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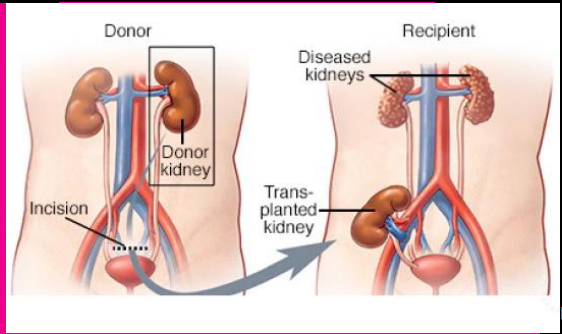


Characterizing Cluster-Based Frailty Phenotypes in a Multicenter Prospective Cohort of Kidney Transplant Candidates

Syed Hani Raza Abidi, Nur Zincir-Heywood, Syed Sibte Raza Abidi, Kranthi Jalakam, Samina Abidi, Amanda Vinson, George Worthen, Karthik Tennankore

Dalhousie University, Halifax, Canada

Introduction

- Frailty: "A state of increased vulnerability due to degeneration in multiple systems" (Worthen et al, 2021)
- Frailty lends a higher risk of death among kidney transplant recipients
- Frailty Index to measure frailty of kidney transplant waitlist candidates
  - Based on deficits across social, function, mobility, health and cognition
  - Informed by a limited number of data parameters
  - Manually derived using variables that meet specific criteria
- Frail patients are at a higher risk of being withdrawn from the kidney transplant waitlist

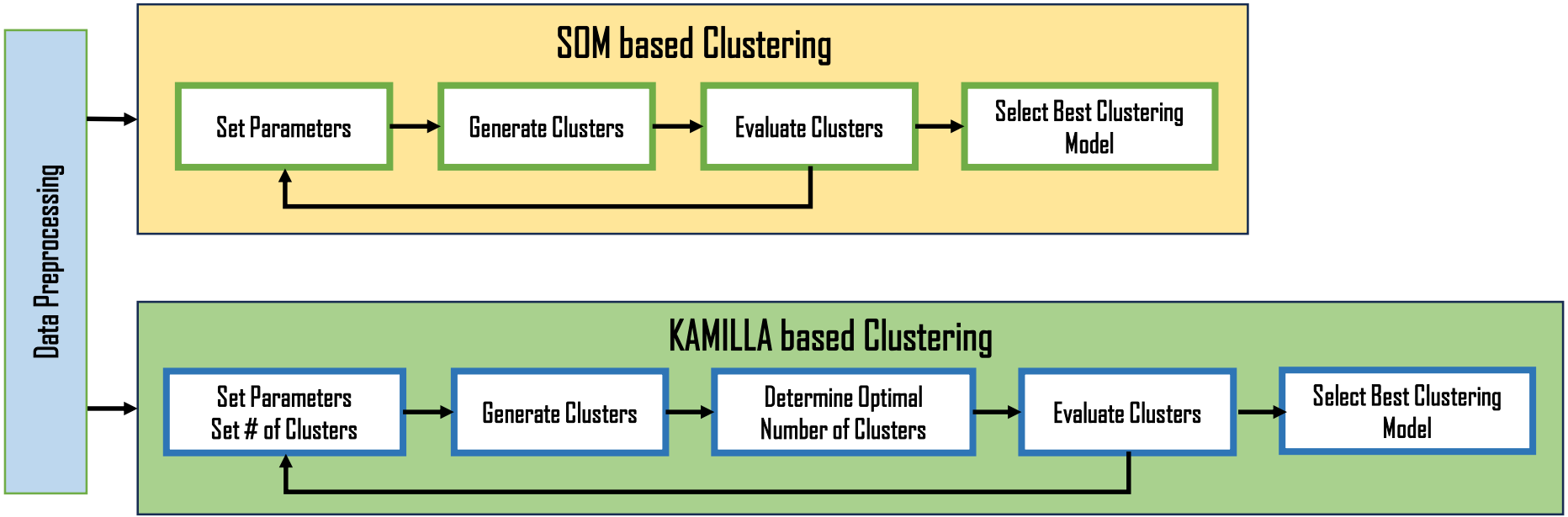
Objectives

- *Can unsupervised learning (clustering) algorithms find groups of patients who are frail and at-risk of kidney transplant failure?*
- Clustering based patient phenotyping
  - Multicenter, prospective dataset of kidney transplant candidates
  - Multi-type (numerical and categorical) data with a large number of features
  - Self-Organizing Maps (SOM) with hierarchical clustering
  - KAMILA (KAy-means for MIxed LArge data sets): density-based clustering
  - Statistical methods to understand clustered feature-level phenotypes of waitlist candidates

Data Description

- Multi-center prospective study evaluating the impact of frailty on outcomes for kidney transplant waitlist candidates (from 2016-2022)
  - Five Canadian transplant centers: London (Ontario), Hamilton (Ontario), Halifax (Nova Scotia), Saint John (New Brunswick), and Montreal (Quebec)
  - 807 kidney transplant recipients
  - 105 variables across a number of domains
    - Demographics, (a) comorbid health conditions (including diabetes, cardiovascular disease and prior malignancy), (b) self-reported functional limitations, (c) self-reported and measured variables relating to cognitive function, social and emotional well-being, and (d) physical examination parameters
  - Dataset contained both categorical and continuous features.

