MP716

# Individual seasonal patterns of normalized protein catabolic rate (nPCR) in hemodialysis patients associated with the death within 3 years

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## Aim

to describe the seasonal patterns of normalized protein catabolic rate (nPCR) and describe the relationship between seasonal patterns of nPCR and 3 year mortality in hemodialysis patients.

## Conclusion

nPCR of hemodialysis patients had seasonal patterns. We succeeded in detecting a cluster associated with seasonal patterns of nPCR and 3 year mortality.

***[Background]***

Variation patterns of clinical and laboratory parameters reflect each patient's characteristics. These variation patterns are relevant for physicians during the clinical evaluation. In hemodialysis patients, the group means of clinical and laboratory parameters reportedly show seasonal variation patterns. However, such seasonal patterns in individual observations are unclear. Further, whether these seasonal patterns are related to mortality is also unclear.

***[Purpose]***

In this single-center study, we aimed to describe the seasonal patterns of normalized protein catabolic rate (nPCR) in group means and individual observations among hemodialysis patients and describe the relationship between seasonal patterns of nPCR in individual observations and mortality.

***[Participants]***

We evaluated 300 patients undergoing maintenance hemodialysis for >12 months between March 2011 and February 2014. Patients who did not have continuous nPCR during the 12 months were excluded. Fifty-one patients died during the 3-year observation period.

***[Methods/Analysis]***

The observation for all patients started in March. nPCR was calculated from blood urea nitrogen, weight before and after dialysis, dialysis time, and blood flow volume on the first week of each month for 12 months. The nPCR values were "smoothed" using the moving average approach. We evaluated the ratio for nPCR in March for each patient with respect to every other month. The group means of nPCR were calculated as the averages of all the patients. After evaluating individual observations, we plotted the ratio of nPCR for each of the 12 months for each patient. The distances between every series of the plot were calculated using the Euclidean approach, resulting in a hierarchical clustering dendrogram (the Ward-method). The clusters of plot series were obtained from the dendrogram. To consider the cluster stable, approximate and unbiased p values were estimated for every cluster. This p-value indicates how strong the cluster is supported by data. We used R version 3.3.2 and Pvclust package. Pvclust calculates p-values for hierarchical clustering via multiscale bootstrap resampling. The relation between clusters and death within 3 years were evaluated at p=0.90, 0.70, 0.60 using Fisher's exact test.

***[Results]***

The group means of nPCR showed a seasonal pattern which demonstrated a decrease in summer and recovery in winter (Figure 1).

We detected thirty-one clusters at p=0.90, forty-one clusters at p=0.70 and thirty-eight clusters at p=0.60 in detecting the cluster associated with seasonal patterns of nPCR and 3 year mortality. All patients were clustered at p=0.60. A cluster was associated with death within 3 years (Table, Figure 2). This cluster had the tendency of an extreme decrease of nPCR in summer and not enough recovery in winter.

***[Limitation]***

The Euclidean approach for measuring distance among variation patterns of patients allows only a rough estimation of the calculated distance. This study was single center study and had small sample. This study did not consider multiple testing.

***[Conclusion]***

The group means of nPCR of hemodialysis patients had seasonal variation patterns, as did other nutritional parameters. Although we used this limited technique, we succeeded in detecting the cluster associated with death. We must refine the technique in terms of distance calculation to examine larger data sets using machine learning approaches.

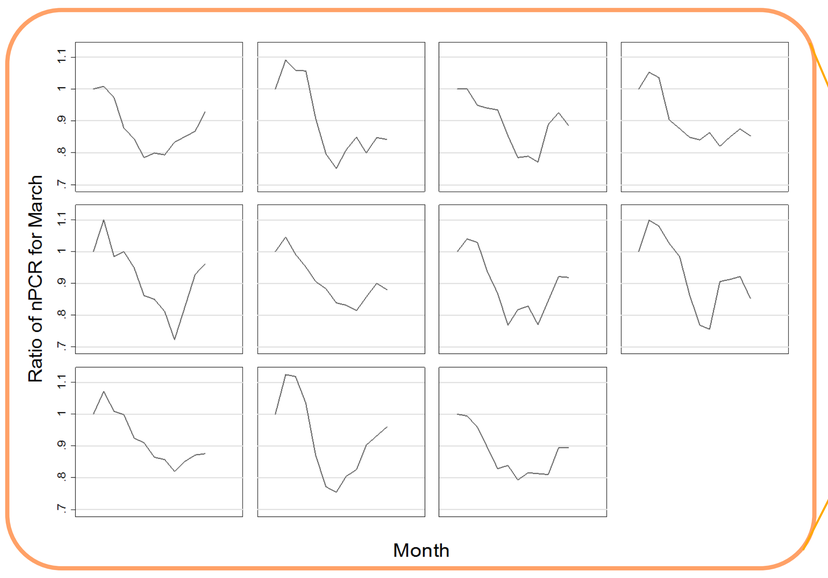


**Figure 2. Individual observations detected seasonal patterns associated with death within 3 years**

This cluster included 11 patients and was detected across p=0.90, p=0.70, p=0.60. This cluster had the tendency of an extreme decrease of nPCR in summer and not enough recovery in winter.

