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Evaluating Factors Influencing Wound Healing: A Mixture Cure Rate Model Approach

Anoushka Khayar
University of Texas at Arlington

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ABSTRACT

The study focuses on healing of chronic wound. A cure rate and probabilities of patients are calculated and visualized by using Proportional Hazards Mixture Cure (PHMC) Model. This study reveals that alkaline wounds tend to heal slower than non-alkaline wounds, with significant differences between male and female patients. To be specific, males generally exhibit slower wound healing in both alkaline and non-alkaline conditions compared to females. This study also reveals the need for future research into biological, environmental and social factors, such as hormonal imbalance, living conditions and caregiver support among the patients.

Keywords: survival, mixture cure model, wound, healing , alkalinity, PHMC

Outline

Importance of Wound Healing Research

- Health Outcomes
- Reduction in Healthcare Costs
- Improved Quality of Life
- Prevention of Complications
- Enhanced Recovery from Surgery

Study Objective

- Analyzing a dataset of patients with chronic wounds
- Using a mixture cure rate model to evaluate factors influencing wound healing

Dataset

- **Sample Size**: 167 patients.
- **Event of Interest**:Wound Healing
- **Key variables:**
  - tstop: Time to complete wound healing (or censoring at 120 days)
  - d120: Indicator of healing within 120 days (1 if healed, 0 if not)
  - Alkalinity: Factor with levels A and B
  - Age: Age of the patient
  - Gender: Gender of the patient (M/F)
  - infection: Presence of infection (yes/no)
  - Wound: Type of wound (venous, diabetic, surgical, other)

Brief Description of the Data

- **Variables**:
  - Continuous: *Age, tstop*
  - Categorical: *Alkalinity, Gender, infection, Wound*
- **Summary Statistics**:
  - **Age**: Mean = 64.09, Min = 29, Max = 97
  - **tstop**: Mean = 109, Min = 28, Max = 120
  - **d120**: 0= 110, 1= 57
  - **Alkalinity**: A = 126, B = 41

Mixture Cure Models

- Mixture cure models are used in survival analysis.
- They handle situations where a portion of the population is ”cured” and will not experience the event.
- Consists of two main components: Incidence (Cure) Model and Latency (Survival) Model.

Incidence (Cure) Model

- Models the probability of being cured.
- Logistic regression:

$$\pi(z) = \frac{\exp(bz)}{1+\exp(bz)}$$

- $1-\pi(z)$ is the probability of being cured depending on z.
- b is a vector of unknown parameters and z represents covariates.

Latency (Survival) Model

- **1. Proportional Hazards Mixture Cure (PHMC) Model**

$$S(t \mid x) = S_0(t)^{\exp(\beta x)}$$

- **2. Accelerated Failure Time Mixture Cure (AFTMC) Model:**

$S(t \mid x) = S_0(te^{\beta x})$, it is the AFTMC model.

where $S_0(t)$ be the baseline survival function of uncured subjects when $x = 0$.

Combined Survival Function

- Overall survival function for the mixture cure model:

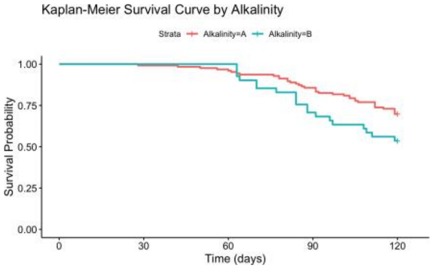
$$S_{\text{pop}}(t \mid x, z) = \pi(z)S(t \mid x) + (1 - \pi(z))$$

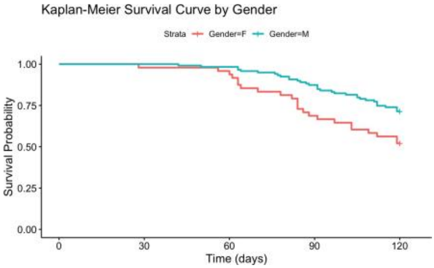
- $\pi(z)$ is the probability of being uncured.

