Japanese Red Cross Society

Transfusion Information

1803-157

Results of Assessment/Surveillance of Transfusion-Related Acute Lung Injury (TRALI)

Transfusion-related acute lung injury (TRALI) is a serious non-hemolytic adverse transfusion reaction characterized by dyspnea due to sudden non-cardiac pulmonary edema during transfusion or within six hours after transfusion. The reported causes include the involvement of anti-leukocyte antibodies (anti-HLA antibody, anti-HNA antibody*1) in blood components for transfusion, and biologically active substances such as active lipids.[1)]

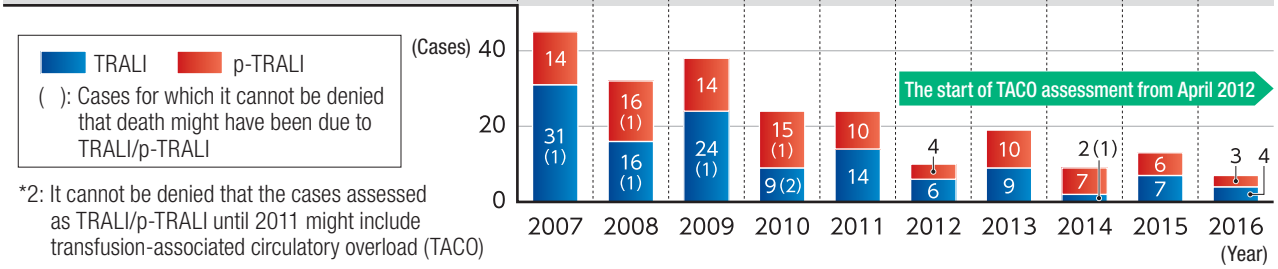
The Japanese Red Cross Society assesses suspected cases of TRALI as non-hemolytic adverse transfusion reactions reported by medical institutions according to the diagnostic criteria (see the reverse side), and conducts tests of anti-leukocyte antibodies on the used blood components for transfusion and the blood of patients. We hereby introduce a summary of these results.

Since cases assessed as TRALI do not show any specific trends in the primary diseases of patients and since it developed with all blood components, it is difficult to predict the onset of such cases. Perform follow-up monitoring of patients after the start of transfusion, and immediately discontinue transfusion if a sudden respiratory disorder appears, and then take appropriate measures such as administration of oxygen and respiratory care.

*1 Anti-granulocyte antibodies

Changes in the number of cases assessed as TRALI/p-TRALI (2007-2016*2)

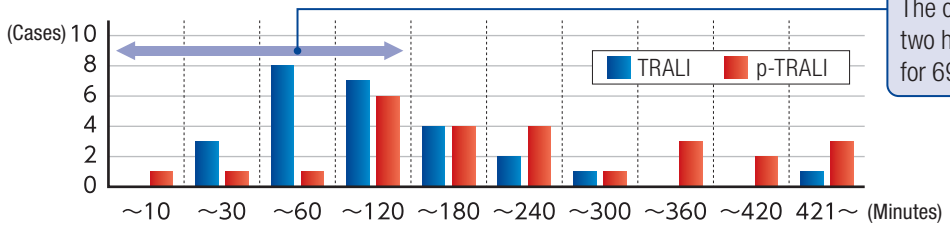
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of reported non-hemolytic adverse transfusion reactions	1,626	1,544	1,541	1,579	1,597	1,595	1,515	1,451	1,533	1,476
Number of cases subjected to TRALI assessment (Ratio to the number of reported non-hemolytic adverse transfusion reactions)	141 (8.7)	141 (9.1)	161 (10.4)	167 (10.6)	177 (11.1)	178 (11.2)	170 (11.2)	156 (10.8)	178 (11.6)	141 (9.6)
Number of cases assessed as TRALI/p-TRALI (Ratio to the cases subjected to the assessment)	45 (31.9)	32 (22.7)	38 (23.6)	24 (14.4)	24 (13.6)	10 (5.6)	19 (11.2)	9 (5.8)	13 (7.3)	7 (5.0)



*2: It cannot be denied that the cases assessed as TRALI/p-TRALI until 2011 might include transfusion-associated circulatory overload (TACO)

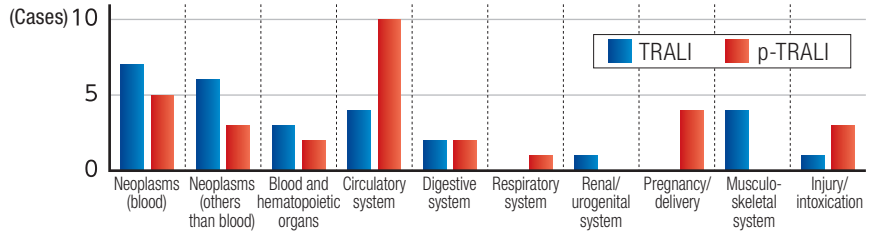
Time of onset / primary disease / blood components (2012-2016)

Time from the start of transfusion to the onset of the symptoms



The onset of the symptoms was within two hours from the start of transfusion for 69.2% of the cases of TRALI.

