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Title: Cutoff Value of Phase Angle by Bioelectrical Impedance Analysis at Admission as a Prognostic Factor in Patients with Acute Heart Failure

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Author Questionnaire

1. **Microscopy**: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

2. **Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **Yes, all done**

3. **Filming location:** Will the filming need to take place in multiple locations? **No**

Current Protocol Length
Number of Steps: 09
Number of Shots: 13

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

1.1. **Lilia Castillo-Martínez:** This study evaluates the prognostic utility of phase angle in acute heart failure, by identifying an optimal cutoff value, and evaluating model performance through multivariable Cox regression with restricted splines.

1.1.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 3.5.3.*

What are the most recent developments in your field of research?

1.2. **Lilia Castillo-Martínez:** Recent developments in this field include the use of Bioelectrical Impedance Vector Analysis or BIVA for precise assessment of hydration status and cell membrane integrity, alongside multivariable survival models incorporating bioelectrical impedancederived biomarkers to improve early identification of high-risk patients.

1.2.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: LAB MEDIA: Table 2.*

What are the current experimental challenges?

1.3. **María Fernanda Bernal-Ceballos:** Current challenges include ensuring accurate, reliable BIA measurements over hospitalization, controlling confounding factors in diverse patient populations, and securing an adequate sample size for accurate estimations in prognostic modeling.

1.3.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

What research gap are you addressing with your protocol?

1.4. **María Fernanda Bernal-Ceballos:** We address the gap in the lack of precise cutoff values for phase angle as a prognostic marker, and the need for reliable and accurate statistical methods to provide accurate predictions of mortality and rehospitalization.

1.4.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 3.5.1.*

What advantage does your protocol offer compared to other techniques?

1.5. **María Fernanda Bernal-Ceballos:** This protocol uses non-invasive, quick, and bedside method, applying Cox regression to identify risk factors and to graphically display adjusted thresholds for precise risk prediction in acute heart failure.

1.5.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 3.1.1.*

Videographer: Obtain headshots for all authors available at the filming location.

Testimonial Questions:

Videographer: Please ensure that all testimonial shots are captured in a wide-angle format, while also maintaining sufficient headspace, given that the final videos will be rendered in a 1:1 aspect ratio.

How do you think publishing with JoVE will enhance the visibility and impact of your research?

1.6. **Lilia Castillo-Martínez, Senior Researcher [National Institute of Medical Sciences and Nutrition Salvador Zubirán]**: Publishing with JoVE enhances research visibility through video-based articles that clearly demonstrate methodologies, facilitating comprehension and reproducibility. Indexed in leading scientific databases, JoVE increases citations and fosters interdisciplinary collaboration. By providing an engaging and accessible format, it amplifies research impact, strengthening knowledge dissemination and recognition within the global scientific community.

1.6.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

Videographer's Note: Shot 1.6.1 was a bit challenging for the author to perform complete without some mistakes, so we decided to split it in two, as follows:

1.6.1: "Publishing with JoVE enhances research visibility through video-based articles that clearly demonstrate methodologies, facilitating comprehension and reproducibility."

1.6.2: "Indexed in leading scientific databases, JoVE increases citations and fosters interdisciplinary collaboration. By providing an engaging and accessible format, it amplifies research impact, strengthening knowledge dissemination and recognition within the global scientific community.

Can you share a specific success story or benefit you've experienced—or expect to experience—after using or publishing with JoVE?

1.7. **María Fernanda Bernal-Ceballos, Researcher**: Publishing with JoVE increased the visibility of our research line on body composition and hydration status alterations. It attracted scientific interest, increased citations, and supported clinical and educational applications.

1.7.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

Ethics Title Card

This research has been approved by the Ethics and Human Biomedical Research Committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

Protocol

2. Setting Up the R Environment and Importing the Dataset

Demonstrator: María Fernanda Bernal-Ceballos

2.1. After installing R and RStudio *(R-Studio)* on the computer, open RStudio **[1]**. Click on the **File** tab, go to **New File**, and select **R script** to display the script file in the upper-left corner above the Console tab **[2]**.