| p-value 0.60 | | | | p-value 0.70 | | | | p-value 0.95 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cluster | Death | Total | Proportion | Cluster | Death | Total | Proportion | Cluster | Death | Total | Proportion |
| A | 9 | 44 | 0.2 | A | 2 | 9 | 0.22 | A | 0 | 2 | 0 |
| | | | | | | | | No cluster | | 7 | |
| | | | | B | 3 | 14 | 0.21 | B | 3 | 14 | 0.21 |
| | | | | C | 3 | 19 | 0.15 | C | 2 | 10 | 0.2 |
| | | | | | | | | D | 1 | 9 | 0.11 |
| | | | | No cluster | | 2 | | No cluster | | 2 | |
| B | 0 | 11 | 0 | D | 0 | 11 | 0 | E | 0 | 11 | 0 |
| C | 1 | 11 | 0.09 | E | 1 | 11 | 0.09 | F | 1 | 11 | 0.09 |
| D | 1 | 6 | 0.16 | F | 1 | 6 | 0.16 | No cluster | | 6 | |
| E | 5 | 11 | 0.45* | G | 5 | 11 | 0.45* | G | 5 | 11 | 0.45* |
| F | 0 | 11 | 0 | H | 0 | 11 | 0 | H | 0 | 4 | 0 |
| | | | | | | | | No cluster | | 7 | - |
| G | 1 | 8 | 0.12 | I | 1 | 4 | 0.25 | I | 1 | 4 | 0.25 |
| | | | | J | 0 | 4 | 0 | J | 0 | 3 | 0 |
| | | | | | | | | No cluster | | 1 | |
| H | 2 | 9 | 0.22 | K | 1 | 2 | 0.5 | K | 1 | 2 | 0.5 |
| | | | | L | 1 | 7 | 0.14 | L | 1 | 7 | 0.14 |
| I | 0 | 6 | 0 | M | 0 | 6 | 0 | M | 0 | 5 | 0 |
| | | | | | | | | No cluster | | 1 | |
| J | 0 | 6 | 0 | N | 0 | 6 | 0 | N | 0 | 4 | 0 |
| | | | | | | | | No cluster | | 2 | |
| K | 1 | 5 | 0.2 | O | 1 | 5 | 0.2 | O | 1 | 5 | 0.2 |
| L | 1 | 5 | 0.2 | P | 1 | 5 | 0.2 | P | 0 | 2 | 0 |
| | | | | | | | | No cluster | | 3 | |
| M | 3 | 8 | 0.37+ | Q | 3 | 8 | 0.37+ | Q | 3 | 8 | 0.37+ |
| N | 0 | 9 | 0 | R | 0 | 2 | 0 | No cluster | | 2 | |
| | | | | S | 0 | 7 | 0 | R | 0 | 7 | 0 |
| O | 1 | 6 | 0.16 | T | 1 | 6 | 0.16 | S | 1 | 3 | 0.33 |
| | | | | | | | | No cluster | | 3 | |
| | | | | V | 0 | 2 | 0 | No cluster | | 2 | |
| | | | | W | 2 | 3 | 0.66+ | No cluster | | 3 | |
| P | 4 | 16 | 0.25 | U | 1 | 2 | 0.5 | T | 1 | 2 | 0.5 |
| | | | | X | 1 | 6 | 0.16 | U | 1 | 6 | 0.16 |
| | | | | No cluster | | 3 | | No cluster | | 3 | |
| Q | 1 | 6 | 0.16 | Y | 1 | 6 | 0.16 | No cluster | | 6 | |
| | | | | | | | | V | 0 | 2 | 0 |
| S | 2 | 10 | 0.2 | Z | 2 | 10 | 0.2 | W | 1 | 6 | 0.16 |
| | | | | | | | | No cluster | | 2 | |
| T | 1 | 11 | 0.09 | AA | 1 | 11 | 0.09 | X | 1 | 11 | 0.09 |
| | | | | | | | | Y | 1 | 2 | 0.5 |
| U | 2 | 10 | 0.2 | AB | 2 | 10 | 0.2 | Z | 0 | 2 | 0 |
| | | | | | | | | No cluster | | 6 | |
| V | 1 | 2 | 0.5 | AC | 1 | 2 | 0.5 | AA | 1 | 2 | 0.5 |
| W | 0 | 10 | 0 | AD | 0 | 10 | 0 | AB | 0 | 3 | 0 |
| | | | | | | | | No cluster | | 7 | |
| X | 1 | 5 | 0.2 | AE | 1 | 5 | 0.2 | AC | 1 | 5 | 0.2 |
| Y | 2 | 7 | 0.28 | AF | 2 | 7 | 0.28 | AD | 0 | 4 | 0 |
| | | | | | | | | No cluster | | 3 | |
| Z | 2 | 15 | 0.13 | AG | 2 | 15 | 0.13 | AE | 2 | 15 | 0.13 |
| AA | 2 | 5 | 0.40 | AH | 2 | 5 | 0.40 | AF | 1 | 2 | 0.5 |
| | | | | | | | | No cluster | | 3 | |
| | | | | | | | | AG | 1 | 2 | 0.5 |
| AB | 3 | 13 | 0.23 | AI | 3 | 13 | 0.23 | AH | 0 | 4 | 0 |
| | | | | | | | | AI | 1 | 3 | 0.33 |
| | | | | | | | | No cluster | | 4 | |
| AC | 2 | 11 | 0.18 | AJ | 2 | 11 | 0.18 | AJ | 2 | 11 | 0.18 |
| AD | 1 | 8 | 0.12 | AK | 1 | 8 | 0.12 | AK | 1 | 8 | 0.12 |
| AE | 1 | 4 | 0.25 | AL | 1 | 4 | 0.25 | No cluster | | 4 | |
| AF | 1 | 10 | 0.1 | AM | 1 | 7 | 0.14 | AL | 1 | 7 | 0.14 |
| | | | | AN | 0 | 3 | 0 | No cluster | | 3 | |

