# Ethnic Differences in Withdrawal of Life Support After Intracerebral Hemorrhage

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## Abstract

*Minorities are less likely to decide on withdrawal of life support (WOLS) after acute severe illness. However, the decision-making process for WOLS after intracerebral hemorrhage (ICH) among Native Hawaiians and other Pacific Islanders (NHOPI) has not been described. To address this gap in the literature, a retrospective study was conducted on consecutive spontaneous ICH patients admitted to a tertiary center in Honolulu between 2006 and 2010. The occurrence of WOLS and time-to-WOLS were the outcome measures. Unadjusted and multivariable logistic regression models were performed to determine associations between NHOPI ethnicity and WOLS. This study assessed 396 patients (18% NHOPI, 63% Asians, 15% non-Hispanic whites [NHW], 4% others) with ICH. NHOPI was associated with lower rate of WOLS than NHW in the univariate analysis (OR 0.35, 95% CI: 0.15, 0.80). However, NHOPI ethnicity was no longer significant when adjusted for age (OR 0.59, 95% CI: 0.25, 1.43) and in the fully adjusted model (OR 0.68, 95% CI: 0.20, 2.39). Although NHOPI with ICH were initially perceived to have less WOLS compared to NHW, this observed difference was largely driven by the younger age of NHOPI rather than from underlying cultural differences that are inherent to their ethnicity.*

## Introduction

Withdrawal of life support (WOLS) is the cessation of life-sustaining treatments; the choice to discontinue and further withhold life-sustaining therapies such as mechanical ventilation, blood pressure medications, antibiotics, or artificial hydration or nutrition, with expected natural death.[1] Since spontaneous intracerebral hemorrhage (ICH) has disproportionally high rates of severe long-term disability and decreased quality of life, the practice of WOLS is frequently considered in many clinical settings.[2-5]

Prior studies have shown differences in end-of-life decision-making by minority groups in the United States. Blacks and Hispanics, the most frequently studied minority groups, have been shown to choose more aggressive care, are less likely to decide on WOLS after acute illnesses, and take longer time to come to the decision on WOLS compared to non-Hispanic whites (NHW).[6-12] However, little is known about the end-of-life care preferences and decision-making of Native Hawaiians and other Pacific Islanders (NHOPI). Due to similarities with other minority groups such as increased health disparities and lack of advanced directives, it is possible that NHOPI may be similar to other minority groups in end-of-life care preferences.[10-15]

The objectives of this study were to compare the prevalence of WOLS between NHOPI and NHW. We hypothesized that NHOPI with ICH have less frequent WOLS compared to NHW

## Methods

### Patients and Data Collection

The Queen's Medical Center (QMC), located in Honolulu, is the largest tertiary center in the state of Hawai'i; the main referral center in the Pacific Basin.[16,17] During the study period, QMC was the only Primary Stroke Center with a dedicated neuroscience intensive care unit (NSICU) for the state of Hawai'i. This study was approved by the QMC Research and Institutional Review Committee.

All patients admitted with ICH between January 1, 2006, and August 31, 2010, were identified through use of QMC's institutional database. Patients with ICH were prospectively identified by a trained database coordinator (S.M.A.). Cases were confirmed for spontaneous ICH by additional review of electronic medical records by a board-certified neurologist (K.N.). Patients admitted with traumatic ICH, ICH related to cerebral aneurysm rupture, and ischemic stroke with hemorrhagic conversion were excluded from the study. For patients who were re-hospitalized at a later date for another ICH, only the data from the initial admission was used for the analysis.

