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Title:
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Date:
2018-06-01

Citation:
Ochi, S., Kato, S., Leppold, C., Morita, T., Tsubokura, M., Oikawa, T., Shineha, R., Kanazawa, Y. & Fujiwara, M. (2018). Can a disaster affect rheumatoid arthritis status? A retrospective cohort study after the 2011 triple disaster in Fukushima, Japan. International Journal of Rheumatic Diseases, 21 (6), pp.1254-1262. https://doi.org/10.1111/1756-185X.13301.

Persistent Link:
https://hdl.handle.net/11343/261076

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Article type   : Original Article

Title: Can a disaster affect rheumatoid arthritis status? A retrospective cohort study after the 2011 triple disaster in Fukushima, Japan

Running title: Rheumatoid arthritis status after a disaster

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Please cite this article as doi: 10.1111/1756-185X.13301

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SO, SK, TM, LC, and MT mainly contributed to the conception or design of the work, analysis, and interpretation of data for the work; AND SO and SK Drafted the work, TM, MT, LC, TO, RS, YK, and MF revised it critically for important intellectual content; AND All did final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgement

We sincerely thank all the staff at the Whole-body counter room at Minamisoma Municipal General Hospital, for kindly analysing the data of internal radiation exposure levels of the patients.

ABSTRACT

Objective: As status of rheumatoid arthritis (RA) is highly affected by environmental factors, a catastrophic disaster may also affect RA activity. Herein we conducted a retrospective cohort study in the disaster area of the 2011 triple disaster in Fukushima, Japan: an earthquake, tsunamis, and a nuclear accident.

Methods: Clinical records of RA patients who attended a hospital near the Fukushima Daiichi Nuclear Power Plant were collected. For those who underwent whole-body counter testing, internal radiation exposure levels were also collected. As clinical parameters may fluctuate in the absence of a disaster, changes in values before and after the disaster were also compared. Logistic regression was conducted to identify factors affecting RA status.

Results: Fifty-three patients (average age, 64.2 years old; females, 83%; average disease duration, 15.7 years) were included in the study. Five patients lived within the no-entry zone, 37 evacuated immediately after the disaster, and 4 temporarily stopped RA treatment. The proportions of patients who showed worsened tender joint count, swollen joint count, and rheumatoid factor values were significantly higher after the disaster compared to those before. Among the 16 patients who underwent whole-body counter testing, only 1 showed a detectable, but negligible, radioactive cesium level. Use of methotrexate was identified as a possible preventive factor for RA exacerbation in this setting.

Conclusion: This is the first study to analyse detailed profiles of RA patients after a disaster. As methotrexate may prevent the disease exacerbation, continuity of care for this common chronic disease should be considered in disaster settings.

INTRODUCTION

Disasters can impact population health in many ways. The health problems that emerge after a disaster are not limited to incidental injuries and acute illnesses associated with disaster damage; rather, secondary events associated with disasters, such as air pollution, mental stress, lifestyle changes, and medication loss, may indirectly lead to exacerbation of chronic diseases, especially non-communicable diseases (NCDs), among residents of the disaster area [1]. With the increasing global burden of NCDs [2], understanding the impact of a disaster on NCDs is critical to the creation of an effective disaster mitigation plan for maintaining population health. However, thus far little evidence is available regarding the impact of a disaster on NCDs.

Rheumatoid arthritis (RA) affects about 0.5-1% of the general population [3] and contributes about 20% of years lived with disability worldwide [4]. RA is characterized by joint inflammation associated with pain and stiffness, which can lead to severe morbidity [3]. As an autoimmune disease, the RA disease status is affected by a variety of external factors that stimulate immune responses; e.g., air pollution [5], mental stress [6], and lifestyle factors such as smoking and eating habits [7], have been reported to affect joint inflammation in RA patients.

