The Changing Profile of Autopsies in Cardiovascular Deaths in the United States, 2003-2018

Clinical autopsy is considered the standard criterion for determining the cause of death.[1] Autopsies also play an instrumental role in promoting benchmark research and science.[1] National Center for Health Statistics data suggest a changing profile in the autopsy rates over the last few decades in the United States,[2] however little is known about the patterns of autopsies performed in deaths attributed to cardiovascular disease (CVD).

We analyzed the National Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research database from 2003 to 2018.[3] Multiple cause of death files were abstracted from the National Vital Statistics System of the National Center for Health Statistics (NCHS). Mortality and autopsy data were extracted from death certificates, and preautopsy CVD mortality was identified using International Classification of Diseases, 10th Revision codes 100-178. We examined the temporal trends in the absolute number of autopsies performed using Joinpoint Regression Program version 4.7.0.0.[4] Annual percent change (APC) with 95% confidence intervals in absolute number of autopsies was calculated using Monte Carlo permutation tests. Results were stratified by age, sex, and race.

Of 16,891,094 total deaths attributed to CVD in the United States between 2003 and 2018, 4,982,893 (30%) individuals were excluded from the analysis due to unknown autopsy status. A total of 773,017 (6%) decedents of CVD received autopsy. Of which underlying reported cause of death was ischemic heart disease (32.6%), stroke (19.2%), heart failure (10.5%), hypertensive heart disease (7.8%), valvular heart disease (1.4%), conduction disorders (0.5%), and other cardiovascular causes (pulmonary heart disease, acute and chronic rheumatic heart disease, pericardial diseases, myocarditis and complications of ill-defined description of heart disease: 28.0%). Overall, the proportion of CVD autopsies performed were higher in adults aged <45 years compared with other age groups, more frequent in men than women, and in blacks than other races.

Between 2003 and 2018, overall number of CVD autopsies/year increased (45,241 to 49,130; average APC, 0.72 [0.02, 1.44]) (Table 1). However, this trend varied across demographic subgroups. Whereas autopsies increased among decedents ≥45 years, a significant decline was noted among adults aged <45 years owing to a reduction since 2005. The number of autopsies increased in men, Asians or Pacific Islanders, American Indians or Alaska Natives, and Hispanics. Conversely, the number of autopsies remained stable among women, whites, and blacks throughout the study period.

Between 2003 and 2018, the number of autopsies in individuals considered to have died from CVD has increased, however, with striking demographic disparities among the decedents. Whereas autopsied deaths have become concentrated among young adults, women continued to have lesser number of autopsies without an improvement over time. Blacks had highest and whites had lowest proportion of autopsies with stable rates over the study period.

These patterns carry certain potential explanations. Since blacks, Hispanics, and American Indians or Alaska Natives tend to experience premature cardiovascular deaths compared with whites,[5] or men or blacks experience higher rates of unattended deaths or sudden cardiac death compared with women or other races, respectively,[5] these groups are more likely to receive autopsies. Data also suggest that health disparities involving reduced diagnostic workup with consequential less-established diagnoses may accentuate the autopsy rates among racial minorities to gain more confidence in the definitive cause of death.[1]

This analysis has various limitations. Hospital accreditation standards, local laws and regulations, family's cultural beliefs can influence the autopsy rates. The purpose of autopsy—whether academic or to ascertain the cause of death—could not be determined. The socioeconomic, sociocultural, and religious determinants affecting autopsy decision were not analyzed.

This nation-level analysis provides some novel insights about autopsy trends with respect to cardiovascular deaths. Despite rising trends in autopsy rates among decedents of CVD, demographic disparities continued to exist and expanded over time.