2.1.1. WIDE: Talent sitting at a computer, launching RStudio. *Videographer: Please film this shot.*

2.1.2. SCREEN: 68203_screenshot_1.mp4 00:03-00:14.

2.2. In the new script file, install the required **survival**, **MASS**, and **pspline** *(pee-spline)* packages **[1]**.

2.2.1. SCREEN: 68203_screenshot_2.mp4 00:05-00:27.

2.3. Load the packages by typing and executing the **library** functions for **survival**, **MASS**, and **pspline [1]**.

2.3.1. SCREEN: 68203_screenshot_3.mp4 00:08-00:16.

2.4. Import the dataset by specifying the name and path of the data file in the command and assign it to an object called **Dataset [1]**.

2.4.1. SCREEN: 68203_screenshot_4.mp4 00:02-00:10.

3. Cox Model Construction, Evaluation, and Spline-Based Risk Visualization

3.1. Determine the Cox proportional hazards regression model adjusted for diabetes mellitus, systolic blood pressure, serum sodium, and phase angle using the Breslow method, and calculate the 95 percent confidence intervals for the model coefficients **[1]**.

3.1.1. SCREEN: 68203_screenshot_5.mp4 00:03-00:11. *Video Editor: Highlight Diabetes_mellitus, Systolic_blood_pressure, Serum_sodium, Phase_angle, method="Breslow" in the top window when the VO says these words*.

3.2. Then, calculate the Akaike Information Criterion, the Bayesian Information Criterion, and the C-statistic along with its 95 percent confidence interval **[1]**.

3.2.1. SCREEN: 68203_screenshot_6.mp4 00:02-00:27.

3.3. For the graphical representation, create the survival object using the **Surv** *(Serve)* function with survival days and outcome as inputs **[1]**.

3.3.1. SCREEN: 68203_screenshot_7.mp4 00:03-00:11.

3.4. Fit the Cox proportional hazards regression model using the survival object and adjust for diabetes mellitus, systolic blood pressure, serum sodium, and a penalized spline of phase angle with 2 degrees of freedom **[1]**. Then, predict the values for the fitted spline and their standard errors using the model **[2]**.

3.4.1. SCREEN: 68203_screenshot_8.mp4 00:03-00:19.

3.4.2. SCREEN: 68203_screenshot_9.mp4 00:01-00:15.

3.5. Finally, plot the fitted model on a graph using the predicted values to visualize the adjusted hazard ratio for phase angle **[1]**. Add the corresponding lines above and below the fitted curve to represent the upper and lower bounds of the prediction interval **[2]**. Identify the cut-off point where the adjusted hazard ratio exceeds 1, indicating that lower phase angle values are associated with an increased risk of in-hospital mortality and 90-day readmission or death **[3]**.

3.5.1. SCREEN: 68203_screenshot_10.mp4 00:01-00:10.

3.5.2. SCREEN: 68203_screenshot_11.mp4. 00:02-00:27.

3.5.3. SCREEN: 68203_screenshot_12.mp4 00:02-00:27.

Results

4. Results

4.1. This table summarizes the prognostic value of various clinical and bioimpedance parameters using multivariable Cox regression models, with outcomes consisting of in-hospital mortality and 90-day readmission or death **[1]**.

4.1.1. LAB MEDIA: Table 2.

4.2. In Model 1 for adverse events, a lower phase angle was independently associated with increased risk **[1]**.

4.2.1. LAB MEDIA: Table 2. *Video editor: Highlight the entire row "Phase angle, °" under "**Model 1**".*

4.3. In Model 2, which included different variables, a lower phase angle remained a significant predictor of adverse outcomes **[1]**.