As huge disasters threaten the livelihood of residents in the affected area, they also inevitably influence the living environment of the residents, thereby affecting RA incidence and status. Factors affecting RA activity may include poor living conditions such as poor sanitation and unhealthy foods at shelters and temporary housing, mental stress caused by loss of family members and possessions, and inactivity due to job loss. In addition, as shelters and temporary housings are often poorly designed for people with disabilities, worsening of joint inflammation may cause further impairment of daily life among patients with RA. Therefore, prevention of RA onset and exacerbation after disasters is important for mitigation of the impact of the disaster on at-risk individuals.

A questionnaire-based study showed that property damage caused by disasters tends to be associated with deteriorated functional status in RA patients [8], while another study reported no significant difference in RA status based on measurement of the erythrocyte sedimentation rate (ESR) titer before and after natural disasters [9]. An increase in the incidence rate of RA among the World Trade Center rescue/recovery workers after the 2011 terrorist attack [10] has also been reported. However, only a limited number of reports have assessed fluctuations in RA status following disasters.

The 2011 Great East Japan Earthquake and the following Fukushima Daiichi Nuclear Power Plant (NPP) accident was a complex disaster consisting of an earthquake, tsunamis, and radiation contamination. This triple disaster brought unforeseen public health challenges to the disaster area. Major health issues have arisen through social disruption, caused largely by fear of radiation. In addition, long-term displacement due to evacuation orders posed health risks such as mental stress and inactivity among affected residents. Mental stress was also caused by stigmatisation against radiation and job losses among farmers and fishermen in radiation-contaminated areas.

Such situations contribute to the assumption that RA status worsens, with an increase in RA incidence, after disasters. Not only stressors by natural disasters but also radiation exposure may affect the immune profiles of patients and thus lead to inflammation flare. A systematic study on autoantibodies among atomic-bomb survivors in Hiroshima and Nagasaki at 1987 showed higher radiation exposure level was significantly associated with higher titer of rheumatoid factor (RF) 40 years after the exposure [11], though no increase in incidence of RA has been reported [12]. However, the situation in Fukushima is quite different from that in Hiroshima and Nagasaki with regard to radiation exposure level. Excessive radiation exposure level of the residents in Fukushima within a year after the NPP accident was assumed to be much lower than that for the survivors, as 23 mGy at maximum for external exposure and 3 mGy at maximum for internal exposure [13, 14], and little, if any, excessive radiation exposure occurred thereafter [15]. By contrast, the average and maximum radiation exposure level among atomic-bomb survivors were estimated as 0.19 Gy (190 mGy) and 50 Gy (50,000 mGy), respectively [11]. Incremental external radiation exposure levels among Fukushima residents due to the NPP accident have been <1 mSv/year [16], which is the upper limitation dose recommended by the Japan National Government; and no reports have described the impact of low-dose radiation exposure on RA status. Therefore, it would be interesting to assess whether such low-dose radiation exposure impacted immune profiles and/or affected autoimmune disease activity.

This study was undertaken to assess disease status among RA patients after the triple disaster using their clinical data at a hospital near the Fukushima Daiichi NPP. The present results address the importance of maintaining provision of healthcare for common NCDs in disaster settings.

METHODS

The situation

On March 11, 2011, an earthquake of magnitude 9.0 and subsequent tsunamis up to 14 m in height struck the northeast coast of Japan. The tsunamis disabled the cooling system of the reactors of the Fukushima Daiichi NPP in Fukushima Prefecture, Japan. The meltdown started soon after the tsunamis, and the first visible explosion, which was suspected to be caused by a hydrogen gas leak, occurred on March 12. Over the following 3 weeks, several suspected hydrogen detonations occurred.

Immediately after the accident, the Japanese National Government designated evacuation zones. The area within the 20-km radius of the NPP was labeled as a no-entry zone, and the 20–30-km radius of the NPP was labelled as an "indoor evacuation" zone. Minamisoma City is located 10-40 km from the NPP (Figure 1). Approximately 70,000 residents in the area were mandated to evacuate and about 15,000 were recommended to stay inside their homes (indoor evacuation) to avoid excessive external radiation exposure. In addition, residents whose houses were destroyed by the tsunami had to evacuate to shelters. In Minamisoma City, 631 out of 70,000 residents were killed, and 2,875 houses were washed away by the tsunami before the evacuation order was made. During this social havoc, mass evacuation occurred in this area due to fear of radiation and security concerns, even though evacuation from the indoor evacuation zone was voluntary.