Methodology

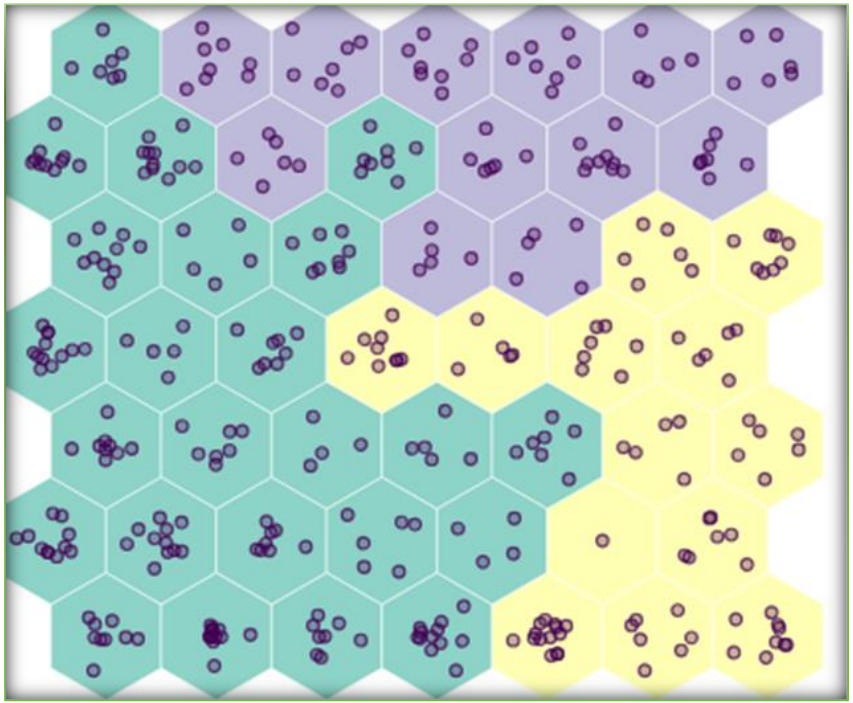


SOM Clustering Experiments

Dimensions	Linkage	Cluster Sizes	Silhouette	Dunn	Calinski-Harabasz
7x7	Complete	198, 90, 79	0.1124315	0.1273989	39.7
10x10	Ward D.2	188, 131, 48	0.0878228	0.1323267	42.9
19x19	Ward D.2	76, 125, 166	0.0850325	0.1398902	40.9
15x15	Ward D	203, 50, 114	0.1000332	0.1334696	40.5
17x17	Ward D.2	87, 67, 213	0.115904	0.1387107	39.6

SOM Results

- 3 patient clusters
  - low-risk, medium-risk, and high-risk
- Variables split patients into three health domains
  - Comorbidity
  - Functionality & Mobility
  - Emotional/Cognitive/Social Health



KAMILA Experiments

Seed Value	Num_Init	Cluster Sizes	Silhouette	Dunn	Calinski-Harabasz
300	25	108, 183, 76	0.1346931	0.102	47.2
150	10	59, 58, 250	0.1375821	0.102	46.7
100	50	203, 104, 60	0.1725514	0.11660	45.8
500	50	201, 105, 61	0.1614899	0.12137	45.9

Cluster based Phenotypes

Variable	Cluster 1	Cluster 2	Cluster 3
Size	N=198	N=90	N=79
Demographics			
Age (years +/- standard deviation)	55 +/-13	48 +/-13	59 +/-12
Female	56 (28%)	54 (60%)	23 (29%)
Comorbidity: N (%)			
Diabetes	68 (34%)	8 (9%)	54 (68%)
Coronary Artery Disease	33 (17%)	3 (3%)	26 (33%)
Prior Cancer	21 (11%)	2 (2%)	13 (16%)
Functionality/Mobility : N (%)			
Exhaustion	28(14%)	44 (49%)	49 (62%)
Weak Grip	58 (29%)	28 (31%)	41 (52%)
Slow Walking Speed	15 (8%)	15 (17%)	18 (24%)
Trouble lifting 10 pounds	3 (2%)	11 (12%)	14 (17%)
Help with Housework	11 (6%)	24 (27%)	23 (29%)
Help with Groceries	19 (10%)	38 (42%)	40 (51%)
Limited in Moderate Activity	25 (13%)	46 (51%)	64 (81%)
Social, Emotional, Cognitive: N (%)			
Feels Alone	16 (8%)	32 (36%)	30 (38%)
Rarely Socializes	60 (30%)	45 (50%)	49 (62%)
Cuts Work Due to Emotional Reasons	2 (1%)	9 (10%)	14 (18%)

Phenotypes

Cluster 1 (198 patients)	Cluster 2 (90 patients)	Cluster 3 (79 patients)
Lowest risk-- mostly independent and emotionally healthy	Moderate risk	Highest risk -- High frailty severity with severe health issues
Few issues with functional limitations	Enough functional capacity Require some assistance for a number of tasks	Functional status: Difficulty performing basic tasks: walking, bathing, climbing stair and groceries
Moderate problems with comorbidity	Minimal burden of comorbidity	High comorbidity burden
Least degree of social and emotional impairment	Impaired social, and emotional function	Emotional and social function: Patients felt lonely and socially isolated
	Youngest, highest proportion of female sex (60%)	

Concluding Remarks

- Frailty is important for all organ transplant candidates and recipients
- Generated cluster-based phenotypes using all patient features
  - Comorbidity and Functionality not related.
  - Functionality and Mental Health related
- SOM produced better results than KAMILA
- Generated phenotypes can be used to identify waitlist candidates who are at higher risk
- Our approach can be applied to other patients being waitlisted for organ transplantation

THANK YOU

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