Interpretation of Pathophysiology by Laboratory Data

(2) Graphic Display of Data, Dynamic Pattern

Masaharu NIWA and Hiroshi SHIMIZU*

Department of Clinical Pathology, School of Medicine, Tokai University
*Department of Medical Informatics, School of Medicine, Tokai University

(Received April 14, 1989)

In order to display the pathophysiology of a patient more efficiently and adequately than in the static radar chart presented in the first report, a dynamic radar chart and serial line graphs using colored lines were presented.

A dynamic radar chart prepared as described particularly in this report, shows the whole data of a patient along with the time course of illness by the space-saving "overlapped-drawing". Moreover serial line graphs are employed for items important for the understanding of a patient's pathophysiology or for items which show obscure change due to overlapping in the dynamic radar chart. Although this line graph is space-occupying it reveals more clearly the changes of data throughout the entire course of a patient's disease.

In this second report the dynamic presentation of data and its interpretation, were presented for nine cases. This was done more efficiently and adequately than in the cases described in the first report where the display and interpretation of pathophysiology of a patient was made using merely the data of a single point.

(Key Words: Blood Chemistry, Graphic Display, Pathophysiology, Radar Chart, Dynamic pattern)

INTRODUCTION

As mentioned in the first report, the pathophysiology, which fluctuates dynamically in nature, is not displayed adequately unless laboratory data are also displayed in a dynamic form. In this paper nine cases using this kind of display were presented.

METHODS

For this purpose we have employed the following two methods (8~12, 14, 15).

1. Dynamic Radar Chart

As shown in Fig. 1, representing a 1/4 segment in comparison with a real one, instead of painting the circular areas A, B, E, F as in the static RC, the horizontal lines connecting the data on the radial lines were divided at constant intervals, painted with different colors in a fixed order and superimposed on a single RC. Rainbow colors were used in the following order, purple → blue → green → yellow → red, in all cases. The interval for each color was changeable according to the speed of change in the pathophysiology of each patient, but was constant in each case. This interval is described on the lower left side in the foot-note of each figure. The dynamic RC indicates the whole time course for one patient. One problem with this space-saving "overlapped drawing" was that the graph was difficult to read in cases showing many data with complicated fluctuations.

2. Serial line Graph

A serial line graph precisely reveals changes throughout the entire course if overlapping or complicated intersections of horizontal lines on the dynamic RC interfere with accurate observation of data fluctuations. For inclusion in a serial line graph, test items that are crucial in the patient's pathophysiology, or show obscure and/or complicated changes in data are selected from the dynamic RC.

An example is shown in Fig. 2. The ordinate was graduated in agreement with the circles on
Colors of lines

early

late stage

*Concentric circles, a 1/4 segment

Fig. 1 Basic structure of a dynamic radar chart

The ordinate was graduated in agreement with the circles U→P in Fig. 1, with the O-SDI site located on the crimson line.

**Lines K→N divide equally the whole clinical course of a patient by the same length of hospitalization day. For further details refer to the body of this report.

Fig. 2 Basic structure of a serial line graph

The RC U→P, with the O-SDI site located on the crimson line. As the abscissa was graduated by the frequency of a test, the actual length of interval in figure varied depending on the number of tests conducted in each period. But the color or the horizontal serial lines representing the day of hospitalization was divided by the line K→N at fixed equal intervals for each case as in dynamic RC.

RESULTS

A. Liver Diseases

1. Case 1 (00916439): Acute Hepatitis, Cholestatic History
A 36 years old male was admitted with fever, general malaise, nausea, vomiting and dark urine. After 120 days of hospitalization he was discharged with improvement.

Static radar chart (S-RC)
Fig. 3 shows the data on the next day after admission.

<table>
<thead>
<tr>
<th>GOT</th>
<th>GPT</th>
<th>TB</th>
<th>DB</th>
</tr>
</thead>
<tbody>
<tr>
<td>elevated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>slightly elevated</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dynamic radar chart
In Fig. 4, the data during the whole course of this patient is displayed with a dynamic radar chart. GOT, GPT, ALP, TB and DB that were elevated or slightly elevated in Fig. 3, maintained these levels during the purple and blue stage (0~48 days), and began to normalize from the green stage (48~72 days). Although in this period, other items such as
GLU, TP, ALB, and CK were decreased, in the final red stage (96 ~ 120 days) they normalized together with all other items. Transient elevation of CK in the blue stage may be caused by laparoscopy and biopsy performed seven days before.