Minamisoma Municipal General Hospital in Fukushima, which is located about 24 km from the Fukushima Daiichi NPP, is the nearest hospital to the evacuation zone (Figure 1). Therefore, detailed records of the physical condition, evacuation status, and laboratory data of RA patients both before and after the disaster were available.

Target patients

Medical records of patients who visited the Department of Rheumatology, Minamisoma Municipal General Hospital were collected. Patients were included in the study if both of the following criteria were fulfilled:

- A diagnosis of RA had been made before the disaster
- Clinical and laboratory data within 6 months before the disaster and within 1 year after the disaster were available

Clinical data

Standardized score for RA disease activity, such as Disease Activity Score (DAS) and Simple Disease Activity Index (SDAI), was not available from the clinical record. The following data were extracted from medical records:

- Background data: age, gender, disease duration, Steinbrocker stage, Steinbrocker functional class, and postal address
- Medications before and after the disaster
- Situation at the time of the disaster: evacuation status, whether or not patients were seen by other physicians, and medication losses
- Disease activity data:
    - Number of tender joints (tender joint count [TJC])
    - Number of swollen joints (swollen joint count [SJC])
    - Laboratory findings: titers of C-reactive protein (CRP), rheumatoid factor (RF), matrix metalloproteinase-3 (MMP-3), and ESR

Internal radiation exposure data

In Minamisoma City, a free screening program for internal radiation exposure from radioactive cesium (Cs-134 and Cs-137) using whole-body counters (Fastscan Model 2251, Canberra Inc, Meriden, CT) was provided beginning in July 2011. For individuals who were screened, the internal contamination levels of radioactive cesium were also collected. Detection limits of the system were set to 220 Bq for Cs-134 and 250 Bq for Cs-137 following a 2-min scan.

Statistical analyses

All statistical analyses were conducted using the STATA/SE 13.1 (Stata Corp LP. College Station, TX), and a p-value <0.05 is considered statistically significant.

a. Comparison of RA activity before and after the disaster

For each clinical parameter, the titers from the second to the last visit before the disaster (pre-pre), titers from the last visit before the disaster (pre), and titers from the first visit after the disaster (post) were obtained. Then, absolute pre- and post- titers were compared using a paired t-test.

b. Comparison of change in activity

Among RA patients, clinical parameters fluctuate even in the absence of a disaster. Therefore, this study also compared changes in values before and after the disaster. Changes were calculated as shown in Figure 2 and the formula below.

Changes in values were calculated as follows:

$$\Delta\text{pre (value)} = \text{pre(value)} - \text{pre-pre(value)}$$

Δpost (value) = post(value) – pre (value)

Values of Δpre and Δpost for each parameter were then compared using a paired-t-test.

c. Identification of risks of increased RA activity

Changes in values were categorized as either positive (increased) changes or no changes. The risks of each parameter decreasing in value were calculated using logistic regression. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) and p-values were reported where applicable.

Ethical consideration

This study was approved by the ethical committee at the Minamisoma Municipal General Hospital.

RESULTS

In total, 53 patients fulfilled the inclusion criteria. The average age at the time of the disaster was 64.2 years, 83.0% of patients were female. Backgrounds of the included patients are shown in Table 1. About 60% of the patients suffered from RA for longer than 10 years. Presumably because of this relatively long disease duration, more than a half of the patients were in Steinbrocker stage IV and about 70% had some difficulty in daily life (Steinbrocker functional class II or higher). Although only 6 (11.3%) patients lived in the no-entry zone, 37 (69.8%) patients evacuated immediately after the disaster and 4 (7.5%) patients temporarily stopped treatment. Twenty nine (54.7%) of patients were temporarily seen by physicians (“Changed physicians” in Table 1) at other hospitals. During pre-disaster visit and post-disaster visit, one patient experienced temporal medication loss, and another patient was given increased dose of MTX after the disaster (6 mg/week before the disaster and 8 mg/week after). Other patients continued the same dose of anti-rheumatic drugs.