4.3.1. LAB MEDIA: Table 2. *Video editor: Highlight the entire row "Phase angle, °" under "**Model 2**".*

4.4. The C-statistic for Model 1 indicated moderate predictive capacity for adverse events **[1]**.

4.4.1. LAB MEDIA: Table 2. *Video editor: Highlight the C-statistic value "0.62 (0.57–0.67)" aligned with "Model 1".*

4.5. In the in-hospital mortality model, a lower phase angle was a highly significant predictor of death **[1]**.

4.5.1. LAB MEDIA: Table 2. *Video editor: Highlight the entire row "Phase angle, °" under "**In-hospital mortality**".*

4.6. Lower systolic blood pressure was also significantly associated with in-hospital mortality **[1]**.

4.6.1. LAB MEDIA: Table 2. *Video editor: Highlight the entire row "SBP, mmHg" under "In-hospital mortality".*

4.7. The in-hospital mortality model had the highest discriminatory ability among all models **[1]**.

4.7.1. LAB MEDIA: Table 2. *Video editor: Highlight the C-statistic value "0.75 (0.66–0.83)" under "In-hospital mortality".*

Pronunciation Guide:

1. Bioelectrical
Pronunciation link:
https://www.merriam-webster.com/dictionary/bioelectrical
IPA: /ˌbaɪ.oʊ.ɪˈlɛk.trɪ.kəl/
Phonetic Spelling: bye-oh-ih-lek-tri-kuhl

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2. Impedance
Pronunciation link:
https://www.merriam-webster.com/dictionary/impedance
IPA: /ɪmˈpiː.dəns/
Phonetic Spelling: im-pee-duhnss

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3. Prognostic
Pronunciation link:
https://www.merriam-webster.com/dictionary/prognostic
IPA: /prɑːgˈnɑː.stɪk/
Phonetic Spelling: prog-naa-stik

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4. Cox (as in Cox regression)
Pronunciation link:
https://www.merriam-webster.com/dictionary/Cox
IPA: /kɑːks/
Phonetic Spelling: koks

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5. Spline
Pronunciation link:
https://www.merriam-webster.com/dictionary/spline
IPA: /splaɪn/
Phonetic Spelling: spline

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6. Vector
Pronunciation link:
https://www.merriam-webster.com/dictionary/vector
IPA: /ˈvɛk.tɚ/
Phonetic Spelling: vek-tuhr

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7. Biomarkers
Pronunciation link:
https://www.merriam-webster.com/dictionary/biomarker
IPA: /ˈbaɪ.oʊˌmɑːr.kɚz/
Phonetic Spelling: bye-oh-mar-kerz

8. Multivariable
Pronunciation link:
https://www.merriam-webster.com/dictionary/multivariable
IPA: /ˌmʌl.tiˈver.i.ə.bəl/
Phonetic Spelling: mul-tee-vair-ee-uh-buhl

9. Hazard
Pronunciation link:
https://www.merriam-webster.com/dictionary/hazard
IPA: /ˈhæz.ɚd/
Phonetic Spelling: ha-zurd

10. Akaike
Pronunciation link:
https://www.howtopronounce.com/akaike
IPA: /ˈɑː.kaɪ.keɪ/
Phonetic Spelling: ah-kai-kay

11. Bayesian
Pronunciation link:
https://www.merriam-webster.com/dictionary/Bayesian
IPA: /ˈbeɪ.zi.ən/
Phonetic Spelling: bay-zee-uhn

12. C-statistic
Pronunciation link:
No confirmed link found
IPA: /siː stəˈtɪs.tɪk/
Phonetic Spelling: see-stuh-tis-tik

13. Sodium
Pronunciation link:
https://www.merriam-webster.com/dictionary/sodium
IPA: /ˈsoʊ.di.əm/
Phonetic Spelling: soh-dee-uhm

14. Systolic
Pronunciation link:
https://www.merriam-webster.com/dictionary/systolic
IPA: /sɪˈstɑː.lɪk/
Phonetic Spelling: sis-tah-lik

15. BIVA (abbreviation of Bioelectrical Impedance Vector Analysis)
Pronunciation link:
https://www.howtopronounce.com/biva
IPA: /ˈbiː.və/
Phonetic Spelling: bee-vuh

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16. Pspline (pronounced pee-spline as scripted)
Pronunciation link:
No confirmed link found
IPA: /piː.splaɪn/
Phonetic Spelling: pee-spline