counterparts initiate hemodialysis with an AVF less frequently independent of medical insurance status and nephrology care [44]. African Americans are also less likely to receive kidney transplantation [40,41], especially live donor kidney transplantation.

In regards to cardiovascular risk differences, a multivariate quantile regression analysis of 3939 patients was done using the U.S. Chronic Renal Insufficiency Cohort Study highlighting cardiovascular risk differences in patients with chronic kidney disease (CKD) by race and ethnicity [45]. Non-Hispanic blacks with moderate and mild CKD were shown to have a significantly higher CVD risk factor score than non-Hispanic whites [45]. However, data published by the Chronic Kidney Disease Prognosis Consortium suggests that there is no difference in cardiovascular mortality across races in patients with CKD [46].

Interestingly, despite inconsistencies with care and cardiovascular risk differences, African American hemodialysis patients over age 40 [47] and over age 50 [48] have shown better survival than white patients. The explanation behind this paradoxical survival advantage is not clear. To further evaluate this survival advantage, Waikar et al. examined whether there are racial differences in the way patients respond to acute renal failure (ARF). They studied ARF in patients hospitalized using the Nationwide Inpatient Sample and reported that African American patients had an 18% lower odds of death than white patients after adjusting for age, sex, and comorbidity [49]. Among the patients requiring dialysis, African American patients had 16% lower odds of death than white patients [49]. Furthermore, stratified analyses of ARF patients also showed that African Americans had substantial lower adjusted odds of death compared to their white counterparts in the settings of cardiac catheterization, CABG, AMI, congestive heart failure, pneumonia, sepsis, and gastrointestinal hemorrhage [49]. They also concluded that in-hospital mortality was lower for African Americans with ARF than whites.

2.4. Contrast-induced nephropathy

Racial and ethnic factors can play a significant role in renal and cardiovascular morbidity and mortality. There is paucity of data in literature looking at the relationship between these factors and contrast-induced nephropathy (CIN). CIN is as an acute worsening of renal function after administration of intravascular radiocontrast, once other causes have been ruled out. It is generally defined as an increase in serum creatinine by 0.5 mg/dL (44 mol/L) or 25% above baseline within 48 h after parenteral contrast

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