Comparisons for each clinical parameter are shown in Table 2. SJC significantly increased after the disaster, and the change in SJC was also significantly higher in the Δpost period compared with the Δpre period. The proportions of worsened TJC, SJC, ESR and RF values were significantly higher after the disaster (Δpost) compared to those before (Δpre). However, the titre of MMP-3 showed no increase during the period.

Then risk factors/beneficial factors were analysed using logistic regression (Table 3). Concomitant use of methotrexate (MTX) significantly decreased the risk of worsened RF (OR:0.23, 95% CI: 0.06-0.92), while no apparent risk factor was identified for other parameters. Higher titre of ESR before the disaster was also associated with low risk of worsened ESR (OR: 0.95, 95% CI: 0.92-0.99). Age, gender, evacuation status, temporary change of physician, and PSL usage did not appear to affect the increase. Background of MTX users and non-users were compared in Table 4. MTX users were significantly younger than non-users. No significant difference were observed in other parameters.

Among the 53 patients, 16 (30%) patients underwent whole-body counter tests. To assess whether a volunteer bias existed among those who underwent whole-body counter tests, the backgrounds of the 16 patients in Table 4 and those of the remaining patients were compared using a Student's t-test; no significant differences were observed (data not shown). Only one 76-year-old male, who underwent the examination 283 days after the accident, showed a detectable but negligible level of radioactive cesium (Cs-134, 227 Bq/body; Cs-137, 177 Bq/body); he experienced an increased SJC and increased ESR and RF titers, but no increase in CRP or MMP-3 (Table 5).

DISCUSSION

This is the first study to compare both clinical and laboratory data of RA patients before and after a disaster. Even though temporary discontinuation of treatment was rare (7.5%), about half of patients experienced deterioration of either subjective symptoms or laboratory data. Furthermore, for some parameters, the deterioration appeared to be accelerated by the disaster. Clinical parameters other than MMP-3 worsened after the disaster. Considering that medication was changed for only two patients during the period, this deterioration might be attributed to the direct and indirect impacts of the disaster.

Increase in RF titre after 40 years from radiation exposure was observed among the atomic bomb survivors in Hiroshima and Nagasaki [11], though some researchers raise the possibility that it was attributed to chronic infections that stimulate antibody production [17]. It is therefore conceivable that massive exposure of radiation immediately after the atomic-bomb attack did change immune profile of the survivors. Even so, the level of radiation exposure was much lower among patients living in Fukushima. Although 71.7% of patients lived within a 30-km radius of the NPP, only one patient showed a detectable level of radiation exposure. He is the oldest among the RA patients, and the date of examination is relatively earlier. Therefore, it is possible that slow metabolism due to high age affected the positivity. The patient also experienced increased RA activity, but it is too early to conclude that such a low dose of radiation impacted his disease status. Rather, considering that a majority of the patients experienced deterioration of clinical parameters, it is unlikely that radiation exposure alone was a major cause of RA flare in the tested disaster area.

In addition, no significant correlation between RA activity and the assessed evacuation zones was observed. These results suggest that the effect of environmental factors on the deterioration of RA status, even if it exists, might have been negligible in the present study. Instead, mental stress and lifestyle changes derived from the disaster appeared to have influenced RA disease status [6, 7].