Data obtained from the database included age, sex, ethnicity, marital status, methamphetamine abuse, and past medical history. The race and ethnicity information were collected from the hospital's administrative database, and were obtained during the registration or admission process using two questions. The first question was whether or not they are "Native Hawaiian or Part-Hawaiian." The second question was an open-ended question to list one race that the patient most closely associated with, based on patient self-identification or family's identification if the patient was incapacitated. The NHOPI race was defined as anyone whose race was coded as "Native Hawaiian or Part-Hawaiian" or any race or ethnicity associated with Polynesia, Melanesia, or Micronesia. Ultimately, ethnicity was categorized as NHW, NHOPI, Asian, or other. Due to the low number of black and American Indian/Alaskan patients, these patients were grouped with those classified as other. Since the admitting team may impact the end-of-life discussion with the family, the data on admitting team was obtained. The admitting team was recorded as neurovascular team if the admitting physician was a neurointensivist or neurohospitalist. All of the neurointensivists and neurohospitalists have been trained in vascular neurology. All other admitting physicians (ie, internal medicine hospitalist, medical intensivist, etc) were coded as "other." Since admission to a specialized unit such as the NSICU may also impact the decision-making process, admission location was obtained and recorded as NSICU or "other." The presence of a pre-existing do-not-resuscitate (DNR) order was noted since this often indicates desire for less aggressive care.[18,19] The patient's initial brain computed tomography (CT) scans were reviewed by an investigator (K.N.) using a previously described standardized

protocol blinded to patient identity and clinical data,[20,21] and ICH volume was calculated using the ABC/2 method.[22] Location of ICH was coded as basal ganglia, lobar, thalamus, brainstem, cerebellum, and primary intraventricular hemorrhage (IVH). Presence of any IVH associated with ICH was also recorded.

## Outcome Measure: Withdrawal of Life Support

WOLS was defined as the physician order to cease all life-sustaining treatments including mechanical ventilation, blood pressure medications, antibiotics, and artificial hydration or nutrition, with the plan not to re-initiate these measures with clinical decline. The accuracy of WOLS was verified by the documentation of physicians, nurses, and respiratory therapists.

## Analysis

Demographics and baseline characteristics of NHOPI and Asians were compared to NHW (reference group). A two-tailed t-test was used for analysis to compare continuous variables. Categorical variables were analyzed using a chi-squared test. The same method was used to compare demographics and baseline characteristics between patients who had WOLS and those who did not have WOLS. Age was used as a continuous variable with a constant odds ratio (OR) for each year and hematoma volume

was used as a continuous variable with a constant OR for each mL. Multivariable logistic regression analysis was performed to assess the relationships between ethnicity and WOLS. Four separate models were created: (1) unadjusted, (2) adjusted for age, (3) adjusted for age and sex, and (4) adjusted for all of the variables with $P < .10$ in the univariate analyses comparing characteristics of those who did and did not have WOLS. The OR and 95% confidence interval (CI) were calculated from the beta coefficients and their standard errors. Levels of $P < .05$ were considered statistically significant. All analyses were performed using SPSS statistical software (SPSS version 22.0, IBM, Chicago, IL).

## Results

A total of 396 patients with spontaneous ICH (18% NHOPI, 63% Asians, 15% NHW, 4% others) who met the study criteria were included. Demographics and clinical characteristics are shown in Table 1. The demographic and baseline characteristic data for the "other" ethnic group was not included in Table 1, but data for "other" ethnic group was included for Table 2 and for all subsequent analyses. Overall, NHOPI were younger ($P < .001$), more likely to have diabetes ($P = .02$), and were less likely to be married ($P = .02$) than NHW.