Serial line graph
A serial line graph was prepared and presented in Fig. 5, using GOT, GPT and TB, the most important items picked up from Fig. 4 for the understanding of the pathophysiology of this patient.

Whole data of these important items are displayed clearly without any intersections or overlapping, and carefully looking at Fig. 5, it is clear that the relation of GOT > GPT is maintained during the whole course of this patient.

Other data
Data in paranthesis mean the normal range adopted in our hospital.

1) Protein fractions (%)  
   ALB: 55.2 (61.3 ~ 74.1), ß: 4.6  
   (1.3 ~ 2.9), ß2: 7.4 (4.1 ~ 10.1), ß: 10.0  
   (7.6 ~ 10.8), γ: 23.0 (9.3 ~ 18.5)
2) Thymol turbidity test (TTT): 10.0 (1 ~ 7)  
   SHU  
   Zinc sulfate turbidity test (ZTT): 7.9  
   (2 ~ 14) KU
3) HBs antigen: (–), antibody: (–)
   α-fetoprotein: 8 (20 l) ng/ml
   Cholinesterase (ChE): 4.4 (2.5 ~ 4.5) × 10^5 U/l

Interpretation
Fig. 3 ~ 5 show the acute parenchymatous damage of liver with cholestasis. High level of γ-globulin, TTT, seem to reflect this pathophysiology. Data 3) serve as a reference.

2. Case 2 (00663573): Fulminant Hepatitis
History
A 53 years old male complained of nausea, anorexia, slight fever, general malaise, and itching. Moreover he noticed that his urine was of a dark colour. Two days later he was admitted because these symptoms and signs increased and he became icteric. He died after 13 days of hospitalization without any improvement.

Static radar chart
Fig. 6 shows the data of the next day of admission.

   elevated GOT, GPT, LDH, ALP, TB, DB

   slightly elevated K
   slightly decreased UA, TP
   decreased ALB

Dynamic radar chart
As GOT, GPT, TB and DB in Fig. 6 are scaled out, in this Fig. 7 the radii of the concentric circles located exclusively outside of the crimson line are scaled 4 fold in the ordinary radar chart. By this scaling, all of the concentric circles in Fig. 7 correspond, from the origin to the outside, -5.0, -2.5, 0, +10, +20, +40 SDI respectively. In the lower part of this figure, the maximum SDI value is described on the right side, and the interval, explained in the foot-note of Fig. 2, on the left side respectively. GOT, GPT and LDH in Fig. 7 decrease gradually keeping the relation of GOT < GPT except in the terminal red stage. TB and DB are scaled over as before, even in this enlarged radar chart.

Items that were at the terminal red stage the maximum or nearly maximum value during the whole course of this case, were GLU, UN, CNN, UA, IP, GAT, LDH, TB and DB. On the contrary, items that showed the minimum values were TP and ALB.

Serial line graph
Fig. 8, that includes the terminal elevation of data, reflects the entire course of GOT, GPT and TB in this case. Taking into consideration the short interval and 4-fold enlarged scale, changes in Fig. 7 and 8 show very severe and rapid progress of liver insufficiency.

Other data
The following data were obtained at the time of admission.

1) White blood cell count: 12.9 (4 ~ 8) × 10^5/μl
   Band-formed leucocytes: 91 (4 ~ 14) %
2) Whole blood NH₃: 176 (0 ~ 90) μg/dl
3) LDH isozymes (%)
   1:20 (21 ~ 30), 2:26 (27 ~ 33), 3:16  
   (19 ~ 25), 4:8 (7 ~ 15), 5:30 (7 ~ 15)
4) ChE: 1.9 (2.5 ~ 4.5) × 10^5 U/l
5) γ-GTP: 130 (5 ~ 105) U/l, LAP: 63  
   (21 ~ 51) U/l
6) HBs antigen and antibodies: negative

Interpretation
Fig. 6 ~ 8 shows a severe grade of acute parenchymatous damage of liver with cholestasis. Low levels of UA, TP, ALB reflect this severe condition. All other data 1) ~ 6) coincide or are referable to this pathophysiology.
Fig. 3 Case 1 (00916439)
Acute Hepatitis