Residents of the disaster area appeared to be highly susceptible to mental stress. For example, loss experiences, such as loss of family members, acquaintances, possessions, and jobs (due to the halt of agriculture and fishery in the contaminated areas), are assumed to be major causes of mental illness. Additionally, the feeling of being stigmatized was also a major cause of mental stress among residents. For some residents, even screening was considered a stressful event: one resident complained that undergoing the whole-body counter test caused him/her to state *'I am treated as a contaminated subject.'*

In addition to mental stress, lifestyle changes might have also worsened RA status. For example, indoor evacuation, living in temporary housing, and job loss led to an inactive lifestyle, which may have deteriorated RA status[18]. In addition, residents often avoided local products and tap water due to fear of internal radiation exposure[19, 20], which may have led to unhealthy eating habits. For example, some of the people anxious about radiation avoided eating any fish, fresh vegetables, or mushrooms, irrelevant of their areas of origin, which resulted in unhealthy dietary intake. Such lifestyle changes after the triple disaster have been reported to have led to deteriorated metabolic profiles [21] and physical inactivity [22]. As food with less unsaturated fat, such as those included in the Mediterranean diet, have been reported to decrease RA activity [7], these changes in eating habits may have also affected RA status.

Interestingly, fluctuation of the titre of MMP-3 was not worsened after the disaster, while all the other parameters were worsened. MMP-3 is a local cytokine that is expressed in synovial tissue, it reflects joint inflammation and destruction more directly compared to other parameters [23]. By contrast, acute phase proteins such as CRP reflects inflammation and it has been suggested that the pathologic mechanisms of joint inflammation may be partially independent of destruction [24]. Therefore, this discrepancy between the titers of inflammation markers (CRP and ESR) and that of MMP-3 may suggest that the deterioration of clinical parameters among RA patients after the disaster is rather temporal phenomenon and may not lead to cartilage destruction, though further research on serum profile among the victims will be needed.

Additional analyses identified the concomitant use of MTX as a potential preventive factor of RA deterioration intermediated by increase in RF. Average age of MTX users were significantly younger than non-users, which may affect the status of RF. However, the association was significant even after controlling for age (Table 3). MTX, an analogue of folic acid, is the most commonly used anti-rheumatic drug and is an anchor drug for RA treatment. Therefore, these results underscore the importance of continuity of MTX treatment. However, immunosuppressant agents such as MTX are not generally included in post-disaster medication supply lists. Considering that RA is a relatively common disease and that exacerbation of joint inflammation interferes with post-evacuation life, the present results suggest that inclusion of MTX and other anti-rheumatic drugs in post-disaster medication supply lists is worth considering.

This study has several limitations. First, assessment of disaster activity does not follow global standards. Although RA activity global assessment tools such as DAS28, CDAI, and simple disease activity index (SDAI) exist, the present data were insufficient for these indices because patient visual assessment scale (VAS) and doctors VAS scores were not available. Second, detailed information about lifestyle changes, which might have affected mental stress or loss experiences among patients, was not available. As the degree of mental stress varies by the duration of evacuation and the size of losses, this study could not assess correlations between mental stress and disease activity. Thirdly, examination of internal radiation exposure level was conducted more than 1 year after the disaster, so it did not reflect radiation exposure soon after the disaster. Even so, this result revealed that only a few patients experienced chronic radiation exposure, and that the exposure level was much less than that in Hiroshima and Nagasaki after the atomic-bomb attack. Finally, the observation period in this study was only 1 year; a latent period between a stressful event and exacerbation of autoimmune disorders may exist. Long-term observation with detailed data from each patient is required to fully elucidate the mechanisms underlying the observed RA flare after the disaster.

CONCLUSION

Exacerbation of RA activity after the triple disaster in Fukushima was demonstrated. Evacuation status and low-dose radiation exposure did not appear to affect disease activity, while other factors such as mental stress and lifestyle changes might have contributed to the deterioration. Although further research is required to elucidate the cause, use of MTX might be a preventive factor for such exacerbation. Continuity of care for this common NCD needs to be considered at the time of relief activities in disaster areas.

Acknowledgement

We sincerely thank all the staff at the Whole-body counter room at Minamisoma Municipal General Hospital, for kindly analysing the data of internal radiation exposure levels of the patients.

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Figure legends

Figure 1. Map of the evacuation zones and the hospital location. Asterisk represents the location of the Fukushima Daiichi Nuclear Power Plant. Solid line is the border of the no entry zone (20 km radius), and dotted line is the border of the planned evacuation zone (30 km radius)

Figure 2. Scheme of data collection time points.