Overview of the smcure Package

- **Function Call:**
  smcure(formula, cureform, offset=NULL, data, na.action=na.omit, model=c("ph", "aft"), Var=TRUE, link="logit", emmax=50, eps=1e-7, nboot=100)
- **Algorithm and Estimation:**
  - Uses Expectation-Maximization (EM) algorithm
- **Model Specification:**
  - Flexible inclusion of covariates
  - Analyzes factors influencing cure and survival

Kaplan-Meier Survival Curves





Cure Probability and Failure Time Distribution Models

	Cure Probability Model		Failure Time Distribution Mode	
Variable	Estimate	Pr(> |Z|)	Estimate	Pr(> |Z|)
Intercept	0.437	0.729		
Alkalinity	0.687	0.062	0.238	0.553
Gender	0.697	0.084	0.230	0.592
Age	-0.023	0.136	-0.010	0.551
Infection	-0.378	0.317	-0.446	0.199
WoundVenous	0.578	0.325	-0.251	0.735
WoundDiabetic	-0.147	0.819	-0.476	0.484
WoundSurgical	0.503	0.621	-0.223	0.810

Cure Probability and Failure Time Distribution Models

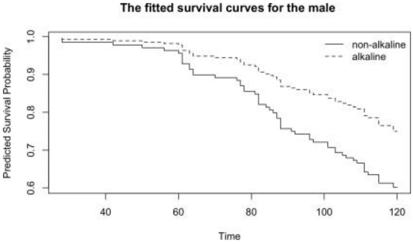
	Cure Probability Model		Failure Time Distribution Model	
Variable	Estimate	$Pr(>\|Z\|)$	Estimate	$Pr(>\|Z\|)$
Intercept	-1.094	< 0.001		
Alkalinity	0.684	0.056	0.239	0.434
Gender	0.826	0.022	0.221	0.470

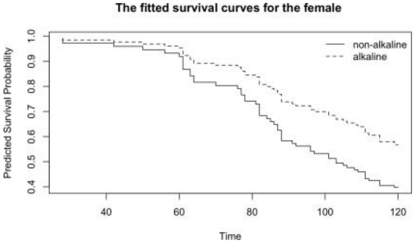
General Cure Rate Formula:

- Cure rate=1- $(\pi(z))= \frac{1}{1+e^{-1.0938356+0.6836659\cdot x_1+0.8257733\cdot x_2}}$

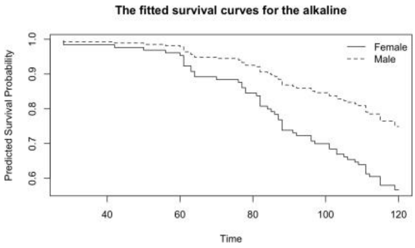
x_1	x_2	Cure Rate
0	0	0.7491033
1	1	0.3975692
0	1	0.5666171
1	0	0.6011286

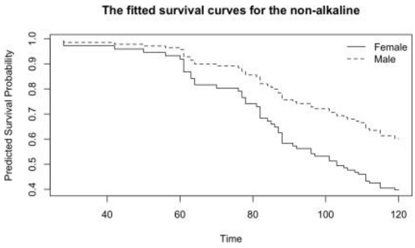
Interpretation of Survival Curves by Gender





Interpretation of Survival Curves by Alkalinity





Summary of Findings

Alkalinity and Gender Impact:

- Higher alkalinity levels are associated with a higher probability of wounds not healing.
- Male patients exhibit a higher likelihood of wounds not healing compared to female patients.

Recommendations

- **Targeted Interventions for High Alkalinity:**
  - Consider treatments or interventions to manage and reduce alkalinity levels in wound areas.
  - Regular monitoring and adjustments to wound care protocols based on alkalinity levels.
- **Gender-Specific Care Protocols:**
  - Develop and implement wound care protocols tailored specifically for male patients.
  - Increased monitoring and follow-up for male patients to ensure timely intervention and healing.

Future Research

- Investigate additional factors that may contribute to wound healing variations between patients.
- Explore potential treatments or strategies to mitigate the negative impact of high alkalinity and gender differences on wound healing.
- Hormonal Influences
- Explore external factors such as frequency of dressing of being used, living condition of individual.

Conclusion

- Summary of findings
- Significance of the study
- Future work

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Q & A

Questions?