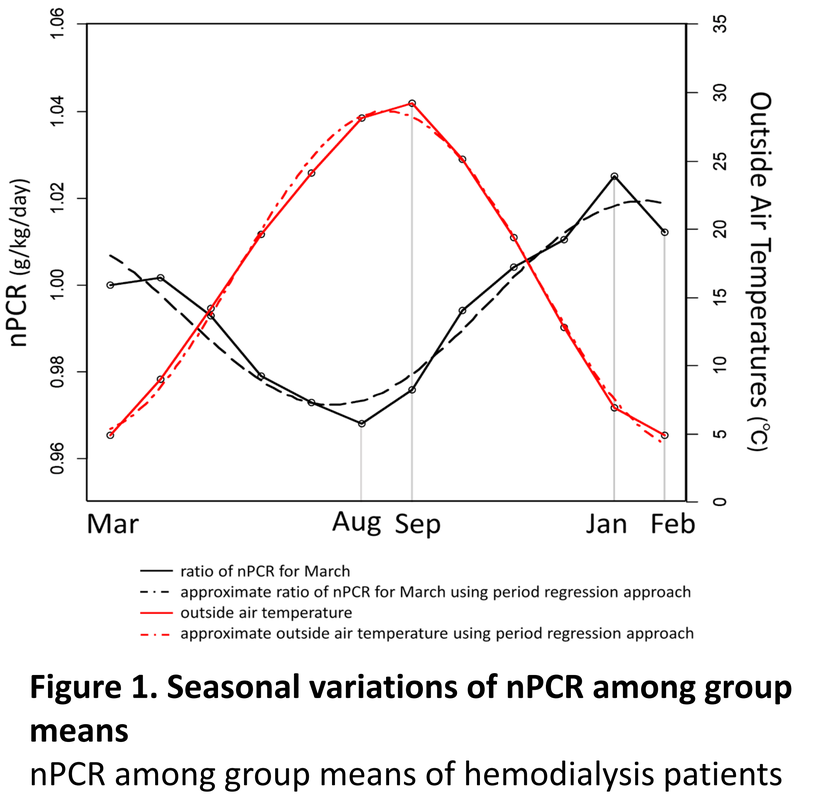


**Figure 1. Seasonal variations of nPCR among group means**

nPCR among group means of hemodialysis patients had seasonal patterns. There was one month deference between the phase of nPCR and outside air temperatures.

**Table. Clusters at every p-value and correlation with death within 3 years.** Association with death *: p<0.05, +: p<0.20

11 clusters (Yellow box and Grey box) were detected across p=0.90, p=0.70, p=0.60. Association between clusters and death within 3 years were evaluated by Fisher's exact test. Yellow box cluster was associated with death.


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