Table 1. RA patient background (N=53).

Table 2. Average clinical parameter scores and changes in the values in each time point.

Table 3. Analysis of factors associated with worsening clinical parameters.

Table 4. Comparison between MTX users and non-users.

Table 5. Background of a patient who showed detectable level of radioactive cesium after the disaster.

Table 1. RA patient background (N=53)

Category		Number	%
Age (years old)	**41-50**	6	11.3%
	51-60	15	28.3%
	61-70	14	26.4%
	71-80	12	22.6%
	81+	6	11.3%
Gender	**Female**	44	83.0%
	Male	9	17.0%
Duration (years)	**<2**	2	3.8%
	2-5	5	9.4%
	6-10	12	22.6%
	11-20	22	41.5%
	21-30	5	9.4%
	31+	7	13.2%
Steinbrocker stage	**I**	3	5.7%
	II	3	5.7%
	III	12	22.6%
	IV	29	54.7%
	Unknown	6	11.3%
Steinbrocker functional classification	**I**	17	32.1%
	II	22	41.5%
	III	9	17.0%
	IV	1	1.9%
	Unknown	4	7.5%
Treatment	**PSL usage**	36	67.9%
	MTX usage	42	79.2%
	Biologics usage	18	34.0%
Distance from the Fukushima Daiichi NPP	**<20km**	6	11.3%
	20-30km	32	60.4%
	>30km	15	28.3%
Evacuation	**Yes**	37	69.8%
	No	13	24.5%
	Unknown	3	5.7%
Changed physician	**Yes**	29	54.7%
	No	22	41.5%

	Unknown	2	3.8%
Medication loss	**Yes**	4	7.5%
	No	47	88.7%
	Unknown	2	3.8%
Days from pre-pre visit to pre visit	**<30days**	5	9.4%
	30-60days	11	20.8%
	60-90days	13	24.5%
	90-120days	14	26.4%
	120-180days	10	18.9%
Days from pre visit to post visit	**<30days**	0	0.0%
	30-60days	8	15.1%
	60-90days	13	24.5%
	90-120days	7	13.2%
	120-180days	14	26.4%
	>120days	11	20.8%

PSL, prednisolone; MTX, methotrexate; NPP, nuclear power plant

Table 2. Average clinical parameter scores and changes in the values in each time point.

	Pre-pre	Pre	Post	Δpre	Δpost	p	Proportion of worsened value (positive Δ) Δpre N	Δpre %	Δpost N	Δpost %	p
TJC	5.2	5.3	5.8	0.0	0.6	0.29	14	26	24	45	0.04*
SJC	2.2	2.1	2.7	0.0	0.5	0.02*	6	11	18	34	0.01*
ESR	39.2	39.8	40.3	1.1	0.0	0.77	20	40	29	57	0.01*
CRP	1.1	1.1	1.0	-0.1	-0.1	0.86	16	31	20	38	0.01*
MMP-3	242.9	190.5	193.2	-42.3	3.1	0.17	24	47	17	33	0.02*
RF	178.3	174.2	178.0	-4.3	3.3	0.60	10	19	20	38	0.02*

TJC, tender joint count; SJC, swollen joint count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; MMP-3, matrix metalloproteinase-3; RF, rheumatoid factor

Table 3. Analysis of factors associated with worsening clinical parameters.