| Table 1. Demographics and Baseline Characteristics | | | | | |
|---|---|---|---|---|---|
| | NHW* n = 61 | NHOPI n = 72 | P | Asian n = 248 | P |
| Age (years), mean (SD) | 68 (16) | 55 (16) | <.001 | 67 (17) | .66 |
| Female, n (%) | 24 (39) | 30 (42) | .79 | 118 (48) | .25 |
| Married, n (%) | 39 (65) | 33 (45) | .02 | 112 (45) | .01 |
| Diabetes, n (%) | 11 (18) | 26 (36) | .02 | 52 (21) | .61 |
| Hypertension, n (%) | 38 (62) | 53 (74) | .16 | 187 (75) | .04 |
| Coronary artery disease, n (%) | 11 (18) | 9 (13) | .37 | 25 (10) | .08 |
| Smoking, n (%) | 9 (15) | 13 (18) | .61 | 34 (14) | .83 |
| Methamphetamine use, n (%) | 2 (3) | 8 (11) | .09 | 15 (6) | .40 |
| Initial GCS, median [IQR] | 13 [6, 15] | 14 [8, 15] | .24 | 14 [8, 15] | .38 |
| Location of ICH on CT, n (%) | | | .27 | | .11 |
| Basal ganglia | 26 (43) | 32 (44) | | 86 (35) | |
| Lobar | 22 (36) | 15 (21) | | 59 (24) | |
| Thalamus | 7 (12) | 12 (17) | | 51 (21) | |
| Brainstem | 2 (3) | 5 (7) | | 16 (7) | |
| Cerebellum | 3 (5) | 3 (4) | | 25 (10) | |
| Primary IVH | 1 (2) | 5 (7) | | 11 (4) | |
| Any IVH, n (%) | 29 (48) | 31 (43) | .60 | 121 (49)** | .84 |
| ICH Volume (mL), mean (SD) | 41 (48)** | 40 (60)** | .90 | 37 (50)** | .64 |
| Admit to NSICU, n (%) | 32 (53) | 41 (57) | .60 | 127 (52) | .86 |
| Admitted to neuro team, n (%) | 30 (49) | 38 (53) | .68 | 116 (47) | .74 |
| Pre-existing DNR order, n (%) | 4 (7) | 3 (4) | .54 | 16 (7) | .98 |

NHW, Non-Hispanic whites; NHOPI, Native Hawaiian Other Pacific Islander; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; CT, computed tomography; IVH, intraventricular hemorrhage; mL, milliliter; NSICU, neuroscience intensive care unit; DNR, do-not-resuscitate; WOLS, withdrawal of life support. Data are displayed in mean (SD), in n (%), or median [IQR]. *NHW is the reference category for NHOPI and Asian statistical comparisons. Data for the ethnic category of other is not included in this table, but is included in Table 2 and the subsequent analyses of Table 3. **Missing data include 1 Asian with Any IVH, 3 NHW with ICH volume, 4 NHOPI with ICH volume, 11 Asian with ICH volume.

| Table 2. Characteristics of Patients With and Without Withdrawal of Life Support | | | |
|---|---|---|---|
| Characteristic | Withdrawal of Life Support n = 89 | No Withdrawal of Life support n = 307 | P |
| Age (years), mean (SD) | 75 (14) | 61 (17) | <.001 |
| Female, n (%) | 48 (54) | 130 (42) | .05 |
| Ethnicity, n (%) | | | .12 |
|    NHW | 19 (21) | 42 (14) | |
|    Asian | 57 (64) | 191 (62) | |
|    NHOPI | 10 (11) | 62 (20) | |
|    Other | 3 (3) | 12 (4) | |
| Married, n (%) | 42 (48) | 144 (48) | .96 |
| Diabetes, n (%) | 22 (25) | 69 (23) | .66 |
| Hypertension, n (%) | 70 (79) | 215 (70) | .11 |
| Coronary artery disease, n (%) | 9 (10) | 37 (12) | .62 |
| Smoking, n (%) | 7 (8) | 53 (17) | .03 |
| Methamphetamine use, n (%) | 1 (1) | 28 (9) | .01 |
| Initial GCS, median [IQR] | 7 (4) | 12 (4) | <.001 |
| Location of ICH on CT, n (%) | | | .29 |
|    Basal ganglia | 37 (42) | 114 (37) | |
|    Lobar | 20 (23) | 79 (26) | |
|    Thalamus | 20 (23) | 52 (17) | |
|    Brainstem | 1 (1) | 22 (7) | |
|    Cerebellum | 7 (8) | 25 (8) | |
|    Primary IVH | 4 (5) | 15 (5) | |
| Any IVH, n (%) | 70 (79) | 119 (39) | <.001 |
| ICH Volume (mL), mean (SD) | 78 (70) | 27 (38) | <.001 |
| Admit to NSICU, n (%) | 60 (67) | 149 (49) | .002 |
| Admitted to neuro team, n (%) | 51 (57) | 142 (46) | .07 |
| Pre-existing DNR order, n (%) | 15 (17) | 9 (3) | <.001 |