Table
Trends in absolute number of autopsies for cardiovascular death in the United States, 2003-2018

	No. of autopsies 2003 − 2018	APC [95% CI], Segment 1	APC [95% CI], Segment 2	Joinpoint year	AAPC [95% CI]
Overall	45,241 − 49,130	4.81 [-0.90, 10.85]	0.11 [-0.18, 0.41]	2005	**0.72 [0.02, 1.44]**
Age, years					
<45	9,901 − 8,463	2.49 [-4.97, 10.53]	**-1.58 [-1.98, -1.18]**	2005	**-1.05 [-1.99, -0.11]**
45-64	21,533 − 25,169	**7.21 [2.67, 11.96]**	-0.01 [-0.49, 0.48]	2006	**1.40 [0.54, 2.26]**
>65	13,807 − 15,498	-1.11 [-2.24, 0.04]	**3.10 [1.71, 4.51]**	2011	**0.83 [0.04, 1.63]**
Women	14,401 − 14,582	2.47 [-4.60, 10.06]	-0.02 [-0.39, 0.34]	2005	0.31 [-0.59, 1.21]
Men	30,840 − 34,548	**5.94 [0.10, 12.11]**	0.15 [-0.13, 0.43]	2005	**0.91 [0.20, 1.62]**
White	35,017 − 37,314	5.27 [-1.21, 12.16]	-0.01 [-0.32, 0.31]	2005	0.68 [-0.12, 1.48]
Black	8,891 − 10,076	3.47 [-4.09, 11.62]	0.19 [-0.20, 0.57]	2005	0.62 [-0.33, 1.58]
Asian or Pacific Islander	1,009 − 1,344	**2.62 [2.16, 3.09]**	-0.84 [-8.40, 7.35]	2016	**2.15 [1.13, 3.18]**
American Indian or Alaska Native	324 − 396	**2.69 [1.20, 4.20]**	-0.41 [-6.47, 6.05]	2014	**1.85 [0.07, 3.67]**
Hispanic	2,982 − 4,624	**8.06 [2.38, 14.06]**	**1.95 [1.37, 2.52]**	2006	**3.14 [2.07, 4.22]**

APC stands for Annual Percent Change and AAPC stands for Average Annual Percentage Change. Bold represents statistically significant results. Segments 1 and 2 are APCs before and after joinpoint year.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Safi U. Khan, MD[a*]
Muhammad Shahzeb Khan, MD[b]
Ann M. Navar, MD, PhD[c]
Haider J. Warraich, MD[d]
Jagmeet Singh, MD[e]
Miguel Cainzos-Achirica, MD, PhD, MPH[f]
Erin D. Michos, MD, MHS[g]

[a] Department of Medicine, West Virginia University, Morgantown, West Virginia
[b] Department of Medicine, John H. Stroger, Jr. Hospital of Cook County, Chicago, Illinois
[c] Department of Cardiology, UT Southwestern Medical Center, Houston, Texas
[d] Department of Medicine, Cardiology Section, VA Boston Healthcare System, Boston, Massachusetts
[e] Department of Internal Medicine, Geisinger Commonwealth School of Medicine, Scranton, Pennsylvania
[f] Division of Cardiovascular Prevention and Wellness, Department of Cardiology, Houston Methodist DeBakey Heart and Vascular Center, Houston, Texas
[g] Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, Maryland
8 October 2020
15 October 2020

1. Gupta A, Premnath N, Kuo PL, Sedhom R, Brawley OW, Chino F. Assessment of racial differences in rates of autopsy in the US, 2008-2017. *JAMA Int Med* 2020;180:1123–1124.
2. Hoyert DL. The changing profile of autopsied deaths in the United States, 1972-2007. *NCHS Data Brief* 2011:1–8.
3. National Center for Health Statistics, CDC. About underlying cause of death 1999-2018. Accessed https://wonder.cdc.gov/ on March 25, 2020.
4. Khan SU, Bashir ZS, Khan MZ, Khan MS, Gulati M, Blankstein R, Blumenthal RS, Michos ED. Trends in cardiovascular deaths among young adults in the United States, 1999 to 2018. *Am J Cardiol* 2020;128:216–217.
5. Winkel BG, Risgaard B, Bjune T, Jabbari R, Lynge TH, Glinge C, Bundgaard H, Haunsø S, Tfelt-Hansen J. Gender differences in sudden cardiac death in the young-a nationwide study. *BMC Cardiovasc Disord* 2017;17. 19-19.

https://doi.org/10.1016/j.amjcard.2020.10.032

Safety and Effectiveness of Long-Term Anticoagulation for Atrial Fibrillation Among Nonagenarians: A Real-World Analysis

The prevalence of atrial fibrillation (AF) increases with age, reaching 10% among those over 80 years old.[1] Long-term anticoagulation (AC) is effective in reducing strokes among patients with AF at increased risk of thromboembolic events.[2] The safety and effectiveness of AC among nonagenarians are poorly understood, since these patients were underrepresented in the pivotal trials of AC.[1] Although age is an independent risk factor for stroke in patients with AF, the net clinical benefit of AC may be mitigated by an increased risk of bleeding.[3,4] We sought to explore the real-world safety and effectiveness of AC among nonagenarians using a large national administrative database.