		OR	95% CI		p
Risk of worsening TJC	**Age**	1.01	0.96	1.06	0.77
	Gender (Male)	0.72	0.16	3.27	0.67
	Evacuation	0.71	0.20	2.55	0.60
	Change physician	1.24	0.39	3.86	0.72
	MTX usage	0.74	0.19	2.82	0.66
	PSL usage	1.31	0.40	4.33	0.66
	PreTJC	0.88	0.76	1.03	0.12
Risk of worsening SJC	**Age**	1.00	0.95	1.06	0.99
	Gender (Male)	0.30	0.03	2.63	0.28
	Evacuation	1.41	0.32	6.14	0.65
	Change physician	2.03	0.53	7.73	0.30
	MTX usage	1.80	0.34	9.58	0.49
	PSL usage	1.25	0.33	4.76	0.74
	PreSJC	1.11	0.91	1.36	0.29
Risk of worsening CRP	**Age**	0.98	0.93	1.03	0.43
	Gender (Male)	0.88	0.19	3.98	0.86
	Evacuation	0.41	0.11	1.49	0.18
	Change physician	0.38	0.12	1.22	0.11
	MTX usage	0.97	0.24	3.87	0.97
	PSL usage	1.04	0.31	3.46	0.95
	Pre CRP	0.88	0.57	1.38	0.59
Risk of worsening ESR	**Age**	1.00	0.95	1.05	0.98
	Gender (Male)	0.88	0.21	3.70	0.86
	Evacuation	0.53	0.15	1.93	0.34
	Change physician	0.49	0.16	1.51	0.21
	MTX usage	0.69	0.18	2.61	0.58
	PSL usage	1.43	0.45	4.58	0.55
	Pre ESR	0.95	0.92	0.99	0.01 *
Risk of worsening MMP3	**Age**	0.99	0.94	1.04	0.60
	Gender (Male)	1.99	0.47	8.45	0.35
	Evacuation	1.36	0.37	4.95	0.64

	Change physician	0.61	0.20	1.88	0.39
	MTX usage	0.82	0.21	3.11	0.77
	PSL usage	0.72	0.22	2.29	0.57
	Pre MMP3	1.00	1.00	1.00	0.87
Risk of worsening RF	**Age**	1.01	0.96	1.07	0.74
	Gender (Male)	0.68	0.12	3.73	0.66
	Evacuation	1.60	0.37	6.91	0.53
	Change physician	1.20	0.35	4.08	0.77
	MTX usage	0.23	0.06	0.92	0.04 *
	PSL usage	2.33	0.56	9.72	0.24
	Pre RF	1.00	1.00	1.00	0.76

CI, confidence interval; TJC, tender joint count; SJC, swollen joint count; MTX, methotrexate; PSL, prednisolone; RF, rheumatoid factor

* p<0.05

Table 4. Comparison between MTX users and non-users

		MTX user	Non-MTX user	p
Age		62.4	71.0	0.02*
Gender		0.2	0.1	0.44
Pre TJC		5.4	4.6	0.58
Pre SJC		2.1	2.1	0.96
Pre CRP		1.3	0.4	0.09
Pre ESR		42.2	29.9	0.18
Dose of PSL		2.3	3.0	0.30
Pre RF		154.7	252.0	0.47
Pre MMP3		200.8	142.6	0.32
Stage	**I**	3 (8%)	0 (0%)	0.73
	II	2 (5%)	1 (10%)	
	II	10 (27%)	2 (20%)	
	IV	22 (59%)	7 (70%)	
Class	**1**	16 (40%)	1 (10%)	0.11
	2	18 (45%)	4 (45%)	
	3	5 (12.5%)	4 (45%)	
	4	1 (2.5%)	0 (0%)	