NHW, Non-Hispanic whites; NHOPI, Native Hawaiian Other Pacific Islander; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; CT, computed tomography; IVH, intraventricular hemorrhage; mL, milliliter; NSICU, neuroscience intensive care unit; DNR, do-not-resuscitate. Data are displayed in mean ± SD or n (%).

Comparison of the patients with and without WOLS is shown in Table 2. Those who had WOLS were older (P < .001), less likely to smoke (P = .03), less likely to use methamphetamines (P = .01), had a lower initial Glascow Coma Scale (GCS) scores (P < .001), higher incidence of IVH (P < .001), had a higher ICH volume in mL (P < .001), were more often admitted to NSICU (P = .002), and had a higher prevalence of pre-existing DNR orders (P < .001) when compared to patients who did not have WOLS.

The multivariable regression models for WOLS after ICH are shown in Table 3. In unadjusted analysis (model 1), NHOPI were significantly less likely to have WOLS compared to NHW (OR 0.35, 95% CI: 0.15, 0.80). However, when adjusted for age (model 2), NHOPI ethnicity was no longer a significant predictor for WOLS (OR 0.59, 95% CI: 0.25, 1.43). In the fully adjusted model NHOPI ethnicity remained an insignificant predictor of WOLS (OR 0.68, 95% CI: 0.20, 2.39). Variables noted to be significantly associated with WOLS in the fully adjusted model

included age (OR 1.06, 95% CI: 1.03, 1.09), ICH volume (OR 1.01, 95% CI: 1.003, 1.02), initial GCS (OR 0.79, 95% CI: 0.72, 0.87), presence of IVH (OR 3.01, 95% CI: 1.44, 6.32) and presence of a pre-existing DNR (OR 3.22, 95% CI: 1.03, 10.50).

## Discussion

This study was performed with the primary hypothesis that prevalence of WOLS after ICH would be less among NHOPI when compared to NHW, as shown in other minority groups.[5-7,10,23-25] Although the results of unadjusted analysis supported the primary hypothesis, that NHOPI are less likely to have WOLS compared to NHW, the impact of age and other clinical factors in all of the subsequent multivariable models dispelled any relationship between NHOPI ethnicity and lower prevalence of WOLS compared to NHW. These results are strikingly different compared to other end-of-life studies of minorities, and suggest that NHOPI and NHW in Hawai'i may share similar