Fig. 6 Case 2 (00663573)
Fulminant Hepatitis

Fig. 4 Case 1 (00916439)

Fig. 7 Case 2 (00663573)

Fig. 5 Case 1 (00916439)

Fig. 8 Case 2 (00663573)
3. Case 4 (00977764): Liver Cirrhosis

History
A 60 years old female was admitted for further investigation of liver dysfunctions. Before admission, strong positive urobilinogenuria and abnormalities in several tests of liver function were found during examination for cystitis by a local physician. She was diagnosed clinically to suffer from liver cirrhosis by the findings inclusive of laparoscopy and endoscopy. After a hospitalization of 96 days she was discharged to be followed up in our out-patient clinic.

Static radar chart
Fig. 9 shows data obtained on the next day of admission.

- elevated GOT > GPT
- slightly elevated UA, IP, LDH, ALP, TB, DB
- decreased ALB

Dynamic radar chart
None of the items in Fig. 10 show so rapid a change as encountered with the previous dynamic RC (Fig. 4 and 7). GOT and GPT elevated during the purple stage (0 ~ 19 days), tended to decrease gradually thereafter. Slightly elevated UA and IP were revealed to be transient. On the other hand slightly elevated ALP, TB and DB, together with decreased ALB at the time of admission, maintained almost the same level during the whole course of the disease. The decreased in ALB was the largest among Case 1 and 2.

Serial line graph
In Fig. 11, the elevation of every item was small, the processes were slow and the relation of GOT > GPT was maintained.

Other data
The following data were obtained at admission.

1) Protein fractions (%)
   - ALB: A46.9, α1:3.1, α2:6.4, β:6.7, γ:37.4
2) ZTT:19.5 KU, TTT:14.4 SHU
3) BSP, 45m: 19 (0 ~ 9) %
4) ChE: 1.7 (2.5 ~ 4.5) × 10³ U/l

Interpretation
Fig. 9 ~ 11 reflect the chronic cirrhotic change of liver parenchym. And other data coincide with this pathophysiology.

B. Advanced Cancers
1. Case 8 (00744107): Breast Cancer

History
A 57 years old female was admitted to receive chemotherapy for breast cancer. However generalized metastases to the bones were already noticed. Additionally thereafter appeared pains of the hip and neck, visual hallucinations, low grade fever, and decrease of consciousness. She died after a hospitalization of about 3 months. This patient had a past history of left radical mastectomy and axillar lymphnode dissection.

Static radar chart
Fig. 12 shows the data of about one month before death.
- elevated UA, CA, GOT, LDH
- slightly elevated CK, ALP, TGL
- slightly decreased GLU, CL, TP, ALB

Dynamic radar chart
Fig. 12 shows the pathophysiology about a month before death, corresponding to the yellow stage in Fig. 13. From admission until this period, almost stationary tendencies were observed, i.e. 1) elevation in UA, K, CA, IP, GOT, LDH, ALP and 2) decrease in CL, TP, ALB, CK, TCH, TB, DB, GLU. These tendencies due probably as a whole mainly to a destructive or consumptive process in this case respectively. Almost all of the abnormal findings at the terminal red stage may be conceived as the progress of these processes. But in some items, the onset of a new pathophysiology (TB, DB, UN), or the effects of energetic treatment (GLU) may be the case of change.

Serial line graph
In Fig. 14, the whole course of CA, IP, and LDH were displayed. Simultaneous elevation of CA and IP may reflect bone destruction, and elevated LDH may be released from tumor cells. The absolute or relative decline of these items at the terminal red stage are unexplainable, but the deterioration of corresponding cells themselves or the aggravation of responses of the whole body may be conceivable factors.

Other data
1) LDH isozymes (%)
   - 1:18, 2:28, 3:28, 4:19, 5:11
2) Principal data at the time of admission.
   - Hb: 11.4 g/dl, WBC: 5.8 × 10³/ul, ChE:
   - 2.5 × 10³ U/l, UA: 5.1 mg/dl, CA: 5.3
   - mEq/l, LDH: 690 U/l

Interpretation
High levels of UA, CA, LDH may reflect the proliferation and destruction of tumor or bone cells. Fixed low level of GLU, TP, and ALB may
Fig. 9  Case 4 (00977764)
Liver Cirrhosis

Fig. 10  Case 4 (00977764)
19 day's interv.