Data from the Nationwide Readmission Database (NRD) 2010 to 2015 were used. The NRD is a de-identified publicly available all-payer database accounting for 58.2% of U.S. hospitalizations.[5] We used ICD-9-CM codes to identify patients with AF (427.31) and on long-term current use of AC (V58.61) then stratified according to age: ≥90 versus <90 years. We excluded patients: (1) <18 years old, (2) died during the index admission, (3) other indications for AC (i.e., pulmonary embolism, deep vein thrombosis, hepatic vein thrombosis, or prosthetic valve), and (4) index hospitalization occurred from July through December to ensure 6-month follow-up since the NRD data do not cross over the calendar year. The primary outcome was the 6-month all-cause readmission rate. Secondary outcomes were 6-month readmission rates for gastrointestinal bleeding, acute ischemic stroke (AIS)/transient ischemic attack (TIA), and intracranial hemorrhage. A sensitivity analysis was performed for 11-month readmission rates by including only index admissions in January of each calendar year. Chi-Square test was used to compare readmission rates between groups and a linear trend test was used to analyze the annual readmission trend. Propensity score matching in a 1:1 pattern was conducted using relevant variables (Table 1). A p value <0.05 was considered statistically significant. This study was exempted by the institutional review board due to the de-identified nature of the database.

A final cohort of 841,495 patients were identified, of whom 77,451 (9.2%) were ≥90 years old. The 6-month readmission rates among ≥90 versus <90 years old were: all-cause − 34.1% versus 34.8% (p < 0.001), gastrointestinal bleeding − 0.9% versus 0.8% (p = 0.003), AIS/TIA − 4.7% versus 2.5% (p < 0.001), and intracranial hemorrhage − 0.2% versus 0.2% (p = 0.19). After propensity score matching, 6-month readmission rates were: all-cause − 34.1% versus 35.0% (p < 0.001), gastrointestinal bleeding − 0.9% 0.8% (p = 0.04), AIS/TIA − 1.6% versus 1.0% (p < 0.001), and intracranial hemorrhage − 0.2% versus 0.2% (p = 0.233). In the sensitivity analysis with 11-month follow up (151,765 patients with 9.8% nonagenarians), the readmission rates were: all-cause − 43.1% versus 44.5% (p = 0.001), gastrointestinal bleeding − 1.1% versus 1.0% (p = 0.24), AIS/TIA − 2.1% versus 1.1% (p < 0.001), and intracranial hemorrhage 0.3% versus 0.3% (p = 0.55). The trend of 6-month all-cause readmission rates from 2010 to 2015 was marginally stable in both groups: ≥90 years old − 35.0% in 2010 versus 34.7% in 2015 (p-trend < 0.001), and <90 years old − 34.8% in 2010 versus 34.9% in 2015 (p-trend = 0.03).

In this nationwide observational analysis of >77,000 nonagenarians with AF on long-term AC, we found that the 6-month all-cause readmission rate was lower, and AIS/TIA was higher compared with those <90 years old. However, rates of gastrointestinal bleeding were only slightly higher, and there was no difference in rates of intracranial hemorrhage. These findings are reassuring about the safety profile−−particularly bleeding complications−−of using long-term AC among selected nonagenarians with AF to prevent stroke.

The results of this study should be interpreted in the context of several limitations. We were unable to ascertain the compliance with AC or if it was stopped after the index admission. There are no data regarding the AC agent or out-of-hospital mortality rates which may lead to misleadingly lower readmission rates. The NRD is an inpatient database and does not capture outpatient encounters. Finally, these results likely apply to relatively healthy nonagenarians who may be more likely to be prescribed AC.

Disclosure: The authors have nothing to disclose, and no relationship with industry.

Funding: Self-funded.