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Letter to the Editor

Reply to: Regional variation in cardiac arrest for patients with sepsis

To the Editor,

We appreciate the comments by Drs. Rush and Hertz in response to our paper regarding the regional variation in the incidence and outcomes of sepsis-associated in-hospital cardiac arrest (SA-IHCA) in the United States (US).[1,2] The authors have three main remarks on the paper and we would like to discuss them individually.

Firstly, we appreciate and entirely concur with the comments made by the authors regarding the reformed design of the National Inpatient Sample (NIS) in 2012 and we acknowledge that this redesign, in addition to an administrative nature of the NIS dataset, could have an impact on recorded number of sepsis-IHCA related admissions between 2007 and 2014. However, these constraints have already been deliberated on the website and described on various occasions in prior studies from the NIS dataset and were not within the scope of our paper to describe in detail, nonetheless, we acknowledge that this could be new information for a readership outside the US.[3]

Secondly, we were partly accurate about the unavailability of information regarding DNR status and its timing, and variation in the implementation of DNR protocol across various hospitals included in the NIS dataset for its entirety (2007−2014) as V49.86 code was only introduced in October 2010.[4] This means that out of 8 years of the study duration, 4 years of discharge records would not incorporate information on DNR status, which we believe was overlooked by Drs. Rush and Hertz. Unavailability of the timing of DNR in our study warrants future prospective studies to overcome this concern in risk prediction models as the wide variation of early DNR implementation across nationwide hospitals have been found to play a pivotal role in prevailing regional variation in IHCA-related outcomes.[5] Using the ICD-9 CM code (V66.7) described by authors, palliative care consultation was found in 11.9%, 14.1%, 11.4%, and 16.0% admissions for SA-IHCA in Northeast, Midwest, South, and West regions, respectively ($p < 0.001$). Nonetheless, the authors should also comprehend that the code for palliative care consultation (V66.7) would not necessarily reveal if palliative care services were actually provided to patients and more importantly, the frequency, timing, and duration of palliative care services rendered to patients which contravenes any major advantage of including this variable in our analysis. In addition, recent studies have shown poor sensitivity (<50%) of this code to precisely capture palliative care services.[6]

Thirdly, we understand the importance of adhering to standard methodology discussed by Khera et al. while performing statistical analysis using the NIS datasets and detailed on the HCUP website.[7] We have used weighted NIS datasets to achieve national estimates of hospitalizations for SA-IHCA as per recommendations. We have considered primary discharge records of sepsis as the denominator and any secondary discharge diagnosis of IHCA as the numerator while calculating the rates of SA-IHCA in hospitals across 4 regions. We have chosen not to report confidence intervals in Fig. 2A as the margin of error was negligible (0.0%−0.1%) for calculated rates across all 4 regions.

Consistent with the unadjusted SA-IHCA related in-hospital mortality rates reported earlier in our paper, an additional sensitivity analysis by multivariable regression models (only for 4 years from 2007 to 2010 with available DNR and palliative care referral ICD-9 CM code) as queried by the authors did essentially confirm higher all-cause mortality in SA-IHCA admissions recorded in the Western (74.4% vs. 73.2%, $p < 0.001$ & aOR 1.10, 95% CI 1.06−1.15, $p < 0.001$) region as compared to Northeast region when adjusted for all demographics, relevant baseline comorbidities (Table 2) using complex sample module and pre-defined survey design. Furthermore, SA-IHCA admissions recorded at Southern hospitals demonstrated lower all-cause mortality as compared to Northeastern hospitals (71.4% vs. 73.2%, $p < 0.001$ & aOR 0.97, 95% CI 0.93−0.99, $p = 0.042$) whereas there was no difference in the all-cause mortality in SA-IHCA admissions between Midwestern and Northeastern hospitals (aOR 0.98, 95% CI 0.04−1.02, $p = 0.278$). These largely parallel results on unadjusted and adjusted analysis could refute any questions raised against employed methodology in our study. Concisely, there is no major change in the mortality risk across regions following SA-IHCA as compared to the reported mortality rates in the published study even with an additional multivariable analysis controlling for sociodemographic characteristics and pre-existing comorbidities. Future research is warranted to understand the governing factors for regional variation and impact of cardiac/extra-cardiac comorbidities and timing of DNR & rendered palliative care services in various hospitals on the incidence of SA-IHCA and subsequent outcomes post-resuscitation.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

This statement is to certify that all authors have seen and approved the manuscript being submitted, have contributed significantly to the work, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to *Resuscitation*.

The authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

On behalf of all co-authors, Rupak Desai, MBBS, the corresponding author, bears full responsibility for the submission.

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