Immunoglobulin G value before treatment is correlated with the responsiveness to initial intravenous immunoglobulin therapy for Kawasaki Disease.

**- Background -**

- Low serum level of immunoglobulin G (IgG) before intravenous immunoglobulin (IVIG) therapy for Kawasaki disease (KD) was reported as one of the risk factors for coronary artery abnormalities (CAAs) by Sawaji in 1998.
- This finding needs to be re-evaluated, because the dosage of IVIG has changed from 0.2-0.4 g/kg for 5 days to 2 g/kg/1-2 days and the incidence of CAAs has been reducing.
- A screening for IVIG non-responders is important since IVIG non-responders are more likely to be affected by CAAs. IgG value before treatment may also be a predictive factor for IVIG non-responders.

**- Objectives -**

- To clarify whether serum IgG value before high dose IVIG therapy is a predictor of CAAs and IVIG non-responders.

**- Methods -**

- We reviewed the clinical records of KD patients who were admitted to Kagoshima Medical Association Hospital in Japan between January 2001 and August 2011.
- The patients who were given IVIG (2 g/kg/1-2 days) within 7 days of illness and who were examined for serum immunoglobulin values (IgG, IgA, and IgM) before treatment were selected.
- Serum immunoglobulin values and coronary artery diameters measured by ultrasound were transformed to z-scores. CAAs were defined as coronary artery z-score above 3.0 at 1 month of illness.

**- Results -**

Fig 1. Subject enrollment

| 303 KD patients were admitted and treated |
| 254 Patients given high dose IVIG within 7 days of illness |
| 197 patients finally fulfilled the inclusion criteria |

There were no differences in each immunoglobulin

Fig 2. Comparison of each immunoglobulin value between KD patients without CAAs and those with CAAs

Fig 3. Comparison of each immunoglobulin value between IVIG responders and non-responders

- Logistic regression analysis revealed that IgG value was an independent factor for IVIG non-responders.
  - Odds ratio: 1.36, 95% CI: 1.002/1.849, p=0.048.
- ROC analysis showed that the value was useful cut-off value.
  - Its sensitivity was 77% and the specificity was 61%.

**- Discussions -**

- In 1991, Newburger showed there was no difference in IgG z-score before treatment between KD patients with CAAs and those without CAAs.
  - At least in KD patients given high dose IVIG, low value of IgGz is not a risk factor for CAAs.
- Inflammatory cytokines, such as IL-6 and TNF-α, increase in acute phase of KD and the levels of these cytokines are higher in KD patients with CAAs and IVIG non-responders.
- Cytokines which are produced by CD (4+) T cell (especially IL-6) prompt B cell activation and production of immunoglobulin.
  - Those findings may be associated with relatively high value of IgGz in IVIG non-responders affected by more severe vasculitis.

**- Conclusions -**

Low IgGz value was not a risk for CAAs in this study. However, KD patients with relatively high value of IgGz before treatment may have a risk of non-responsiveness to initial IVIG.