Fig. 11  Case 4 (00977764)
19 day's interv.

Fig. 12  Case 8 (00744107)
Breast Cancer

Fig. 13  Case 8 (00744107)
7 day's interv.

Fig. 14  Case 8 (00744107)
7 day's interv.
be due to the consumptive condition. LDH isozymes show five-finger shaped pattern characteristic of malignancy.

C. Endocrine and Metabolic Diseases

1. Case 10 (00982725): Hypoparathyroidism

History

A 26 years old female was complaining of continual paresthesias since thyroidecotomy for Basedow's disease had been performed twelve years ago. She was admitted because cramping in the extremities appeared additionally regardlessly day or night, beginning three months previously. She was discharged after a hospitalization of 52 days with improvement after various therapies including Vitamin D and calcium administration.

Static radar chart

Fig. 15 shows the data on the next day of admission.

- elevated GLU,
- slightly elevated NA, IP, TP, LDH, CK
- slightly decreased UA, K, TB, DB,
- decreased CA

Dynamic radar chart

Fig. 16 shows that the elevation of GLU and the slight decrease of UA at the purple stage (0 ~ 11 days) were transient. On the other hand the elevation of NA and the decrease of K were unexplainably permanent. Decrease of CA was found to be frequent except in the green stage (22 ~ 33 days), slight elevation of IP was observed during the whole course. Elevation of LDH and CK at the purple stage declined thereafter, this was especially prominent in the case of CK.

Serial line graph

In Fig. 17 the precise fluctuations of IP, CA and CK could be followed during the whole period. The transient elevation of CA at the green stage may be caused by the administration of the calcium preparation for therapeutic purposes. Except for this stage, the relation of IP to CA are similar to Fig. 23 showing a tendency to renal insufficiency.

Other data

1) Serum calcitonine: 0.37 (0.2) ng/ml
2) Serum Ca ion: 36 (50 ~ 60) %
3) Serum γ globulin: 20 ~ 30 (9.3 ~ 18.5) %

Interpretation

Taking into consideration the clinical histo-

2. Case 11 (00532452): Primary Aldosteronism

History

A 49 years old female was admitted with the complaint of hypertension and weakness of the extremities. Detailed examination revealed in the vein of the right adrenal gland an abnormal figure and high content of aldosterone. She was discharged after a hospitalization of 34 days with improvement by appropriate therapy. After 2 months, she was readmitted for a surgical operation and the corresponding gland containing the adenoma was entirely removed.

Static radar chart

Fig. 18 shows the data on the day after admission.

- elevated NA, CK
- slightly elevated GLU
- slightly decreased IP
- decreased K

Dynamic radar chart

The elevation of NA, LDH and CK, together with the decrease of K found in the purple stage (0 ~ 7 days) of Fig. 19, normalized gradually during hospitalization. The abnormalities of IP and GOT encountered in the same stage, revealed to be transient. GLU fluctuated frequently during the whole course.

Serial line graph

In Fig. 20 the fluctuations of NA, K and LDH are displayed in detail.

Other data

1) Blood pressure: 170/90 mmHg
2) Contents in the vein of right adrenal gland:
   - Aldosterone: 400 (2 ~ 12) ng/dl
   - Renin: 0.1 (0.3 ~ 2.0) ng/dl
3) ECG: hypokalemic pattern
4) 50g-OGTT (oral glucose tolerance test): diabetic type
5) Urinary 17HCS, 17KS: within normal
Fig. 15 Case 10 (00982725) Hypoparathyroidism

Fig. 16 Case 10 (00982725) 11 day's interv.

Fig. 17 Case 10 (00982725) 11 day's interv.

Fig. 18 Case 11 (00532452) Primary Aldosteronism

Fig. 19 Case 11 (00532452) 7 day's interv.

Fig. 20 Case 11 (00532452) 7 day's interv.
Interpretation
High NA and low K were caused by the over-production of aldosterone. The relations of, 1) elevated CK and LDH to muscular weakness and paralysis of extremities, 2) elevated GLU to impaired glucose tolerance, both may be due to the hypokalemia underlying this disease. Other data 1)~5) coincided with this pathophysiology.