Classification of the primary diseases of patients (ICD10)



"Neoplasm" and "blood and hematopoietic organ" accounted for 57.1% of all cases of TRALI. This shows the same trend as the state of transfusion for each disease in Tokyo.*3

On the other hand, p-TRALI shows a trend of many cases with transfusion during surgical procedures (e.g., "circulatory system") and "pregnancy/delivery."

*3 Bureau of Social Welfare and Public Health, "Surveillance of Transfusion"

Number of cases and frequency of development by each blood component

(Frequency based on the total number of bags supplied)

Blood component	Total number of bags supplied	TRALI	p-TRALI
Red cells	16,867,390	8 (Approx. 1/2,100,000)	5 (1/approx. 3,400,000)
Platelets	4,155,656	7 (Approx. 1/590,000)	4 (1/approx. 1,000,000)
Plasma	4,832,026	7 (Approx. 1/690,000)	2 (1/approx. 2,400,000)
Multiple types of component	-	6 (–/–)	19 (–/–)

Results of the surveillance of anti-leukocyte antibodies (2012-2016)

(1) Number of cases in which anti-leukocyte antibodies were detected in the blood component for transfusion

Number of cases assessed	Anti-HLA antibody only	Anti-HNA antibody only	Anti-HLA antibody + anti-HNA antibody	Positive rate
TRALI (28 cases)	13	1	2*4	57.1%
p-TRALI (30 cases)	9	2	0	36.7%

*4 Anti-HLA antibodies and anti-HNA antibodies were respectively detected in cases in which multiple blood components for transfusion were used

(2) Number of cases in which the cross-match study of the leukocytes of patients was positive in (1) (number of positive cases / number of cases in which the study was conducted)

Number of cases assessed	Anti-HLA antibody only	Anti-HNA antibody only	Anti-HLA antibody + anti-HNA antibody	Positive rate
TRALI (12 cases)	9/9	1/1	1/2	91.7%
p-TRALI (7 cases)	3/5	0/2	-	42.9%

Anti-leukocyte antibodies that exist in blood components for transfusion were detected in 16 of the 28 cases of TRALI (approximately 57.1%), which is higher than the detection rate of other cases of non-hemolytic adverse transfusion reactions.[2)]

Since the retention rate of anti-HLA antibody tends to be higher in women (antibody production due to pregnancy/delivery), the Japanese Red Cross Society has preferentially manufactured "Fresh Frozen Plasma, Leukocytes Reduced NISSEKI" from 400 mL of blood from men (Male Dominant FFP: MDF) since April 2011 as a safety measure.

(3) Number of cases in which anti-leukocyte antibodies were detected in the blood of patients

Number of cases assessed	Anti-HLA antibody	Anti-HNA antibody	Positive rate
TRALI (28 cases)	7	0	25.0%
p-TRALI (30 cases)	2	1	10.0%

The reactivity is unknown because a cross-match study on the used blood components for transfusion has not been conducted; however, the positive rate of anti-HLA antibody was similar to that of anti-HLA antibody in the blood of the patient in other cases of non-hemolytic adverse transfusion reactions.[3)]

TRALI and possible TRALI[4)]

1. Diagnostic criteria of TRALI

a. ALI (acute lung injury)
   i. Acute development
   ii. Hypoxemia
   $PaO_2/FiO_2 \leq 300$ or $SpO_2 < 90\%$ (room air),
   or other clinical symptoms of hypoxemia
   iii. Bilateral infiltrative shadows on the front view of the chest X-ray
   iv. No evidence of elevated left atrial pressure (circulatory overload)
b. No ALI before the transfusion
c. Development during the transfusion or within six hours after the transfusion
d. No risk factors* of ALI other than transfusion temporally related

2. Possible TRALI

a. to c. are the same as the diagnostic criteria of TRALI
d. There are risk factors of ALI other than transfusion temporally related

*** Risk factors of ALI**
[Direct lung injury]
Aspiration, pneumonia, inhalation of hazardous substances, pulmonary contusion, near-drowning
[Indirect lung injury]
Severe sepsis, shock, multiple injury, burn, acute pancreatitis, cardiopulmonary bypass, drug overdose

In case any of adverse reactions and/or infections related to transfusion of blood components, please notify the medical representatives of your local JRC blood center immediately. Please provide the residual products, the recipient samples, and any other related materials; it is helpful to investigate and/or identify the cause. For storage of residual products and the recipient samples, refer to the "Guidelines for lookback studies of blood products."

1) Toy P et al. Transfusion-related acute lung injury: incidence and risk factors. Blood. 2012;119:1757-67.
2) Transfusion Information 1107-128 "Results of Surveillance of Adverse Transfusion Reactions and HLA Antibody"
3) Rikizo Taira, Izumi Miwa, Naoko Goto, et al. Investigation Results of Patients Who Developed Non-Hemolytic Transfusion Reactions: A Japanese Red Cross Society Study. Japanese Journal of Transfusion and Cell Therapy. 2017; 63:708-715.
4) Kleinman S et al. Towards an understanding of transfusion-related acute lung injury: statement of a consensus panel. Transfusion. 2004;44:1774-89.

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* For more information, please contact the medical representatives of your local JRC blood center.

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