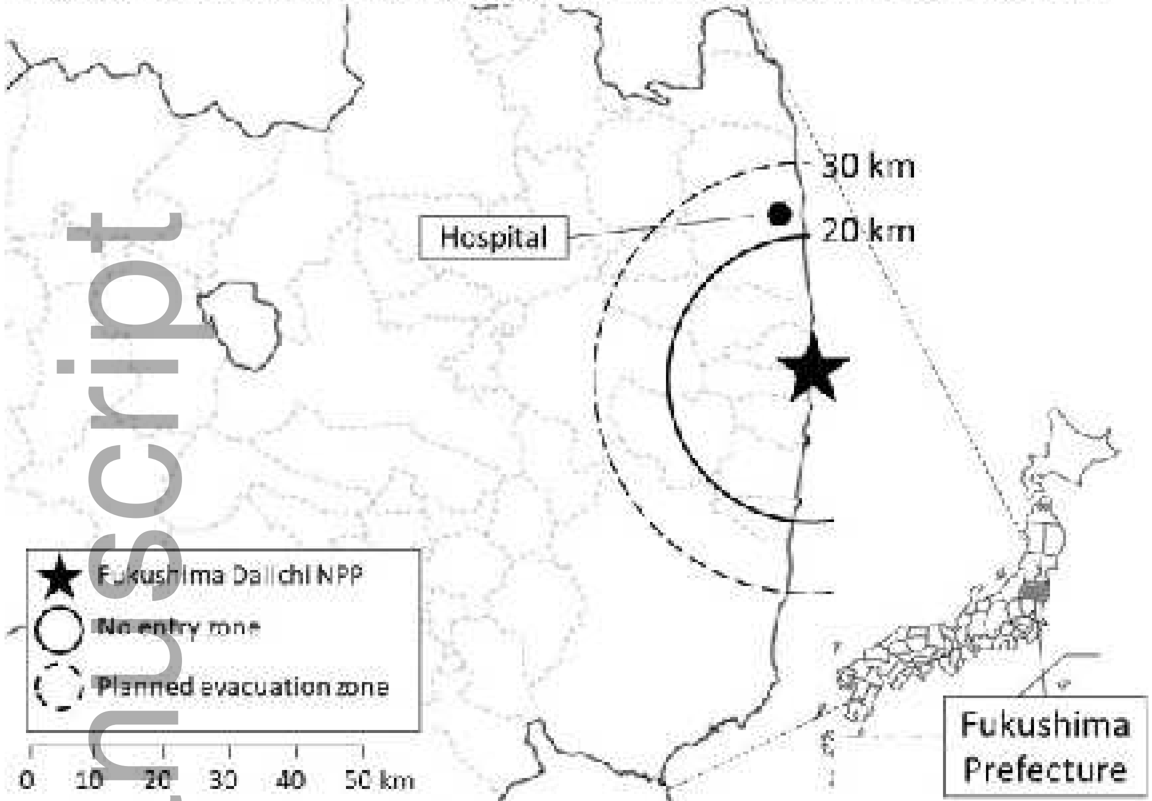
* p<0.05

Table 5. Backgrounds of a patient who showed detectable level of radioactive cesium after the disaster.

	Age*	Gender	Exam date	Days from disaster	Cs-134 (Bq/body)	Cs-137 (Bq/body)	Evacuation	Changed physician	Medication loss	Increased SJC	Increased ESR	Increased CRP	Increased RF	Increased MMP-3
Patient 1	76	M	21-Dec 2011	283	227	177	No	No	No	Yes	No data	Yes	Yes	No

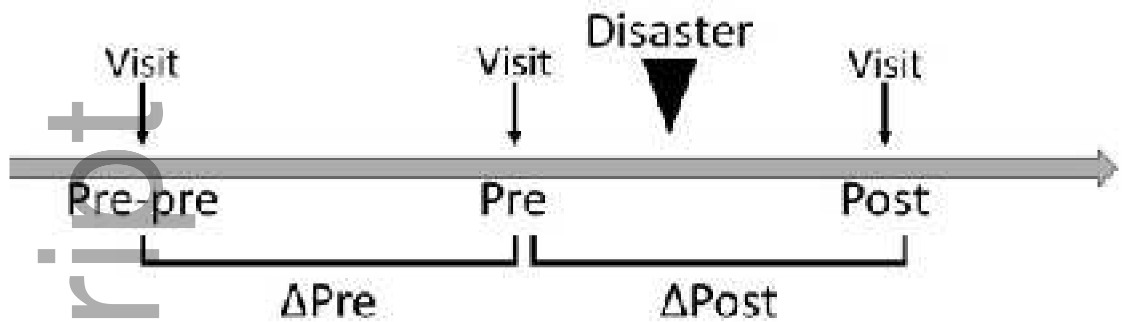
* At the time of the disaster

Figure 1. Map of the evacuation zones and the hospital location.



apl_13301_f1.jpg

Figure 2. Scheme of data collection time points.



apl_13301_f2.jpg