D. Kidney Diseases
1. Case 17 (00698091): Chronic Nephritis
History
A 52 years old female visited our out patient clinic with complaint of anorexia, nausea, and decrease of body weight for 3 weeks. After consultation, the disturbances of kidney functions were pointed out. Ten days later she was admitted through the emergency clinic owing to malaise of lower limbs as well as left-sided abdominal pain. After about 2 months, this patient was discharged with transient improvement. However four months later, she was admitted again with sudden aggravation of her general condition and died eventually after a three-days hospitalization.
Static radar chart
Fig. 21 show the data on the next day of admission.
- elevated UN, CNN, UA, IP
- slightly elevated K
- slightly decreased CL, ALB, DB
- decreased NA
Dynamic radar chart
Although UN, CNN and UA were elevated initially, then decreased thereafter gradually in Fig. 22, maintaining their levels as before even at the time of transient discharge. The elevation of K, IP, and the decrease of NA, CL, CA were revealed to be constant during the whole course. Decrease of ALB and TP proceeded gradually reflecting the aggravation of the general condition.
Serial line graph
Detailed fluctuations of IP, CA and K during the whole course of this case can be followed clearly by looking at Fig. 23. In the figure the fluctuations of IP and CA, are to some extent mirror-images of each other. Abnormalities of the electrolytes in this case show almost typical patterns which occur simultaneously with azotemia.

Other data
The following data were obtained after admission.
1) Blood pressure: 130~180/70~110 mmHg
2) Urine volume: 400~900 (1,000~1,200) ml/day specific gravity: 1.005~1.008 (1.012~1.023)
Interpretation
Fig. 21~23 show the pattern of chronic renal insufficiency with azotemia and electrolyte abnormalities. Other findings are consistent with this pathophysiology.

E. Diseases with Elevated CK
1. Case 20 (00996904): Acute Myocardial Infarction
History
A 65 years old female was admitted to the CCU on an emergency basis for treatment of dyspnea and coma. Early in the morning of admission, she was found unconscious in a knee-chest position. She had a history of precordial discomfort about seven months previously, but no abnormalities, including ECG, were found at that time. She died after being hospitalized for nine days.
Static radar chart
Fig. 24 shows the data 29 hours after the onset of attack.
- elevated GLU, UA, GOT, GPT, LDH, CK
- slightly elevated UN
- slightly decreased IP, TP, ALB
Dynamic radar chart
Because almost all of the enzyme levels are scaled out in Fig. 24, a four-folded scaling was employed in Fig. 25 and 26 the same as in the case with fulminant hepatitis (Fig. 7, 8). GOT and GPT that were initially elevated at the purple stage (0~2 days) declined gradually thereafter. LDH and CK were continually high during the whole course, reached maximum level at the terminal red stage, simultaneously with ALP, TB and DB. Elevation of GLU was found occasionally. Although difficult to evaluate in Fig. 25 employing a 4-folded scale, slight elevation of UA and UN were observed. CA, TP, ALB, TCH, probably also NA and CL, that showed minimum level at the red stage, may reflect the terminal consumptive condi-
Fig. 21 Case 17 (00698091)
Chronic Nephritis

Fig. 22 Case 17 (00698091) 00698091
12 day's interv.

Fig. 23 Case 17 (00698091)

Fig. 24 Case 20 (00996904)
Acute Myocardial Infarction

Fig. 25 Case 20 (00996904)
2 day's interv. max. 40-SDI

Fig. 26 Case 20 (00996904)
2 day's interv.

12 day's interv.
tions. Decrease of IP were observed at the purple and blue stages, but the mechanism is unexplainable.

Serial line graph
In Fig. 26 detailed fluctuation of GPT, CK, and TB during the whole course are displayed.

Other data
1) WBC: 10.3 (4.8) × 10^6/ul
2) EKG: elevation of ST

Interpretation
Abnormally high levels of enzymes and probably slightly elevated UA show their release from necrotic myocardium into the blood stream. The elevation of GPT, ALP, TB and DB may reflect liver complication. Transient elevation of GLU, and UN may relate to fever, pain, and un easiness which happened concomitantly with the acute attack. Other data may show that the tests were performed at an early stage of attack.