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| Table 3. Multivariable Models for Withdrawal of Life Support | | | | |
|---|---|---|---|---|
| Characteristic | Model 1<br>Unadjusted<br>OR (95% CI) | Model 2<br>Adjusted for age<br>OR (95% CI) | Model 3<br>Adjusted for age and sex<br>OR (95% CI) | Model 4<br>Fully adjusted<br>OR (95% CI) |
| Ethnicity* | | | | |
|   Asians | 0.60 (0.33, 1.08) | 0.55 (0.29, 1.05) | 0.54 (0.28, 1.02) | 0.65 (0.27, 1.59) |
|   NHOPI | 0.35 (0.15, 0.80) | 0.59 (0.25, 1.43) | 0.58 (0.24, 1.40) | 0.68 (0.20, 2.39) |
|   Others | 0.46 (0.12, 1.80) | 0.52 (0.12, 2.32) | 0.52 (0.12, 2.31) | 0.43 (0.05, 3.88) |
| | | | | |
| Age | | 1.06 (1.04, 1.07) | 1.05 (1.03, 1.07) | 1.06 (1.03, 1.09) |
| Female sex | | | 1.30 (0.78, 2.15) | 1.38 (0.67, 1.84) |
| ICH Volume, mL | | | | 1.01 (1.003, 1.02) |
| Initial GCS | | | | 0.79 (0.72, 0.87) |
| IVH | | | | 3.01 (1.44, 6.32) |
| Methamphetamine use | | | | 0.19 (0.02, 1.77) |
| NSICU admit | | | | 2.02 (0.68, 5.96) |
| Pre-existing DNR | | | | 3.22 (1.03, 10.50) |
| Smoking | | | | 0.79 (0.24, 2.6) |
| Admission to neurovascular team | | | | 0.44 (0.17, 1.17) |

NHOPI, Native Hawaiian Other Pacific Islander; ICH, intracerebral hemorrhage; mL, milliliter; GCS, Glasgow Coma Scale; IVH, intraventricular hemorrhage; NSICU, neuroscience intensive care unit; DNR, do-not-resuscitate. Data are displayed in odds ratio (95% Confidence Interval). *Reference group for ethnicity is NHW, Non-Hispanic whites.

end-of-life decision-making process.[5-7,22,23] In the full model, the major clinical predictors for WOLS after ICH were older age, hematoma volume, IVH, initial GCS and pre-existing DNR. Although unadjusted observation implies a possible racial difference in the prevalence of WOLS, we believe this was largely driven by the younger age of NHOPI compared to NHW. NHOPI in this study were, on average, more than a decade younger than NHW. NHOPI have been previously shown to have ICH at a younger age when compared to NHW and other studies have echoed this sentiment of the occurrence of ICH at a younger age in minority groups. Previous studies have shown that younger patients are associated with lower prevalence of WOLS compared to older patients.[26]

The magnitude of age disparity in this study is highly alarming and dramatizes the health inequities facing this population. Prior studies have shown that NHOPI are more likely to be obese, smoke, have diabetes, and have hypertension when compared to NHW.[27-29] The aforementioned are all risk factors for cardiovascular disease (CVD), and as a subcategory of CVD, stroke. In the state of Hawai'i, CVD is the cause of over one-third of all deaths, and on average, NHOPI die from CVD at an average age that is 7 years younger than NHW and the rest of the state.[27-29]

Limitations of this study include single-center nature of the study, which limits the generalizability of the results. Furthermore, there may have been selection bias toward accepting only severe cases of ICH from other hospitals. Thereby, the results of this study may not be representative of decision-making in the NHOPI community in the state of Hawai'i, decreasing its external validity. The small sample size limits the conclusions drawn from this study to preliminary observations. Since pre-specified power calculations were not made, the negative results do not prove a lack of association. Due to the retrospective nature of the study, we were unable to characterize all of the intricate end-of-life discussions that likely took place, including each patient's previously stated wishes, known values, religion/spirituality, socioeconomic status, social support, etc, that ultimately led to the decisions to proceed with WOLS. Also, we could not assess each physician's attitude toward limitation of care and the main factors that led to the decision to proceed with WOLS. We did not have specific exam findings such as dilated pupils, Cushing reflex, or other clinical signs of brain herniation or hemodynamic instability that may have affected the provider's decision-making to initiate care limitation. Based on the retrospective nature of this study, we cannot draw any conclusions about the appropriateness of the WOLS use in these patients.

## Summary
In summary, NHOPI hospitalized with ICH were observed to have less WOLS compared to NHW with ICH. However, this observed difference in the practice of WOLS was largely driven by the impact of younger population of NHOPI and not by any inherent ethnic differences between the two groups.

## Conflict of Interest
None of the authors identify a conflict of interest.

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