F. Hematological Diseases
1. Case 22 (00837962): Chronic Myelogenous Leukemia

History
A 43 years old female complained since childhood of a tendency to fatigue, anemia, and occasional nasal bleeding. She was admitted for further investigations because the symptoms of common cold have appeared additionally for the last half months, and she was noted to have a leucocytosis by a local physician. She died eventually after a hospitalization of about a half year.

Static radar chart
Fig. 27 shows the data of the third day after admission.
- elevated LDH
- slightly elevated NA, GOT, TGL
- slightly decreased CK, TB.

Dynamic radar chart
Elevation of LDH at the initial and terminal stage in Fig. 28, may reflect the relapses and remission in the course of this disease. A possible explanation for the initial decrease and the terminal increase of GLU, may be caused for the former by the artifactual hypoglycemia due to leukocyte glucose utilization in vivo, and for the latter by the energetic treatment inclusive of glucose infusion. Among items that showed terminal decrease, TP, ALB, CK, TB and DB may relate to the consumptive or anemic con-
condition. On the contrary the terminal increase of UN, UA, GOT, GPT and LDH may be affected with the agonal abnormal conditions.

**Serial line graph**

In Fig. 29, LDH, ALB and GLU were followed during the whole course of this case.

**Other data**

1) Leucocyte
count: 178.4 $\times 10^3$ /µl

Hemogramm, myeloblast: 52.5, promyelocyte: 28.5%

Philadelphia chromosome: detected

2) Hb: 10.4 g/dl. Thrombocyte count: 9.8

(14~40) $\times 10^4$ /µl

3) LDH isozymes (%)

1:23, 2:48, 3:24, 4:4, 5:1

**Interpretation**

The only evident data in the radar chart is the elevation of LDH, orginated from the proliferated leucocytes. Decreased TB and DB relates to anemia. Other abnormal findings were revealed to be transient. Other data 1) and also the data 3), in which the increase of LDH is found, correlate with the pathophysiology of this disease. So long as those kinds of biochemical data are employed for the interpretation of the pathophysiology in the hematological field, the acquisition of effective data are inevitably restricted. To obtain more informative data, those biochemical items constructing a radar chart must be replaced by hematologically important ones.

**DISCUSSION**

Examined parameters of patients, e.g., blood chemistry, however, multiple the data may be, or however delicate their display, ultimately reflect the pathophysiology only at the time-point of specimen collection. Furthermore, the pathophysiology of a living body, in particular the levels of components of blood chemistry fluctuate constantly and dynamically: especially glucose, neutral fat, CK and NEFA levels are markedly affected by food intake, exercise and medication.

However, when such tests are repeated many times, it is rather easy in most cases to judge whether changes in these data are essential to the pathophysiology, or whether they are transient. This is true for data on the blood acid-base balance, which fluctuates markedly over a short period (2, 3). Actually in a clinical setting various tests are serially conducted for the diagnosis of a disease, evaluation of the effects of treatment, and estimation of prognosis.

These circumstances indicate that any display of data should include their serial changes to demonstrate the pathophysiology more efficiently and adequately. Various examples have been devised to display in a dynamic figure the data of a patient i.e. trend (20) or vector display (2, 3, 19), simultaneous overlapped display of the figures of a patient for each stage (21). Our current attempts are in line with such a view.

We believe that our work, described here, has clarified the usefulness of a graphic display of data, but such a display naturally has limitation of precision and reliability for pathophysiological differentiation. This will be overcome only by a more objective and quantitative from of interpretation, which will be demonstrated in the next report.

**ACKNOWLEDGMENTS**

The authors wish to thank Mr. Masaki Mizuno and Mrs Mariko Matsushita (née Katayama), for their invaluable help in preparing various graphs with computer during their study for the thesis in 1983.

**REFERENCES**


8) Niwa M, Haida M, Ito K, Shimizu H and Mizuno M: Graphical presentation of the chemical data assayed
by Technicon SMAC. Revista Brasileira de Analises Clinicas 16: 137, 1984
13) Niwa M: Why not use the standard deviation index as a common scale for data quantification? Clinical Chemistry 33:1294, 1987